Dutch statutory board report and financial statements of CureVac N.V.

for the fiscal year ended December 31, 2022

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Dutch Statutory Board Report

1. Introduction

In this Annual Report, unless otherwise indicated or the context otherwise requires, all references to "CureVac" or the "Company," "we," "our," "ours," "ourselves," "us" or similar terms refer to CureVac N.V. and, where appropriate, its subsidiaries, including CureVac Netherlands B.V. and CureVac SE (formerly known as CureVac AG).

We own or have rights to various trademarks and trade names, including CureVac® and the CureVac logo that we use in connection with the operation of our business. This Annual Report may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. We do not intend our use or display of other entities' trademarks, trade names or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other entity. Solely for convenience, the trademarks, trade names and service marks in this Annual Report are referred to without the symbols ® and ™, or SM, but the omission of such references should not be construed as any indication that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

1.1 Preparation

This Annual Report has been prepared by CureVac's management board (the **"management board")** and has been approved by CureVac's supervisory board (the "**supervisory board**") pursuant to Section 2:391 of the Dutch Civil Code ("**DCC**"). It also contains (i) CureVac's financial statements within the meaning of Section 2:361(1) DCC and (ii) to the extent applicable, the information to be added pursuant to Section 2:392 DCC. This Annual Report relates to the fiscal year ended December 31, 2022 and, unless explicitly stated otherwise, information presented in this annual report is as at December 31, 2022. The financial statements included in sections 9 and 10 of this Annual Report have been prepared in accordance with the International Financial Reporting Standards, as adopted by the European Commission ("**EU IFRS**") and Part 9 of Book 2 of the DCC. The report of CureVac's independent auditor, Ernst & Young Accountants LLP, is included in section 11. The Dutch Corporate Governance Code 2016 ("**DCGC**") recommends that this Annual Report includes reports from the management board and the supervisory board. The elements that the DCGC recommends to be covered by the report from the management board and the report from the supervisory board are covered throughout this Annual Report, which is signed by each of our managing directors and each of our supervisory directors.

1.2 Forward-Looking Statements

This Annual Report contains statements that constitute forward-looking statements. Many of the forward-looking statements contained in this Annual Report can be identified by the use of forward-looking words such as "anticipate," "believe," "could," "expect," "should," "plan," "intend," "estimate" and "potential," or other similar expressions.

Forward-looking statements appear in a number of places in this Annual Report and include, but are not limited to, statements regarding our intent, belief or current expectations. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Such statements are subject to risks and uncertainties, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various factors, including, but not limited to, those identified under the section entitled "Risk Factors" in this Annual Report. These risks and uncertainties include factors relating to:

- our ability to obtain funding for our operations necessary to complete further development and commercialization of our product candidates;
- the initiation, timing, progress, results, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work, the period during which the results of the trials will become available and our research and development programs;
- the timing of and our ability to obtain and maintain regulatory approval for our product candidates;

- the ability and willingness of our third-party collaborators to continue research and development activities relating to our product candidates and cost associated with the cancellation of manufacture and supply agreements in the event of termination of our research and development programs;
- the exercise by the Bill & Melinda Gates Foundation of withdrawal rights;
- our and our collaborators' ability to obtain, maintain, defend and enforce our intellectual property protection for our proprietary and collaborative product candidates, and the scope of such protection;
- the rate and degree of market acceptance of our products;
- our ability to commercialize our product candidates, if approved;
- our ability and the potential to successfully manufacture our drug substances and delivery vehicles for preclinical use, for clinical trials and on a larger scale for commercial use, if approved;
- general economic, political, demographic and business conditions in the United States and Europe;
- the impact of unstable market and economic conditions such as rising inflation and interest rates and the conflict involving Russia and Ukraine on our business;
- our ability to implement our growth strategy;
- our ability to compete and conduct our business in the future;
- our ability to enroll patients for our clinical trials;
- the availability of qualified personnel and the ability to retain such personnel;
- regulatory developments and changes in the United States, Europe and countries outside of Europe including tax matters;
- our ability to overcome the challenges posed by pandemics (such as COVID-19), to the conduct of our business;
- other factors that may affect our financial condition, liquidity and results of operations; and
- other risk factors discussed under section 4.3 Risk Factors.

You should read this Annual Report carefully with the understanding that our actual future results may be materially different from and worse than what we expect. If our forward-looking statements prove to be inaccurate, the inaccuracy may be material. Other sections of this Annual Report include additional factors which could adversely impact our business and financial performance. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame or at all. Moreover, we operate in an evolving environment. Thus, new risk factors and uncertainties emerge from time to time and it is not possible for our management to predict all risk factors and uncertainties, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. We qualify all of our forward-looking statements by these cautionary statements.

Forward-looking statements speak only as of the date they are made, and we do not undertake any obligation to update them in light of new information or future developments or to release publicly any revisions to these statements in order to reflect later events or circumstances or to reflect the occurrence of unanticipated events or otherwise, except as required by law.

2. Company and business overview

2.1 History and development of the Company

On April 7, 2020, CureVac B.V. was incorporated under the laws of the Netherlands and became the holding company of CureVac AG in connection with our initial public offering on August 14, 2020, as part of a corporate reorganization (the "Corporate Reorganization"), the legal form of CureVac B.V. was converted from a Dutch private company with limited liability (besloten vennootschap met beperkte aansprakelijkheid) to a Dutch public company (naamloze vennootschap), and the articles of association of CureVac N.V. became effective. Following the Corporate Reorganization, CureVac N.V. became the holding company of CureVac AG. On September 26, 2022, CureVac AG entered into a plan of merger with CureVac Beteiligungsverwaltungs AG, with CureVac SE as the surviving entity and both CureVac AG and CureVac Beteiligungsverwaltungs AG as disappearing entities, and the historical consolidated financial statements of CureVac AG included in this Annual Report became part of the historical consolidated financial statements of CureVac N.V. Our legal and commercial name is CureVac N.V.

Our principal executive offices are located at Friedrich-Miescher-Strasse 15, 72076 Tübingen, Germany and our telephone number at this address is +49 7071 9883 0. Our additional offices are in Wiesbaden (Germany), Louvain La Neuve (Belgium), Amsterdam (Netherlands), Basel (Switzerland) and Boston (Massachusetts, United States).

Since August 14, 2020, our common shares have traded on Nasdaq under the symbol "CVAC." Our agent for service of process in the United States is CureVac Inc., located at 250 Summer St. 3rd Fl., Boston, Massachusetts 02210.

The SEC maintains an internet website that contains reports and other information about issuers, like us, that file electronically with the SEC. The address of that website is www.sec.gov. Our website can be found at www.curevac.com. The information on our website is not incorporated by reference into this Annual Report, and you should not consider information contained on our website or any websites mentioned in this Annual Report to be part of this Annual Report.

Our capital expenditures for 2022, 2021 and 2020 amounted to €101.6 million, €135.4 million and €39.6 million, respectively These expenditures were primarily for equipment and intangibles used in our research and development activities, as well as for the development of a GMP production process on a large industrial scale (GMP IV).

As the result of our organic growth, our workforce has increased over the last three years from an approximate average workforce of 440 in fiscal 2019 to more than 1,000 in fiscal 2022.

2.2 Business overview

Overview

We are a global biopharmaceutical company developing a new class of transformative medicines based on messenger ribonucleic acid that has the potential to improve the lives of people. Our vision is to revolutionize medicine and open new avenues for developing therapies by enabling the body to make its own drugs. Messenger ribonucleic acid, or mRNA, plays a central role in cellular biology in the production of proteins in every living cell. We are the pioneers in successfully harnessing mRNAs designed to prevent infections and to treat diseases by mimicking human biology to synthesize the desired proteins. Our technology platform is based on a targeted approach to optimize mRNA constructs that encode functional proteins that either induce a desired immune response or replace defective or missing proteins using the cell's intrinsic translation machinery. Our current product portfolio includes clinical and preclinical candidates across multiple disease indications in prophylactic vaccines, oncology and molecular therapy.

In prophylactic vaccines, we are advancing our second-generation mRNA backbone against coronavirus (SARS-CoV-2) and a range of infectious diseases, including influenza in collaboration with GSK.

The improved second-generation mRNA backbone features targeted optimizations designed to improve intracellular mRNA stability and translation for increased and extended protein expression. These optimizations potentially allow for strong and early immune responses at low doses, which is intended to also support the development of multivalent vaccines to target rapidly spreading COVID-19 variants or different influenza strains as well as combination vaccines against different viral diseases.

COVID-19 Program (second-generation mRNA backbone)

The collaboration on COVID-19 vaccine candidates with GSK was initiated in April 2021, and aims to research, develop and manufacture mRNA vaccines targeting the original SARS-CoV-2 strain as well as emerging variants.

CV2CoV was introduced as the first representative of our joint COVID-19 vaccine program based on our second-generation backbone. The vaccine candidate is a non-chemically modified mRNA, encoding the prefusion stabilized full-length spike protein of the original SARS-CoV-2 virus, formulated within Lipid Nanoparticles, or LNPs. On June 30, 2021, we published preclinical data in Nature Communications demonstrating full protection by CV2CoV and our first-generation vaccine candidate CvnCoV, from lethal infection caused by SARS-CoV-2 ancestral strain BavPat1 or the Beta variant (B.1.351) in a transgenic mouse model. On August 4, 2022, we further published in the journal Vaccines data from a preclinical study in rats, showing that CV2CoV is able to induce high levels of antigen production in an in vitro setup as well as strong and dose-dependent immune responses in vivo. In a subsequent Nature publication issued on November 18, 2021, we further presented preclinical data investigating immune responses as well as the protective efficacy of CV2CoV in comparison to CvnCoV, against SARS-CoV-2 challenge in non-human primates. A direct comparison of CV2CoV with a licensed mRNA vaccine in non-human primates was able to show that neutralizing antibody levels measured following full vaccination of animals with either 12µg of CV2CoV or a 30µg standard dose of the licensed mRNA vaccine were highly comparable. On April 21, 2022, the preclinical data for CV2CoV and the second-generation mRNA backbone was extended by a study conducted in collaboration with the Friedrich-Loeffler-Institute, comparing immune responses and protective efficacy of monovalent and bivalent mRNA vaccines encoding Beta and/or Delta variants, primarily in a transgenic mouse model and a Wistar rat model. On March 30, 2022, we announced the start of a Phase 1 clinical trial with CV2CoV. The Phase 1 dose-escalation study is being conducted at clinical sites in the United States and evaluates the safety, reactogenicity and immunogenicity of a single booster dose of CV2CoV in the dose range of 2µg to 20µg.

Within the joint vaccine program with GSK, we also extended our technology platform to chemically modified mRNA constructs to allow for data-driven selection of the best candidate. We announced the start of a Phase 1 clinical trial with a chemically modified COVID-19 mRNA vaccine candidate based on our second-generation backbone, CV0501, on August 18, 2022. CV0501 specifically targets the Omicron BA.1 variant. The study is being conducted at clinical sites in the United States, Australia, and the Philippines and evaluates the safety, reactogenicity and immunogenicity of a single booster dose of CV0501 in the dose range of 3µg to 200µg.

On January 6, 2023, we announced that the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the COVID-19 program. In January and April 2023, we also announced positive preliminary data from the CV0501 Phase 1 trial. The data are based on cohort sizes of up to 20 participants in the younger adults age group (age 18-64) and 10 participants in the older adults age group (age ≥65). Reported safety data cover the fully recruited dose groups of 3, 6, 12, 25, 50, 100 and 200µg in the younger adult age group and 12, 25, 50, 100 and 200µg in the older adult age group. CV0501 was shown to be generally well tolerated. Immunogenicity data in both age groups showed relevant titers of neutralizing antibodies beginning at the lowest tested dose. On day 29 at the 12µg dose level, CV0501 generated a ratio of post-boost to pre-boost serum neutralizing titers against the Omicron BA.1 variant of 8.1. in younger adults and 13.3 in older adults. The data read-out for both age groups are currently being finalized. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant variants. A pivotal Phase 3 trial may be initiated in 2024, contingent on discussion with regulatory authorities.

Seasonal Flu Program (second-generation mRNA backbone)

Influenza was disclosed as the first indication from the initial collaboration we started with GSK in July 2020, which focuses on the development of new products for different targets in the field of infectious diseases.

The first non-COVID-19 vaccine candidate within the broader infectious disease program applying our second-generation backbone we tested in collaboration with GSK is the influenza candidate, CVSQIV, a differentiated multivalent vaccine candidate featuring multiple non-chemically modified mRNA constructs to induce immune responses against relevant targets of four different influenza strains. On February 10, 2022, we announced the start of a Phase 1 dose-escalation study in Panama evaluating the safety, reactogenicity and immunogenicity of CVSQIV in the dose range of

3µg to 28µg. Preliminary safety data reported on April 28, 2022, showed a benign reactogenicity profile across the tested dose groups.

In line with the mRNA development strategy to also test chemically modified mRNA and similar to the setup of the COVID-19 vaccine program, CureVac and GSK announced the start of a Phase 1 dose-escalation study with a chemically modified influenza vaccine candidate, Flu SV mRNA, on August 18, 2022. The candidate is a monovalent candidate. The Phase 1 dose-escalation study is being conducted in Canada, Spain and Belgium to evaluate the safety, reactogenicity and immunogenicity of FLU SV mRNA.

On January 6, 2023, the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the seasonal flu vaccine program. In the Phase 1 study of the monovalent Flu-SV-mRNA, expressing an H1N1 hemagglutinin antigen (subtype of influenza A), five doses ranging from 2 to 54µg with up to 25 subjects per dose cohort were evaluated in younger adults (age 18-45). In this age group, preliminary safety and reactogenicity data showed that the monovalent Flu-SV-mRNA candidate was generally well tolerated with no safety concerns observed to date across all tested dose levels. A single dose of Flu-SV-mRNA (dose level undisclosed) was assessed for safety and reactogenicity in older adults (age 60-80) and was also observed to be safe and well tolerated with no grade 3 adverse events in the 32 subjects who were administered the mRNA construct. Immunogenicity of the monovalent Flu-SV-mRNA was assessed in parallel with a licensed seasonal flu vaccine comparator in both age groups. In younger adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA increased up to approximately 3.3 times those elicited by the licensed flu vaccine comparator in younger adults. In older adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA were approximately 2.3 times those elicited by the licensed flu vaccine comparator. In the same age group, the percentage of subjects achieving seroconversion was 89.7% for Flu-SV-mRNA and 56.2% for the licensed flu vaccine comparator.

The vaccine candidate for future clinical 7abellipment is expected to target all four strains recommended by the WHO for influenza vaccines. A Phase ½ study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

mRNA-based medicines represent a novel class of medicine that have the potential to address limitations of conventional treatment modalities. We believe the modular nature of mRNA has the potential for higher efficacy, greater speed and lower cost of production as compared to conventional treatment modalities. mRNA delivery enables direct production of any protein (secreted, membrane and intracellular) in the body and has shown a wide range of activity. The flexible chemical structure of mRNA, utilizing only four nucleotide buildings blocks, allows us to encode for a broad range of proteins with simple sequence changes, offering design versatility, specificity and limited off-target effects. Transient expression of mRNA limits the risk of irreversible changes to the cells' DNA and allows for flexible dosing based on a patient's needs as well as the opportunity for repeat dosing. We are leveraging these inherent advantages of mRNA-based medicines in the development of our mRNA technology platform.

We have built an extensive expertise in the fields of mRNA biology, optimization and production. We have continued to invest in developing our technology platform, which we refer to as the RNAoptimizer, over the past 21 years. Our differentiated technology platform is designed to optimize each component of the mRNA-based medicine. Our RNAoptimizer platform is built on three core pillars:

- ***Protein design:*** optimizing the specific properties of encoded protein;
- ***mRNA optimization:*** optimizing characteristics such as half-life and translation efficacy of the mRNA molecule; and
- ***mRNA delivery:*** selecting the best-suited delivery system from our diverse portfolio of proprietary and third-party delivery systems.

By leveraging each of these pillars, we have observed improved required protein expression levels while modulating the interaction with the immune system in preclinical and clinical trials. We continue to invest in all levels of optimization to improve the methods we currently employ and to further advance our mRNA-based medicines.

We consider our manufacturing process an important part of our strategy that allows us to match our flexible and versatile technology platform with equally flexible and versatile manufacturing setups. In house, we currently operate three GMP-certified suites, with the capacity to supply our clinical programs and support potential early

commercialization activities. We are in the process of building a fourth GMP large-scale production facility at CureVac's headquarters in Tübingen, which is being designed to cover all manufacturing steps from starting material to formulation, and which could potentially supply materials for hundreds of millions of doses of our vaccine product candidates to support our future commercial launches. In addition to our GMP manufacturing facilities, we are developing a novel downsized, integrated, and automated process for manufacturing of mRNA vaccines and therapeutics, which we refer to as The RNA Printer®. In March 2022, we established the CureVac RNA Printer GmbH as a whollyowned CureVac company to advance The RNA Printer®. The new entity is designed as a platform and services company, providing a dedicated operational environment to further develop and establish The RNA Printer® as a manufacturing end-to-end solution. With its modular design and decentralized concept, we believe The RNA Printer® could be used to facilitate broad access to mRNA technology and enable mRNA product developments (e.g., for rapid supply of new mRNA-based vaccines in pandemic situations as well as patient access to advanced and personalized mRNA-based therapies in oncology).

Our approach seeks to mitigate clinical and developmental risk across multiple levels to advance and expand our broad product portfolio. We have made advances in utilizing the potential of our technology platform through rational disease selection. We consider a number of factors in our disease selection process including unmet medical need, immune response, duration of expression, dosing requirements, delivery, and targeted tissue types, among other factors. Our programs target the underlying modes of action of the disease that play a critical role in the pathology of the disease. We are initially targeting diseases that require an active immune response (such as prophylactic vaccines and oncology) and require transient expression of mRNA in tissue types that are more easily accessible. We believe these initial indications are amenable to localized delivery using a lipid nanoparticle, or LNP, delivery system. Following the encouraging results from our current prophylactic vaccines program in clinical studies and based on our advanced understanding of mRNA biology and immune stimulation control, we have expanded our product portfolio to also target indications that require an immune silent approach (such as protein delivery), given the need for higher doses, repeated dosing and longer expression of the protein. These initial indications are using LNP delivery systems. Our access to a broad range of delivery systems allows us to target multiple tissue types.

COVID-19 candidate CvnCoV (first-generation mRNA backbone)

On October 12, 2021, we announced the strategic decision to withdraw our first-generation COVID-19 vaccine candidate, CvnCoV, from the approval process with the European Medicines Agency, or EMA, and to focus our COVID-19 vaccine program on the development of second-generation mRNA vaccine candidates in collaboration with GSK. The decision was aligned with the evolving dynamics of the pandemic response toward greater need for more differentiated vaccines. The rolling submission with the EMA was originally initiated in February 2021 to assess CvnCoV's compliance with standards for vaccine efficacy, safety and pharmaceutical quality as a prerequisite for a formal market authorization application. Later in 2021, the EMA informed us that it would not start reviewing the provided CvnCoV data packages before 2022. As a result, we estimated that the earliest possible approval of CvnCoV would come in the second quarter of 2022. By this time, we expected candidates from the second-generation vaccine program to be progressing through clinical development. Consequently, CvnCoV was also withdrawn from a rolling submission with Swissmedic, Switzerland's authority responsible for the authorization and supervision of therapeutic products, initiated in April 2021, to review the safety, efficacy and pharmaceutical quality of CvnCoV as a prerequisite for market authorization.

All clinical studies with first-generation candidate, CvnCoV, have completed the scheduled safety follow-up times for all trial participants as per the respective trial protocols. These include a Phase 1 study in Germany (initiated in June 2020), a Phase 2a study in Peru and Panama (initiated in September 2020), the Phase 2b/3 (HERALD) study in Europe and Latin America (initiated in December 2020), a Phase 3 study in healthcare workers in Germany (initiated in December 2020), and a Phase 3 study in participants with comorbidities in Belgium (initiated in April 2021).

Data analyses of the Phase 2b/3 (HERALD) study and Phase 3 study in healthcare workers in Germany have been finalized. Primary data of the Phase 2b/3 (HERALD) trial was published in The Lancet Infectious Diseases on November 23, 2021. Data of an interim analysis of the Phase 1 trial in Germany was published in Wiener klinische Wochenschrift on August 10, 2021. Safety and immunogenicity data of the Phase 2a clinical trial in Peru and Panama was published in Vaccine: X on July 1, 2022. Neutralizing antibody data against the ancestral strain and the beta variant after a third dose of CvnCoV in the same trial were published in Vaccines on March 25, 2022.

Previously announced studies to be initiated with CvnCoV, including a Phase 2 clinical trial, focusing on immunogenicity in older adults above the age of 65 years old compared to younger adults and a flu-co-administration

study, planned to be initiated together with Bayer AG to assess compatibility with established seasonal vaccines in an older population, were cancelled.

To assess the benefit of booster vaccinations, CvnCoV was also included in the Cov-Boost trial sponsored by the University of Southampton, UK. The Cov-Boost trial started in June 2021 across 18 sites in the United Kingdom and dosed overall 2,878 participants with a third dose vaccine. Initial results from the Cov-Boost trial were published in The Lancet on December 2, 2021.

Our pivotal Phase 2b/3 trial for CvnCoV, which included approximately 40,000 participants, reported interim analysis outcomes on May 28, 2021, and on June 16, 2021. In the highly dynamic variant environment, the HERALD trial met the prespecified success criteria for efficacy against symptomatic COVID-19 of any severity and for efficacy against moderate-to-severe COVID-19, as defined in the protocol. Vaccine efficacy against COVID-19 of any severity was 48.2% in the overall primary efficacy analysis set of SARS-CoV-2 I participants, and 52.5% in those aged 18–60 years. Vaccine efficacy against moderate-to-severe COVID-19 was 70.7% overall and 77.2% in participants aged 18–60 years. There were too few participants aged 61 years or older who developed COVID-19 to allow a meaningful estimate of efficacy in this age group. HERALD was conducted in an unprecedented evolving landscape with an increasing number of SARS-CoV-2 variants adding additional challenges to the assessment of COVID-19 vaccine candidates. About 50% of cases of COVID-19 in our trial were caused by variants of concern, 35% were caused by variants of interest, as classified by WHO in September 2021, and about 3% were caused by wild-type, with the remaining 11% caused by other variants.

Beyond the GSK COVID-19 and general infectious disease collaboration, our next advanced prophylactic vaccine program, CV7202, is being developed for prophylactic vaccination against rabies. CV7202 is an mRNA based on our first-generation backbone that encodes the rabies virus glycoprotein, RABV-G, formulated with Lipid Nanoparticles. Safety, reactogenicity, and immunogenicity of CV7202 was investigated in a Phase 1 clinical trial that has completed the scheduled follow-up time for all trial participants as per trial protocol. In January 2021, we published data from our Phase 1 trial of CV7202 in Vaccine. CV7202 induced adaptive immune response as shown by rabies-specific virus-neutralizing antibodies above the World Health Organization thresholds considered to be protective, after the second dose in all subjects, at the lowest 1µg and 2µg dose levels. We also showed that the lowest dose levels (1µg and 2µg mRNA) were generally well tolerated. We are currently assessing the path forward for advancing CV7202.

Oncology

In oncology, we plan to build a meaningful portfolio and create long-term value to accelerate growth beyond the recent progress in prophylactic vaccines. Developing new oncology candidates is characterized by similar medical challenges as in infectious diseases, including selection and accessibility of disease-relevant antigens, enhancing antigen-induced immune activation, and triggering immune responses led by a strong induction of tumor-killing T cells.

Taking advantage of recent technology platform advances, particularly our second-generation mRNA backbone in COVID-19 and flu, we are evaluating targeted expansions of our unique mRNA approaches for the development of cancer vaccines. This targeted expansion is based on three strategic pillars:

1. Validation and optimization of our broad mRNA technology approach for T cell mediated tumor control

2. Build-up of a pipeline of cancer vaccine candidates targeting antigens predicted to be immunogenic and presented on tumors in cancer patients

3. Addition of complementary platform technologies for validation and optimization of vaccine design focusing on T cell activation

A key component to deliver on this strategy is the build-up of a powerful antigen discovery engine. To gain access to state-of-the-art antigen discovery technologies we announced a partnership with Belgium-based company myNEO on May 25, 2022, and the acquisition of Netherland-based Frame Cancer Therapeutics on June 8, 2022.

Together with immunotherapy company myNEO, we aim to identify specific antigens found on the surface of tumors for the development of novel mRNA immunotherapies. myNEO utilizes a broad range of underlying genomic alterations to identify constantly emerging, novel classes of antigens of defined tumor types. Incorporating new ranking

methodologies based on tumor cell antigen processing and presentation is expected to allow for selection of antigens with the highest confidence of success for potential clinical testing.

With the acquisition of Frame Cancer Therapeutics, a private company focused on advanced genomics and bioinformatics, to identify both shared and unique neoantigens across different cancer types, we complement existing in-house expertise to identify and validate promising antigens for mRNA cancer vaccine candidates. The former Frame Cancer Therapeutics site was inaugurated as CureVac Netherlands and will further develop the proprietary technology platform, which has the potential to identify a broad panel of neoantigens and tumor-associated antigens that go beyond conventional approaches and could strongly increase the likelihood of developing highly effective cancer vaccines that activate the human immune system against cancer.

The field of immuno-therapy has advanced with the progression of available technologies to extract data from patient samples, such as next-generation sequencing. Conventional approaches have so far focused on the exome, the protein-coding part of the genome, which represents only about 1.5% of the total genetic information. More recently, breakthrough developments in sequencing capacity have enabled the extraction of vastly larger amounts of data that allows us to utilize the remaining 98.5% of genetic information. The technologies brought in house with the acquisition of Frame Cancer Therapeutics are based on whole-genome-sequencing for every patient sample and combine it with short as well as long-range RNA sequencing to map the full inventory of genomic changes. More specifically, downstream of the sequencing, a software package integrates all the data to retrieve the exact changes in the DNA of the tumor cells compared to healthy cells. Correlation of this data with changes in the RNA transcription of the tumor results in entirely new and potentially antigenic tumor antigens that we plan to test as targets for a portfolio of new cancer vaccine candidates. These new antigens are not only entirely foreign to the body but are also uniquely expressed in the tumor and not in healthy tissue. In their foreignness, these constructs are expected to raise stronger immune responses than antigens derived from exome-based conventional approaches.

The highly synergistic antigen discovery technologies of Frame Cancer Therapeutics and myNEO are expected to significantly accelerate CureVac's oncology strategy to build a meaningful portfolio of new cancer vaccine candidates. Within this strategy, we follow two approaches. The first approach assesses tumor antigens shared by different cancer patients for the development of off-the-shelf cancer vaccines. The second approach is tailored to the individual tumor setup of a patient for personalized therapy. We plan to advance new antigens for both approaches based on our second-generation mRNA backbone. To assess the safety and immunogenicity of our second-generation backbone in an oncology setting, we expect to initiate a proof-of-principle study in the second quarter of 2023, assessing an mRNA construct encoding eight epitopes from tumor associated antigens in patients with surgically resected Glioblastoma Multiforme.

In our oncology strategy, we are committed to drive innovation by also leveraging The RNA Printer®, CureVac's automated end-to-end manufacturing solution for GMP-grade mRNA vaccines and therapeutics. The highly standardized system is expected to allow for rapid and highly flexible availability of mRNA to screen new targets and transition promising mRNA product candidates more efficiently into the clinic. Designed for small-scale quantities, the automated GMP-grade output of The RNA Printer® is designed to open avenues for personalized mRNA-based cancer therapies. The system is currently undergoing regulatory approval processes to obtain its first manufacturing licenses.

Our clinical oncology candidate, CV8102, is a complex of single-stranded non-coding RNA, which has been optimized to maximize activation of cellular receptors that normally detect viral pathogens entering the cells (such as toll-like receptor 7, or TLR7, toll-like receptor 8, or TLR8, and retinoic acid inducible gene I, or RIG-I pathways), mimicking a viral infection of the tumor. Clinical data support the hypothesis that CV8102 is able to recruit and activate antigen-presenting cells at the site of injection to present tumor antigens released from tumor cells to T cells in the draining lymph node. This potentially leads to activation of tumor-specific T cells, which can kill tumor cells at the injected site, but also at distant non-injected tumor lesions or metastases. CV8102 is currently being evaluated in a Phase 1 clinical trial as a single agent and in combination with anti-PD 1 antibodies. The trial consists of two parts. The first dose-escalating part assesses CV8102 in 58 patients with solid tumors, namely cutaneous melanoma, adenoidcystic carcinoma, squamous cell carcinoma of skin, and squamous cell carcinoma of head and neck, or HNSCC. As of June 21, 2021, in the single-agent cohort, we observed one patient with a complete response and two patients with a partial response according to RECIST 1.1. In addition, twelve patients experienced a best response of stable disease. In the PD 1 combination cohort, one PD 1 refractory melanoma patient experienced a partial response according to RECIST 1.1. In addition, three patients experienced a best response of stable disease. On November 10, 2021, we added an

extensive analysis of immune cell activation. The data showed efficient stimulation of the immune system characterized by the induction of interferon alpha and interferon gamma. Serial tumor biopsies from individual patients demonstrated increased infiltration of T cells in the micro-environment of injected as well as non-injected tumors.

In February 2021, we initiated an expansion of our Phase 1 study to confirm the safety, tolerability and efficacy of CV8102 at a 600µg dose in 40 patients with advanced melanoma. On November 11, 2022, we presented preliminary data from the expansion study. As of August 30, 2022, preliminary efficacy was observed in the cohort of 30 patients treated in combination with anti-PD-1 antibodies, 40% of whom were pretreated with anti-CTLA-4 antibodies. In this anti-PD-1 combination cohort, five out of 30 patients (17%) experienced a partial response according to RECIST 1.1. Responses appeared durable for up to one year from the start of treatment. No objective responses were observed in the 10 patients of the single-agent cohort, 50% of whom were pretreated with anti-CTLA-4 antibodies. Analysis of immune cell activation confirmed that CV8102 single agent or combination treatment, after the first dose, activated systemic pathways of immune response. Preliminary analysis of the tumor microenvironment in a subgroup of patients showed the positive outcome of increased infiltration of T cells, following intra-tumoral injection in 4 out of 8 (single agent cohort) and 10 out of 18 (anti- PD1 combination cohort) analyzed paired biopsy samples.

Final study results are expected to be submitted for publication in a peer reviewed journal in the first half of 2023. A scientific paper assessing the mode of action and efficacy of CV8102 for local immunotherapy in preclinical models was published on November 2, 2022, in Cancer Immunology, Immunotherapy.

In the context of our strategic focus on antigen discovery and hence the development of mRNA-based cancer vaccine candidates that target tumor-specific antigens, the clinically valid11abellmmuno-modulatory characteristics of CV8102 represent a potentially complementary technology. We would therefore only consider a potential further clinical development of CV8102 based on an integration into our cancer vaccine developments, for example, as a poten11abellmmuno-modulatory adjunct to a defined mRNA cancer vaccine candidate.

Molecular Therapies

In molecular therapies, we published preclinical mouse data in liver fibrosis in the Journal of Hepatology in August 2021. Progression of liver fibrosis is associated with the gradual decrease of hepatocyte nuclear factor 4 alpha, or HNF4 alpha, an important regulator and key factor in liver metabolism. In the published study, four independent mouse models of the disease were treated with mRNA encoding HNF4A. The treatment was able to restore HNF4A levels and thereby significantly reduced liver injury. The study was conducted in collaboration with the REBIRTH-Research Center for Translational Regenerative Medicine and Department of Gastroenterology, Hepatology and Endocrinology at the Hannover Medical School, Hannover (Germany). It provides the first preclinical data demonstrating the therapeutic applicability of mRNA encoded HNF4A in the treatment of liver fibrosis and cirrhosis.

We further expect to publish data from our collaboration with the Schepens Eye Research Institute.

Our development efforts for molecular therapy are based on delivering optimized mRNAs to trigger production of antibodies or therapeutic proteins. Using our technology, we can instruct human cells to produce or secrete specific proteins in the nucleus, cytoplasm, cellular organelles, cell membrane. Based on this "healthy" information delivered by mRNA, our cells can produce proteins, which are required to treat the disease caused by missing or inactive proteins. Molecular therapy spans broad therapeutic areas and has the potential to be used as a treatment against infectious diseases in passive immunization (protection against an infectious disease with the encoding of the adequate protective antibody) and toxins (protection against a toxin with the encoding of the adequate protective antibody) and to be applied in many disease indications including cancer (mRNA encoded cancer antibodies), cardiovascular diseases, and autoimmune diseases. Our mRNA optimization process, which is a core pillar of our RNAoptimizer platform, is designed to increase protein expression with the aim to reach therapeutic levels. In preclinical studies in non-human primates, we have demonstrated that antibodies encoded by mRNA can be produced in hepatocytes very rapidly and can reach therapeutic levels in the blood stream. We are currently advancing undisclosed programs in preclinical studies across eye disorders as well as delivering therapeutic antibodies.

To date, our revenues have consisted of upfront licensing payments, product sales and compensation for research and development services, all of which relate to our license and collaboration agreements. For the years ended December 31, 2020, 2021 and 2022, €48.9 million, €103.0 million and €67.4 million, respectively, or 100%, of our total revenue, in each respective year, was derived from our license and collaboration agreements.

The following is a summary of revenue by geographic area. Revenue is attributed to geographic region based on the location of our license and collaboration partner:

	2020		2021		2022	
North America	71.3	%	—	%	—	%
Europe	28.7	%	100.0	%	100.0	%
12abellf the World	—	%	—	%	—	%

We have built an intellectual property portfolio in the United States, Europe and other major geographies. As of April 3, 2023, we own approximately 803 issued patents worldwide, including 102 issued U.S. patents, 50 issued European patents (which have been validated in various European countries resulting in a total of approximately 518 national patents in European countries), and 183 issued patents in other foreign countries, 122 pending U.S. patent applications, 85 pending European patent applications, 262 pending patent applications in other foreign countries and 17 pending PCT patent applications. Our patent portfolio includes claims relating to our RNA technology platform, our CVCM delivery system, our proprietary LNP technology and our CV8102, CV7202, CVSQIV, and our SARS-CoV-2 product candidates.

We are led by a team of veterans with extensive experience in the biopharmaceutical industry, including experience in nucleic acid therapy, oncology, rare and infectious diseases and antibodies. Our management team as well as our supervisory board members have broad expertise in the clinical, regulatory and commercialization aspects of oncology, prophylactic vaccines and protein therapy as well as in drug development, process development and manufacturing for mRNA therapies. As of December 31, 2022, we had 1,049 employees, including 242 employees with advanced scientific degrees. Since our founding in 2000, we have raised €1.71 billion in gross proceeds from equity financings.

Our Product Portfolio

Our differentiated mRNA technology platform is designed to address a broad range of diseases across multiple therapeutic areas. Given the strengths of our platform, the broad potential of mRNA-based medicines and our rational approach to disease selection, we have chosen to leverage our platform to initially focus on advancing our product candidates in the areas of prophylactic vaccines, oncology and molecular therapy.

A disease indication may require an approach that triggers an immune response (immune active) or that does not require immune activation (immune silent). Each of the disease indications that we are targeting require different levels of immune activation for the mRNA-based medicines to be effective. For the immune active side of our technology, we focus on RNA or mRNA-based medicines in prophylactic vaccines and oncology. For the immune silent side of our technology, we have expanded our preclinical product portfolio to include mRNA therapies based on the expression of therapeutic proteins (including ocular, liver and lung applications).

Our lead programs include:

- Our second-generation construct CV0501 against SARS-CoV-2 is a monovalent construct applying modified mRNA developed in collaboration with GSK. We initiated a Phase 1 study in August 2022, which provided positive preliminary results in January 2023.

- Our second-generation vaccine candidate Flu SV mRNA against influenza is a monovalent construct applying modified mRNA developed in collaboration with GSK. We initiated a Phase 1 study in August 2022, which provided positive preliminary results in January 2023.

- In oncology we focus on building a meaningful portfolio of novel cancer vaccine candidates based on the differentiated antigen discovery technologies we acquired with Frame Cancer Therapeutics and our partnership with myNEO. Within this portfolio, we follow two approaches. The first approach assesses tumor antigens shared by different cancer patients for the development of off-the-shelf cancer vaccines. The second approach is tailored to the individual tumor setup of a patient for personalized therapy. A proof-of-principle study, assessing an

mRNA construct encoding multiple epitopes from eight tumor associated antigens in patients with surgically resected Glioblastoma Multiforme is planned to start in the second quarter of 2023.

Our key partnered programs include:

- We have partnered with GSK for the development of COVID-19 vaccine candidates based on our second-generation mRNA backbone, including CV0501 and CV2CoV, and vaccine candidates based on our second-generation mRNA backbone against other infectious diseases, including Flu SV mRNA and CVSQIV against influenza.

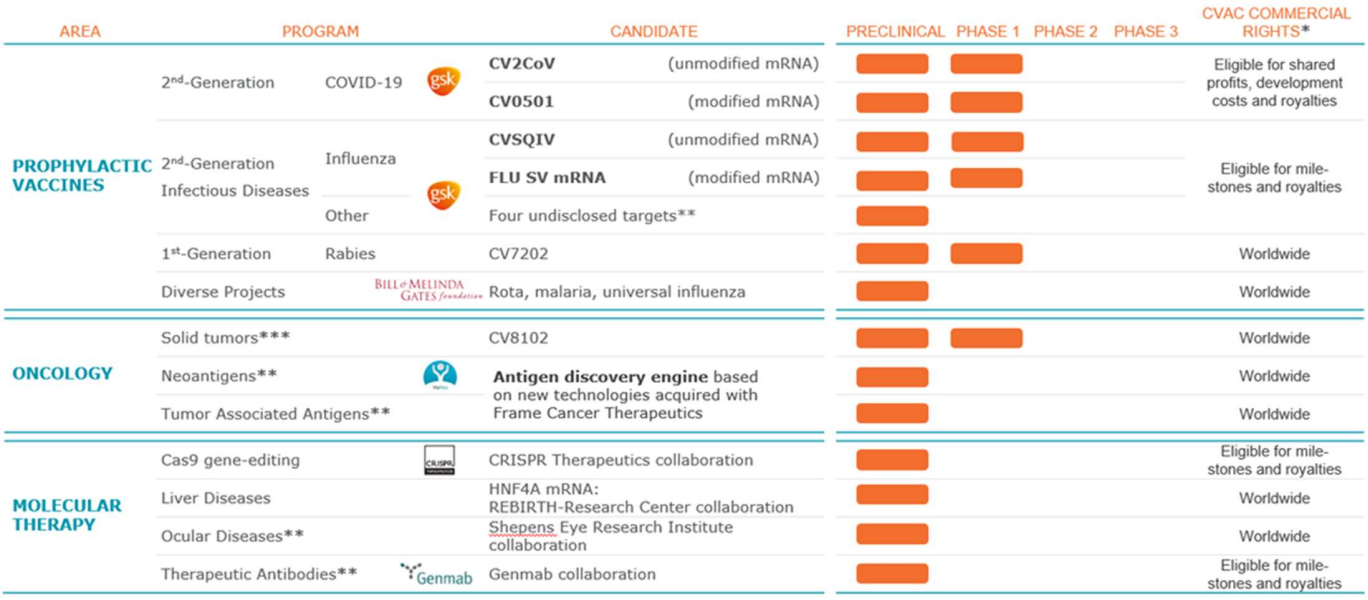
- We have partnered with the immunotherapy company myNEO to identify specific antigens on the surface of tumors for the development of novel mRNA-based cancer vaccine candidates. The partnership leverages myNEO's biological datasets and integrated machine learning and bioinformatics platform to identify and validate specific tumor antigens predicted to elicit a strong immune response.

- We have partnered with CRISPR Therapeutics for the development of novel Cas9 mRNA constructs for use in gene editing therapeutics, with improved properties such as increased potency, decreased duration of expression and reduced potential for immunogenicity. CRISPR Therapeutics has an exclusive license to the improved constructs in three of their *in vivo* gene editing programs.

- We have a broad strategic partnership with Genmab to leverage our mRNA technology platform to develop up to four mRNA-based novel therapeutic antibodies. This represents the first publicly announced strategic partnership focused on differentiated mRNA-based antibodies.

- We have received grants from the Bill & Melinda Gates Foundation to develop prophylactic vaccines designed to prevent picornaviruses, influenza, malaria and rotavirus.

- We also have several academic collaborations, including with SERI for target discovery research in mRNA-based eye therapy.



* For further details on our collaboration agreements, see section 2.2 Business Over–iew - Collaborations and section 3.1 Operating Results — Our Collaborations and Related License Agreements and Advance Purchase Agreements."

** Unidentified indication.

***Cutaneous melanoma, adenoid cystic carcinoma, squamous cell carcinoma, squamous cell carcinoma of head and neck.

Our Strengths.

We are developing a broad portfolio of product candidates currently in preclinical or clinical development stages that we believe position us at the forefront of targeted immune active and immune silent mRNA medicines. Our key strengths include:

- ***We have a differentiated mRNA technology platform that has the potential to address a wide range of diseases.*** As the pioneers in the field of mRNA-based medicines, we have a deep understanding of mRNA biology, its interaction with the cellular translation machinery as well as the immune system. We have built our differentiated RNA optimizer platform to incorporate these insights over the past 22 years. We optimize mRNA to preserve critical protein-RNA interactions. Given the potential advantages of the mRNA-based medicines over existing treatment modalities, such as potential for broad application, wide range of activity, flexibility, design versatility, transient expression and a single manufacturing process, we believe that we have the potential to address a broad range of diseases across multiple therapeutic areas. Our technology platform has been validated in clinical and preclinical studies in selected disease indications.

- ***We have an optimized second-generation mRNA backbone, which catalyzes the expansion of our clinical development pipeline in prophylactic vaccines as well as oncology.*** Our proprietary second-generation mRNA backbone targets improved intracellular mRNA translation for increased and extended protein expression, resulting in earlier and stronger immune responses compared to our first-generation mRNA backbone applied for our initial COVID-19 candidate, CVnCoV. The second-generation mRNA backbone broadly spans unmodified and modified mRNA, as well as monovalent and multivalent vaccine formats to diversify and advance our product development pipeline. We aim to be at the forefront of delivering second-generation mRNA-based vaccines against a range of relevant infectious diseases and are executing on a broad mRNA vaccine program in collaboration with GSK. Second-generation backbone-based vaccines are expected to allow for flexible protection against one or more emerging COVID-19 variants and to enable new mRNA vaccines against other infectious diseases, such as influenza, as well as potential combination vaccines against different viruses. Based on the recent clinical validation of the second-generation mRNA backbone in COVID-19 and flu we are also broadening our foundation in oncology and preparing to build a meaningful portfolio of cancer vaccine candidates based on the second-generation mRNA backbone in combination with promising new tumor antigens predicted to elicit strong immune responses.

- ***We have a broad portfolio of mRNA-based medicines in preclinical and clinical development stages being designed for efficacy, safety and protein expression at relatively low doses.*** The potential of our technology optimized for immune activation in prophylactic vaccines and oncology has been observed in multiple clinical studies. We are developing our product candidates and have conducted preclinical studies and initiated Phase 1 trials of vaccine candidates based on our second-generation mRNA backbone for COVID-19 and influenza. In 2023, clinical development is planned to be continued in both indication with an upcoming Phase 2 in COVID-19 and combined P½e 1/2 study in flu. In oncology, we plan to build a meaningful portfolio of novel cancer vaccines based on our second-generation mRNA backbone to create long-term value and accelerate growth beyond the recent progress in prophylactic vaccines. A key component to deliver on this strategy is the buildup of a powerful antigen discovery engine. In the immune silent area molecular therapy, our approaches optimized for protein therapies have been evaluated in multiple preclinical disease models.

- ***We have a strong prophylactic vaccines clinical development pipeline driven by the technological advantages of our versatile second-generation mRNA backbone.*** Our development focus in the immune activation area is on our second-generation mRNA backbone COVID-19 and flu vaccine candidates jointly developed with GSK. Together with GSK, we extended our technology platform to chemically modified mRNA constructs. We announced the start of a Phase 1 clinical trial with a chemically modified COVID-19 mRNA vaccine candidate based on our second-generation backbone, CV0501, on August 18, 2022. CV0501 specifically targets the Omicron BA.1 variant. The study is being conducted at clinical sites in the United States, Australia, and the Philippines and evaluates the safety, reactogenicity and immunogenicity of a single booster dose of CV0501 in the dose range of 3 to 200µg. In January and April, we announced positive preliminary data from the CV0501 Phase 1 trial. The data are based on cohort sizes of up to 20 participants in the younger adults age group (age 18-64) and 10 participants in the older adults age group (age ≥65). Reported safety data cover the fully recruited dose groups of 3, 6, 12, 25, 50, 100 and 200µg in the younger adult age group and 12, 25, 50, 100 and 200µg in the older adult age group. CV0501 was shown to be generally well tolerated. Immunogenicity data in both age groups showed relevant titers of neutralizing antibodies beginning at the lowest tested dose. On day 29 at the 12µg dose level, CV0501 generated a ratio of post-boost to pre-boost serum neutralizing titers against the Omicron BA.1 variant of 8.1. in younger adults and 13.3 in older adults. The data read-out for both age groups are currently being finalized. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant variants. A pivotal Phase 3 trial may be initiated in 2024, contingent on discussion with regulatory authorities. CureVac and GSK also announced the start of a Phase 1 dose-escalation study with a chemically modified influenza vaccine candidate, Flu SV mRNA, on August 18, 2022. The candidate is a monovalent candidate. The Phase 1 dose-escalation study is being conducted in Canada, Spain and Belgium to evaluate the safety, reactogenicity and immunogenicity of FLU SV mRNA. In the Phase 1 study of Flu-SV-mRNA, expressing an H1N1 hemagglutinin antigen (subtype of influenza A), five doses ranging from 2 to 54µg with up to 25 subjects per dose cohort were evaluated in younger adults (age 18-45). In this age group, preliminary safety and reactogenicity data showed that the monovalent Flu-SV-mRNA candidate was generally well tolerated with no safety concerns observed to date across all tested dose levels. A single dose of Flu-SV-mRNA (dose level undisclosed) was assessed for safety and reactogenicity in older adults (age 60-80) and was also observed to be safe and well tolerated with no grade 3 adverse events in the 32 subjects who were administered the mRNA construct. Immunogenicity of the monovalent Flu-SV-mRNA was assessed in parallel with a licensed seasonal flu vaccine comparator in both age groups. In younger adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA increased up to approximately 3.3 times those elicited by the licensed flu vaccine comparator in younger adults. In older adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA were approximately 2.3 times those elicited by the licensed flu vaccine comparator. In the same age group, the percentage of subjects achieving seroconversion was 89.7% for Flu-SV-mRNA and 56.2% for the licensed flu vaccine comparator. The vaccine candidate for future clinical development is expected to target all four strains recommended by the WHO for influenza vaccines. A P½e 1/2 study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

- ***We have the ability to target different tissue types based on our delivery systems.*** We have access to a number of mRNA delivery systems, including third-party and our proprietary systems, which allow us to target distinct tissues in an optimal way. Our initial clinical programs are based on localized delivery or using the LNP delivery system. Our prophylactic vaccine programs rely on LNP-based delivery systems administered intramuscularly and provide access to the immune cells. Moreover, LNP-based systems deliver mRNA efficiently to the hepatocytes in the liver, if administered intravenously. Protein expressed in the liver may either restore a specific function in the liver itself or produce secreted proteins for release into circulation. We rely on third-party state-of-the-art LNP delivery systems for our current clinical programs, but we are also developing our own proprietary LNP delivery system. In our proprietary LNP programs, we demonstrated that changes to the ratio and/or composition of the LNP constituents can be applied to fine tune LNP physico-chemical properties and steer immune responses as well as overall biological activity.

- ***We have invested in building our in-house manufacturing infrastructure, capabilities and expertise to rapidly, efficiently and cost-effectively produce mRNA-based medicines at commercial-scale.*** We have continued to invest in our manufacturing platform since 2000 and have manufactured thousands of mRNA. We consider our manufacturing process an important part of our strategy that allows us to continuously improve our technology platform and maintain flexibility in clinical development. We are currently producing clinical trial material for our upcoming Phase 2 in COVID-19 and P½e 1/2 in flu using CureVac's proprietary mRNA platform. Our manufacturing setup allows us to drive innovation and to maintain flexibility as well as to pivot quickly in clinical development and potential commercialization. In house, we currently operate three GMP-certified suites, with the capacity to supply our clinical programs and support potential early commercialization activities. We are in the process of building a fourth GMP large-scale production facility at CureVac's headquarters in Tübingen, which is being designed to cover all manufacturing steps from starting material to formulation, and which could potentially supply hundreds of millions of doses of our vaccine product candidates to support our future commercial launches. All our mRNA-based active ingredients for various fields of application originate from a common technology platform and are based on standardized source materials, which enables us to produce mRNA-based medicines using a platform process concept.

- ***We have entered into strategic partnerships with leading biopharmaceutical companies and research and nonprofit institutions to expand the applications of our technology platform.*** We have a history of partnering with leading biopharmaceutical companies such as GSK, myNEO, CRISPR Therapeutics, Genmab, and Bayer. We also have received research grants from the Bill & Melinda Gates Foundation and CEPI for the development of several prophylactic vaccines. Our academic collaborations are focused on identifying and evaluating novel targets in selected therapeutics areas. These partnerships and collaborations allow us to expand the application of our platform and bring in external expertise and capabilities.

- ***We have built an intellectual property portfolio in a variety of markets for our platform and product candidates.*** As pioneers in the field of mRNA therapies, we have built an intellectual property portfolio in the United States and other major geographies, which is one of the broadest and most diverse intellectual property portfolios in the field. As of April 3, 2023, we own approximately 801 issued patents worldwide, including 102 issued U.S. patents, 50 issued European patents (which have been validated in various European countries resulting in a total of approximately 516 national patents in European countries), and 183 issued patents in other foreign countries, 122 pending U.S. patent applications, 85 pending European patent applications and 262 pending patent applications in other foreign countries and 17 pending PCT patent applications. These patents include claims relating to our mRNA technology platform, our CVCM delivery system, our proprietary LNP technology, CV8102, CV7202, CV2CoV and other product candidates. We believe our patent applications and other patents are the most cited among mRNA companies' intellectual property.

- ***We have a long history of mRNA research and development and are led by an experienced management team.*** We are led by veterans of the biopharmaceutical industry with extensive experience in nucleic acid therapy, oncology, rare and infectious diseases and antibodies. Our management team as well as our supervisory board members have broad expertise in the clinical, regulatory and commercialization aspects of oncology, prophylactic vaccines and rare diseases as well as in drug development, process development and manufacturing for mRNA-based medicines. Members of our management team have held senior positions at Novartis, Bristol-Myers Squibb, Ipsen, Sanofi, GSK, Merck KGaA, Schering Plough, AstraZeneca, Genmab, LION Bioscience, Pixium Vision, Sirona Dental Systems, Sygnis Pharma AG and other companies. As of December 31, 2022, our broader team included 242 individuals with advanced scientific degrees working on advancing our mRNA platform.

Our Strategy

Our goal is to build a leading, fully integrated mRNA-based medicines company that can transform the lives of people. The key components of our strategy include:

- ***Continue to invest in our proprietary technology platform to be the leading mRNA platform company.*** We intend to invest in our proprietary technology platform to broaden its potential across therapeutic areas, in addition to broadening our pipeline in existing therapeutic areas. We believe our continued investment will enable us to further optimize the three core pillars of our technology platform — protein design, mRNA optimization and mRNA delivery — and to further enhance our treatment approaches by offering higher selectivity, greater protein expression, potential combination therapies and reduced or flexible dosing. We are continuing to build on our deep expertise in mRNA-based medicines based on what we have learned from our current programs to apply to our future programs.

- ***Utilize a rational disease selection approach to minimize clinical and commercial risk for our programs and broader platform.*** Our strategy is to maximize the potential of our technology platform through our rational disease selection approach to clinical development. We are initially targeting diseases that require an active immune response (such as prophylactic vaccines and oncology) and require transient expression of mRNA in tissue types that are more easily accessible. We are also developing a product portfolio targeting diseases that require an immune silent approach (such as molecular therapy).

- ***Rapidly advance our lead product candidates through clinical development and regulatory approval.*** Our product candidates are currently in preclinical or clinical development stages. In January 2023, we announced that the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the COVID-19 and flu programs jointly developed with GSK. In COVID-19, we are conducting a Phase 1 study with our monovalent second-generation mRNA backbone COVID-19 vaccine candidate, CV0501, initiated in August 2022. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant COVID-19 variants. A pivotal Phase 3 trial may be initiated in 2024, contingent on discussion with regulatory authorities. Within the broader second-generation infectious disease program we are developing in collaboration with GSK, we are conducting a Phase 1 study with our monovalent second-generation mRNA backbone influenza candidate, Flu SV mRNA, initiated in August 2023. The vaccine candidate for future clinical development is expected to target all four strains recommended by the WHO for influenza vaccines. A P½e 1/2 study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

  We believe that by initially targeting diseases with high unmet medical need, we will be able to rapidly advance our programs through clinical development. We intend to pursue the appropriate regulatory pathways available to further accelerate our development efforts.

- ***Continue to invest in our manufacturing capabilities across all manufacturing steps from starting material to formulation to further add scale and flexibility for potential commercialization.*** We believe that our manufacturing capabilities are a key strategic advantage that offer us flexibility, scalability, versatility and reliability in discovery and development. We are currently building our commercial-scale GMP IV facility, which is being designed to cover all manufacturing steps from starting material to formulation and would allow us to further scale up, reduce manufacturing time and reduce production costs. In addition, we are developing a new integrated and automated process for manufacturing of mRNA vaccines and therapeutics, The RNA Printer®. In March 2022, we established the CureVac RNA Printer GmbH as a fullyowned CureVac company to advance The RNA Printer®. The new entity is designed as a platform and services company, providing a dedicated operational environment to further develop and establish The RNA Printer® as a manufacturing end-to-end solution. With its modular design and decentralized concept, we believe The RNA Printer® could be used to facilitate broad access to mRNA technology and enable mRNA product developments (e.g., for rapid supply of new mRNA-based vaccines in pandemic situations as well as patient access to advanced and personalized mRNA-based therapies in oncology).

- ***Selectively seek strategic partners to develop and commercialize product candidates in certain therapeutic areas and geographies.*** We plan to continue to seek additional partnerships with other leading biopharmaceutical companies with specialized capabilities, including development and commercialization expertise in selected therapeutic areas and geographies. We may pursue partnerships that allow us to expedite the discovery and development of product candidates, complement our internal development expertise, broaden the breadth of our technology platform, and provide us with non-dilutive financing, while allowing us to retain economic rights to our product candidates that we view as strategically important. Our approach of partnering with a number of biopharmaceutical companies allows us to execute on a broad range of programs simultaneously, while mitigating our drug development risk.

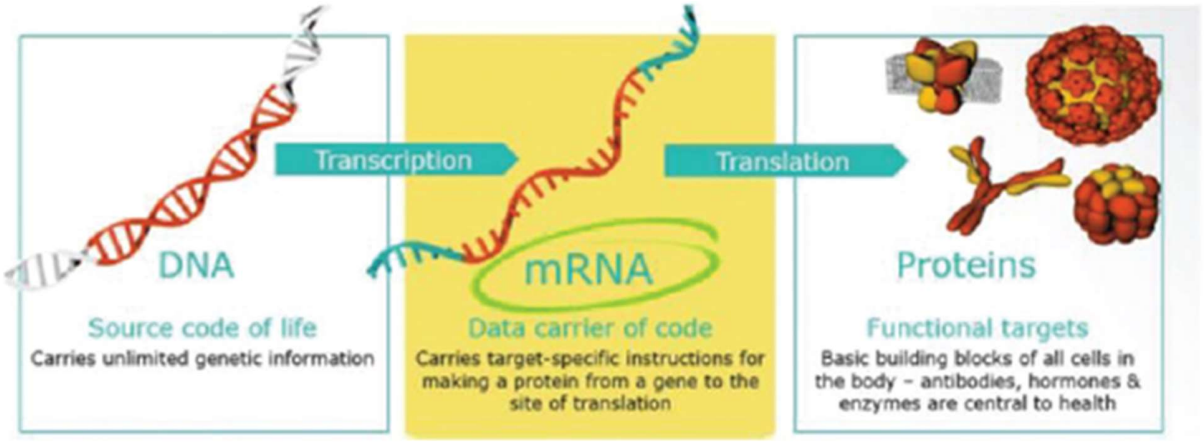
- ***Seek strategic acquisitions or in-licenses of technology or assets that are complementary to our programs and technology platform.*** mRNA-based medicines is an emerging field with ongoing advancements and discoveries. As the pioneers in the field, we have made significant strides in advancing and optimizing our technology platform over the past 22 years. We may seek acquisitions and in-licensing opportunities that can augment our internal expertise, expand our competitive differentiation and further enhance our mRNA technology platform. In June 2022, we announced the acquisition of Frame Cancer Therapeutics, a private company focused on advanced genomics and bioinformatics, to identify both shared and unique neoantigens across different cancer types. The acquisition complements existing in-house expertise to identify and validate promising antigens for mRNA cancer vaccine candidates. The acquired technologies will support the development of a strong antigen discovery engine, which has the potential to identify a broad panel of neoantigens and tumor-associated antigens that go beyond conventional approaches and could strongly increase the likelihood of developing highly effective cancer vaccines that activate the human immune system against cancer.

- ***Strengthen and expand our intellectual property portfolio to protect our scientific and technical know-how.*** We intend to continue to strengthen and expand our intellectual property to protect our advances in scientific and technical know-how. Our intellectual property strategy is focused on covering advancements in our technology platform, manufacturing processes, and product candidates. In addition to patent protection, we also rely on trade secrets and confidentiality agreements to protect other proprietary information that is not patentable or that we elect not to patent.

Overview of mRNA Therapeutics

The Role of mRNA

mRNA is a molecule instructing the translation of genetic information encoded in DNA by cells into proteins, which carry out essential cellular functions. As depicted in the figure below, genetic information stored in DNA is transferred to mRNA in a process called transcription in the cell nucleus. In transcription, double-stranded DNA is temporarily unwound and copied into single-stranded mRNA by the enzyme RNA polymerase. mRNA is then transported to the cytoplasm where it instructs synthesis of proteins through a process called translation. In translation, cellular structures called ribosomes decode mRNA bases in groups of three (called codons) as amino acids. Each codon specifies a particular amino acid, and amino acids are the building blocks of protein molecules which perform distinct functions within the body.



Limitations of Existing Treatment Modalities

There are several existing treatment modalities that seek to address the underlying cause of absent or defective proteins associated with diseases, including protein replacement therapy, gene therapy, gene editing, RNA interference and small molecule therapies. Other treatment modalities seek to harness the immune system, including antibody therapies and traditional prophylactic vaccines. Each of these treatment modalities have certain limitations as discussed below:

- *Protein Replacement Therapy:* While this approach has been successfully used to treat a subset of protein-based disorders, it is mostly limited to proteins that function outside of the cell.

- *Antibody Therapy:* Antibody therapeutics are largely administered intravenously and, being proteins themselves, have applications largely limited to surface molecules. In addition, antibodies have historically faced challenges due to their relatively large size, inadequate pharmacokinetics and tissue accessibility as well as unwanted interactions with the immune system.

- *Gene Therapy:* Gene therapy is usually a one-time intervention meant to provide lasting levels of therapeutic protein. While expected to be a one-time treatment, the duration of treatment efficacy is still largely unknown and it may not be amenable to repeat dosing due to neutralizing antibodies against the gene therapy vehicle. In addition, large-scale manufacturing is costly, time consuming and complex.

- *Gene Editing:* Despite its promise, gene editing is still in the early-stages of development and has potential risks related to unwanted on and off-target DNA modifications, incomplete targeting or mosaicism that hinder intended modifications. Similar to gene therapies, manufacturing complexities and costs for gene editing are also challenging.

- *RNA Interference:* RNA interference has potential in silencing certain genes but has limitations in replacing defective or missing proteins, as well as highly expressed proteins. Most of the current efforts in this treatment modality are focused on genes expressed in the liver, with limited evidence of applications in extra-hepatic tissues.

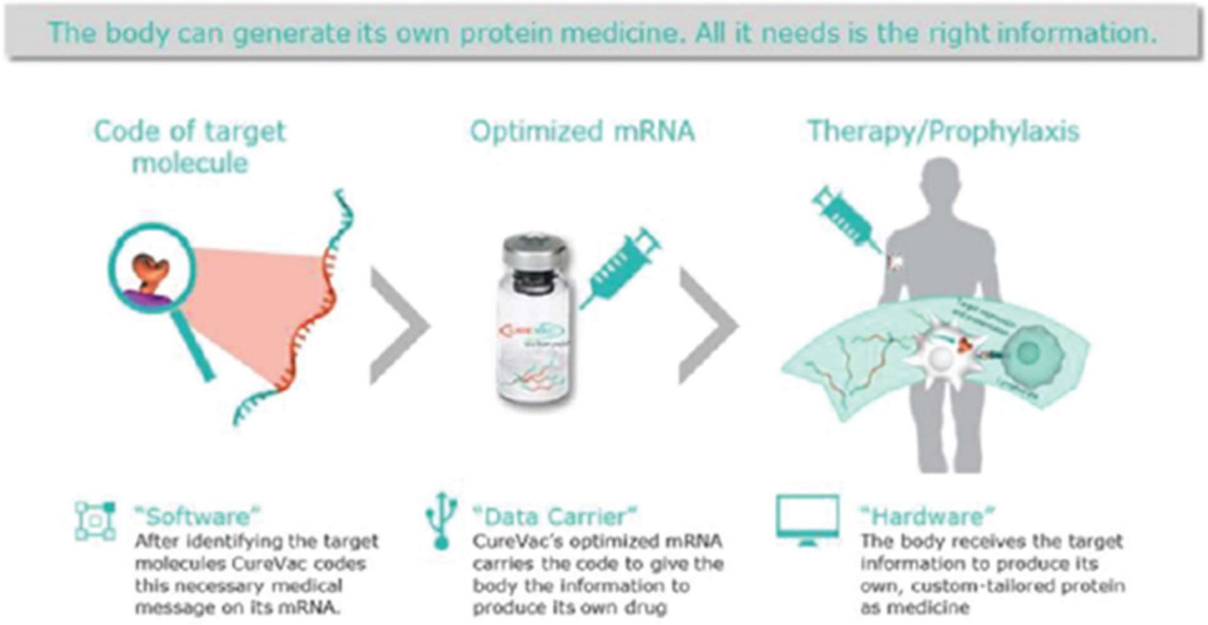
- *Small Molecule:* While small molecules offer advantages over other treatment modalities in terms of biodistribution, tolerability, and delivery, they do not directly address specific gene defects and have a high potential to cause off-target toxicities.

- *Traditional Prophylactic Vaccines:* While traditional prophylactic vaccines are one of the most successful and cost-effective global health interventions, their complex development and costly production processes create a high barrier to entry, long development cycle and limitation in developing vaccines with high serotype coverage.

mRNA as a Novel Treatment Modality

mRNA, as the universal template for protein synthesis, can direct the synthesis of any protein in the body. To treat a medical condition, we identify a target protein and encode the information required to synthesize this protein on the mRNA. The mRNA, optimized using our platform, carries this code to give a patient's body the information to produce its own, custom-tailored protein as medicine.

mRNAs are typically characterized by their rate of translation into protein and their short and predictable, yet steerable half-life. We optimize these mRNA properties for specific therapeutic needs to provide the most efficacious mRNA-based medicine. mRNAs provide the flexibility to deliver medicines that are required for a limited time as well as the opportunity to deliver repeated doses that can be adjusted to patient needs. The development and manufacturing of mRNA-based medicines can also proceed much more quickly than traditional protein-based therapies, including antibodies.



Key potential advantages of mRNA therapies that could position it as a novel treatment modality include:

- *Broad application:* mRNA has the ability to produce all types of proteins, including secreted, membrane and intracellular proteins. This enables broad applicability across a variety of diseases.

- *Natural biology:* mRNAs mimic human biology to produce proteins in the body in contrast to recombinant proteins that are manufactured using processes that are foreign to the body.

- *Wide range of activity:* mRNAs can be used to create therapies that can be applied as an agonist, an antagonist or for vaccines.

- *Flexibility:* A large number of alternative mRNA candidates can be generated in a short time and tested to optimize both the mRNA and protein format.

- *Design versatility:* Therapeutic protein expressed from mRNA *in situ* can be designed for efficacy without being limited by the constraints which recombinant proteins are subject to.

- *Specificity:* mRNA-based medicines encode proteins which offer much higher specificity of interactions compared to small molecule drugs, which limits any potential off-target effects.

- *Repeat dosing:* mRNA-based medicines can be dosed repeatedly given their low immunogenicity.

- *Transient expression:* Short-lived expression of mRNA limits the risk of unforeseen adverse effects of lasting protein expression (as seen in gene therapy and gene editing) and allows for modified dosing schedules adjusted based on a patient's needs.

- *Manufacturing:* mRNA production process is largely independent of the encoded protein as changes to the mRNA sequence do not affect its chemical and physical properties, allowing for higher efficiency, greater speed and lower cost of production.

Historical Challenges with Developing mRNA Treatments

Using mRNA as a treatment has long been of interest given its potential to address limitations of existing treatment modalities. However, mRNA has historically been limited by the following theoretical and practical hurdles:

- *Stability:* Naked mRNA is rapidly degraded by RNase enzymes present throughout the body which limits the duration of its therapeutic effect. An effective mRNA would need to be masked from these enzymes.

- *Uptake by cells:* Uptake of naked mRNA into cells is relatively inefficient. A more effective mRNA-based medicine would need a delivery system that delivers mRNA efficiently into cells.

- *Expression level:* Protein expression levels from synthetic mRNA obtained by *in vitro* production have been considered too low historically for therapeutic purposes, which underlines the need for an optimized mRNA construct.

- *Immunogenicity:* Non-optimized mRNA in the body rapidly activates receptors on immune cells which triggers the innate immune response and can lead to shut down of protein translation in cells. An effective mRNA-based medicine needs to modulate the immune system according to the disease indication being targeted.

- *Tissue targeting:* Each indication requires delivery to a specific tissue. An effective mRNA-based medicine would need a delivery system that efficiently delivers mRNA to a specific target tissue with low off-target delivery and toxicity.

- *Manufacturing:* mRNA manufacturing technology must be scalable and cost-effective to enable large production for multiple clinical trials and commercialization.

Our Technology Platform

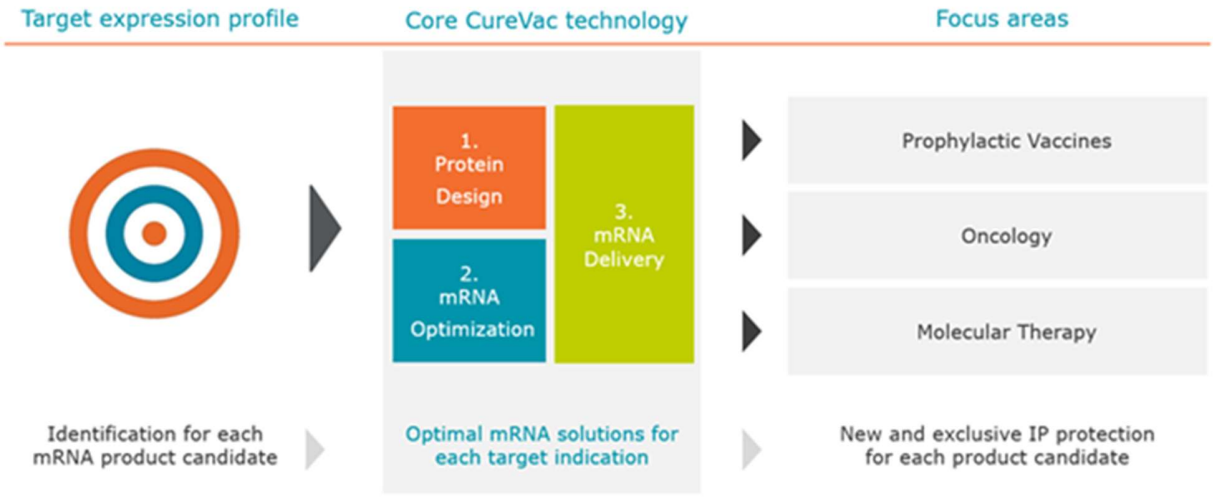
The therapeutic potential of mRNAs was discovered by our co-founders in 2000. As the pioneers in the field of mRNA, we have built extensive expertise in mRNA biology, optimization and production. We have developed our technology platform, called RNAoptimizer, through continued investments over the past 22 years. We believe that we

have created the broadest and most versatile platform to develop optimized mRNA-based medicines that has potential to offer differentiated profile in terms of safety, stability and expression.

Our optimization approach covers three pillars: protein design, mRNA optimization and mRNA delivery. Our approach is based on the extensive data libraries we have generated to date. To improve protein expression from *in vitro* produced mRNA, we isolated high numbers of human natural mRNAs from different cells and identified elements which stabilize mRNA and improve their interaction with the cellular translation machinery. In 2022, we extended our technology platform to chemically modified mRNA constructs. We continue to invest in all levels of optimization to improve the methods we currently employ and continue advancing mRNA-based medicines.

We have a long track record of performing clinical trials with multiple product candidates since 2008. The data generated in these clinical trials has allowed us to better understand the biology of mRNA and to further accelerate development in new therapeutic areas and approaches. We were the first company to demonstrate that mRNA vaccines can induce protective antibody titers in naïve human subjects with a previous version of our current rabies vaccine product candidate.

Our product candidates consist of two major components: the protein-coding mRNA and a delivery vehicle. Once we have established delivery capability to a target tissue, we can design new product candidates that vary only in the mRNA component, which we expect will allow for rapid target and development candidate identification. We believe that this will enable our platform to be flexible and scalable as we develop additional product candidates.



Our process for creating novel mRNA therapies comprises the following three pillars:

- ***Protein Design:*** Our goal is to define the amino acid sequence to optimize specific properties of the encoded protein.

- ***mRNA Optimization:*** Our goal is to define the nucleotide sequence of the mRNA encoding the optimized protein to improve the properties of the mRNA molecule.

- ***mRNA Delivery:*** Our goal is to define mRNA encapsulation and delivery to select the optimal formulation for each specific indication and tissue.

First Pillar: Protein Design

Proteins play a central role in biology, including formation of the structural framework of the body, aiding in intra- and extracellular transport, biological catalysts (such as enzymes), controlling the activity of cells, and enabling signal transduction throughout the body. Accordingly, mutations that alter the function of a protein that plays a critical

role inside the body can disrupt normal development and cause disease. Diseases could be caused by low expression, over expression, or abnormal structures for specific proteins.

We target diseases that are caused by these abnormal or missing proteins. Once our team identifies the protein of interest for a specific vaccine or therapeutic target with a defined target product profile, protein design further improves the potential efficacy by adaptation of the amino acid sequence. Protein design is based on modulation of beneficial protein characteristics that are not present in the naturally occurring protein. We have a library of validated protein domains that can be leveraged using a combinatorial approach to optimize the properties of the target protein.

Our protein design process considers multiple factors before the protein is encoded in the mRNA, including half-life, stabilization of tertiary structure, oligomerization, secretion, and immunogenicity. We have the ability to modify each of these parameters while ensuring that these modifications work in harmony with the required function of the target protein.

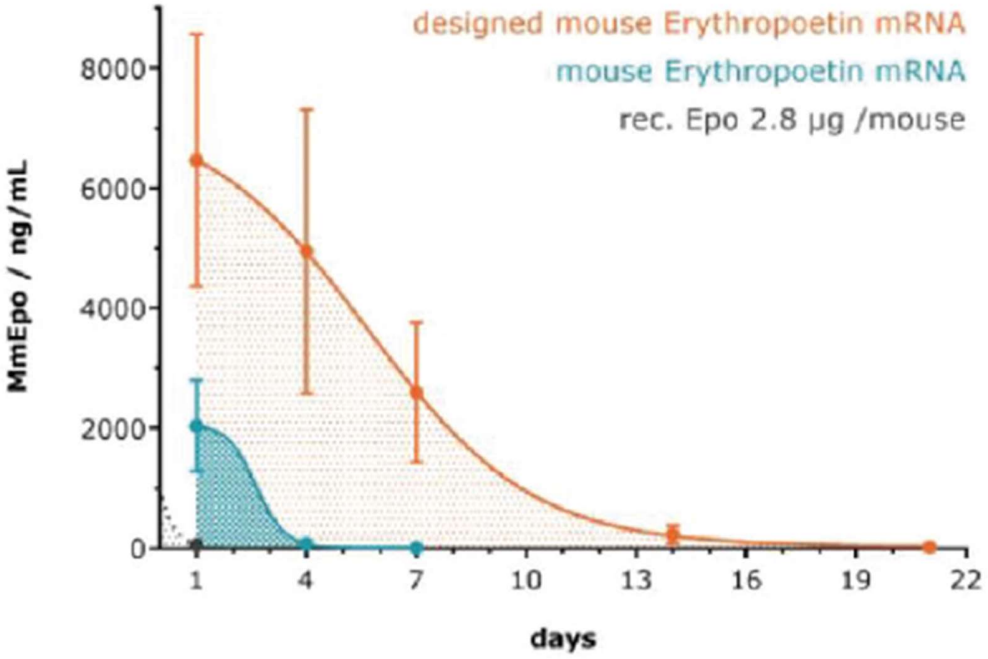
Protein design always depends on the function of the individual protein of interest. The protein can serve as a therapeutic protein without any activation of the immune system or the protein can serve as an antigen with the goal of inducing strong immune responses against it. We employ different optimization strategies to support these distinct functions and requirements. For example, we can enhance certain parameters to extend the half-life or localization of a protein in the case of therapeutic proteins while making sure that RNA sensors remain muted to avoid activation of the immune system. For vaccines, our goal is to induce an optimal immune response mimicking response induced by bacterial or viral infections. Therefore, protein design is always bespoke and multi-factorial to support distinct functions and requirements of the specific target protein.

Below are several specific examples of protein modifications by which we designed a protein's properties relative to the wild-type protein:

Extended Half-Life of Secreted Protein

This approach relies on the addition of supplementary short domains to the coding sequence of the protein of interest. Although this fusion increases protein size, the additional domains recruit binding proteins already present in blood which promote stabilization of the target protein by preventing proteolytic degradation. To support the efficient persistence of a secreted protein in the bloodstream, we can improve the half-life of this protein by adding specific, endogenous domains. By tailoring the pharmacokinetic profile of secreted proteins, we have the ability to reduce the frequency of dosing, generating a better therapeutic window, and using less material.

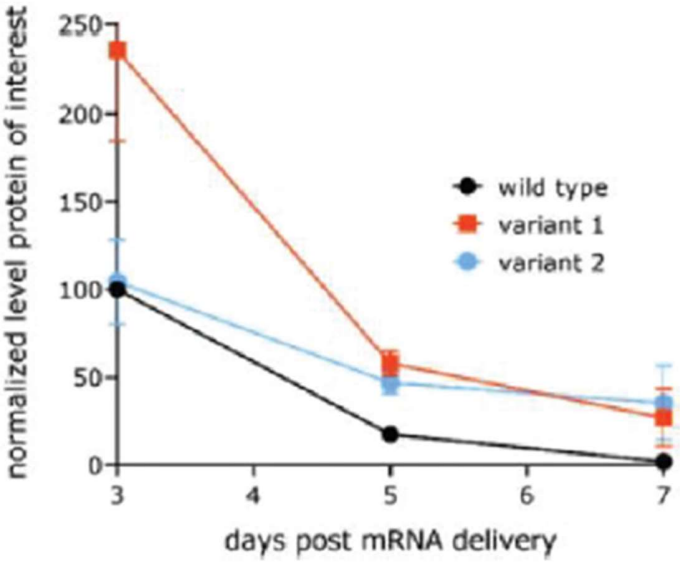
For example, wild-type erythropoietin (Epo) is a protein that has a very short half-life of three to four hours in the bloodstream. In a preclinical model, mice were dosed with mouse Epo and protein engineered mouse Epo, both encoded with our optimized mRNA. Dosing with the engineered mouse Epo protein showed an increase in serum titers and pharmacokinetic profile. We were able to increase the half-life and availability of functional Epo in blood from four days to two weeks by fusing endogenous Epo to a selected domain. Notably, both mRNA-encoded Epo proteins showed significantly higher protein expression levels than the injected recombinant Epo, which was cleared from the bloodstream after a single day.



Mice received a single injection in the tail vein of recombinant protein (control) or mRNA encoding proteins. Mice received 2.8 µg of recombinant mouse Epo protein. Wild-type Epo encoded by our optimized mRNA and engineered Epo protein encoded by our optimized mRNA were administered at a dose of 0.4 mg/kg giving rise to relevant serum titers of functional Epo and different pharmacokinetic profiles.

Extended Half-Life of Intracellular Protein

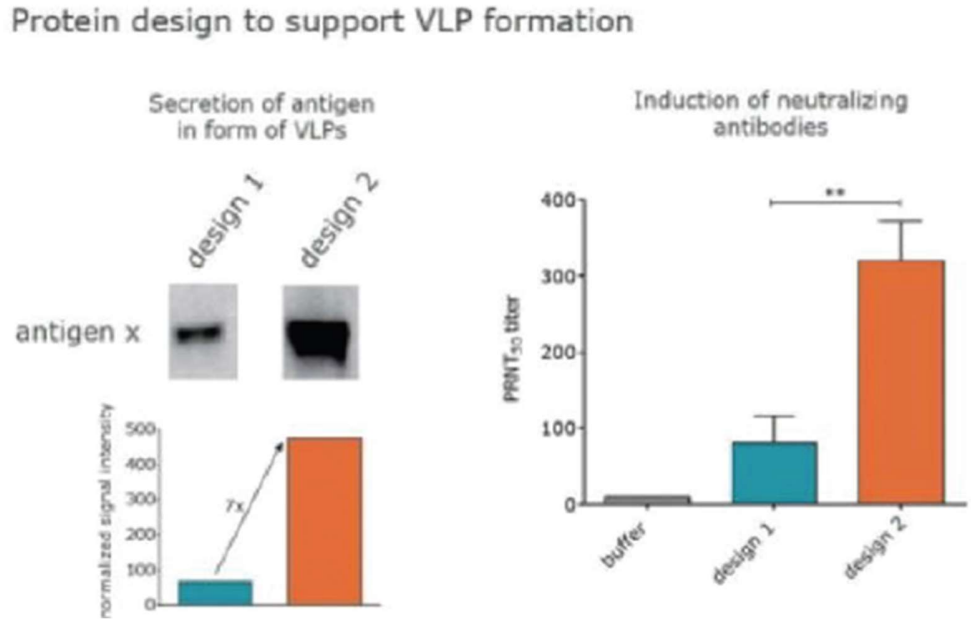
Similar approaches can also be applied to intracellular proteins, promoting the half-life of functional target proteins. In the example below, protein variant 1 represents the fusion of a protein of interest with a selected protein domain, while variant 2 represents a construct with a single point mutation within the protein of interest. In contrast to the wild-type protein, both engineered protein variants enabled the detection of protein even one week after mRNA delivery to hepatocyte cells in culture.



Intracellular abundance of engineered protein variants in comparison to unmodified wild-type protein. Protein levels were determined by whole cell Western Blot analysis in human hepatocytes, followed by normalization to signals from a cytosolic loading control and relative to the wild-type protein. Same doses used in wild-type and engineered protein variants.

Increased Oligomerization

Protein oligomerization is a process that converts monomers to macromolecular complexes through polymerization. We can engineer protein oligomerization by adding domains capable to perform this process to the target protein. As antigens need to be secreted and build clusters to form virus-like particles, or VLPs, this oligomerization process is beneficial in boosting the immune response.



Protein sequence of viral antigen was optimized (design 2) by adding an element promoting secretion and clustering of antigen. In the left-hand side of the graphic, secretion of antigen in form of clusters was confirmed by Western Blot analysis of supernatants from transfected human cells. In the right-hand side of the graphic, vaccination of mice with an mRNA vaccine based on this improved protein design resulted in higher immunogenicity, measured by induction of virus neutralizing antibodies.

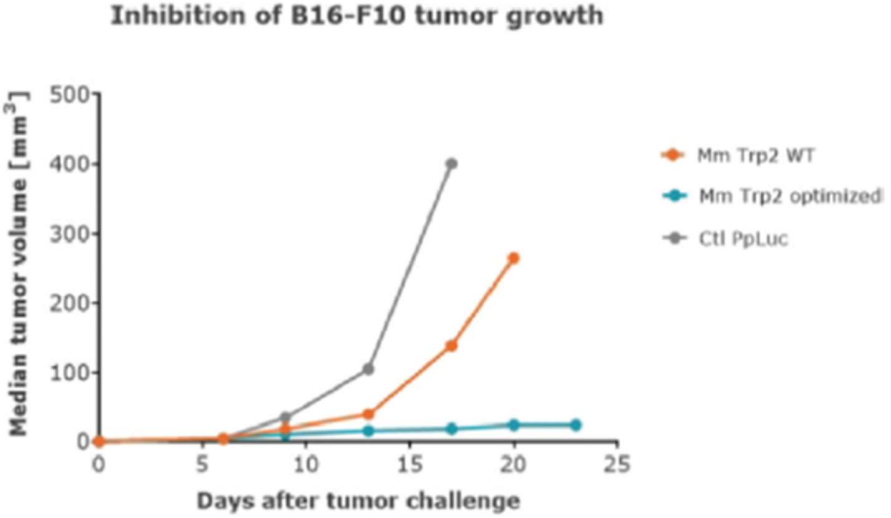
Improved Secretion

The potency of secreted target proteins can be improved by using alternative, more powerful signal peptides. These signal peptides are responsible for transporting the target protein from the cytoplasm to the outside of the cell, where the secreted protein fulfills its primary function. We screen large libraries of signal peptides to optimize secretion of any given target protein and in any cell type of choice.

For example, we selected a set of 87 verified signal peptides to maximize secretion. These were combined with the novel target protein via automated cloning to enable facile screening and selection of the most potent product candidate. In the figure below, the top hit from this screen increased the secreted protein levels in primary human muscle cells by three-fold relative to the native signal peptide.

Modified Immunogenicity

If the target protein serves as a therapeutic agent, it is important to curb the protein's natural immunogenicity. Our protein design process analyzes and replaces immunogenic epitopes, masking immunogenic epitopes and thereby rendering the target protein more immunosilent. In contrast, we also have the ability to improve immunogenicity for certain applications (for example in a cancer vaccine) by protein design. These protein sequence adaptations promote immunogenicity and suppress tumor growth in mouse models, as shown in the below example.



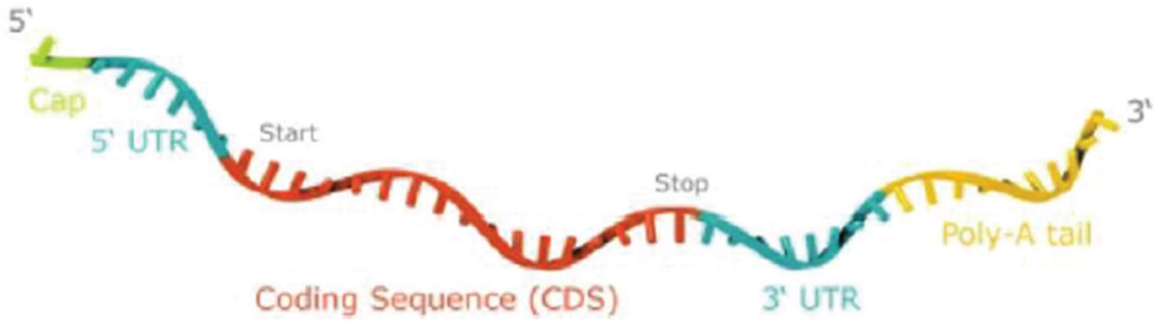
Therapeutic vaccination with mRNA vaccine encoding optimized Trp2 cell antigen inhibited tumor growth in murine melanoma model. Syngeneic mice were challenged subcutaneously with melanoma cells. When tumors were palpable, mice were vaccinated intradermally twice a week with LNP-formulated mRNA encoding either wild-type murine antigen

Trp2 or Trp2 designed to improve antigen presentation. Mice vaccinated with LNP-formulated irrelevant mRNA (PpLuc) served as control.

Second Pillar: mRNA Optimization

Overview of mRNA Biology

mRNA is a linear polymer comprising four monomers called nucleotides: adenosine (A), guanosine (G), cytidine (C), and uridine (U). The sequence at any mRNA's center instructing the synthesis of the protein encoded by it is the open reading frame (ORF, also known as coding sequence). The ORF is a continuous stretch of groups of three nucleotides (called codons) that is decoded and translated into protein by the ribosome. The process of translation begins at the first codon of the ORF, always an AUG (the start codon). The start codon signals to the ribosome where to start protein synthesis. The ribosome then progresses along the ORF one codon at a time, adding the amino acid to the protein chain fitting to the codon. A stop codon at the end of the ORF (UAA, UAG, or UGA) signals to the ribosome to terminate protein synthesis. In every cell, hundreds of thousands of mRNAs are translated into hundreds of millions of proteins every day. A typical protein contains 200-600 amino acids; therefore, a typical mRNA coding region ranges from 600-1,800 nucleotides.



In addition to the coding sequence, mRNAs contain the following elements:

- Untranslated regions, or UTRs — UTRs are sequences that are not translated into protein. The 5' UTR precedes the start codon, the 3' UTR follows the stop codon. These regions play important roles in gene expression, including mRNA stability, mRNA localization and translational efficiency via protein-RNA interactions. Some of the elements in the UTRs form characteristic secondary structures that are involved in mRNA regulation.

- 5' cap — The cap structure is required to recruit ribosomes and additional proteins involved in translation to the mRNA.

- 3' polyadenosine, or poly-A, tail — The 3' poly-A tail is a long sequence of adenosine nucleotides (often several hundred) at the 3' end of mRNA. This tail promotes mRNA export from the nucleus and translation and protects mRNA from degradation. In addition, the 3' end of the mRNA can include a stretch or sequence of nucleotides following the 3' poly-A tail.

Our Approach

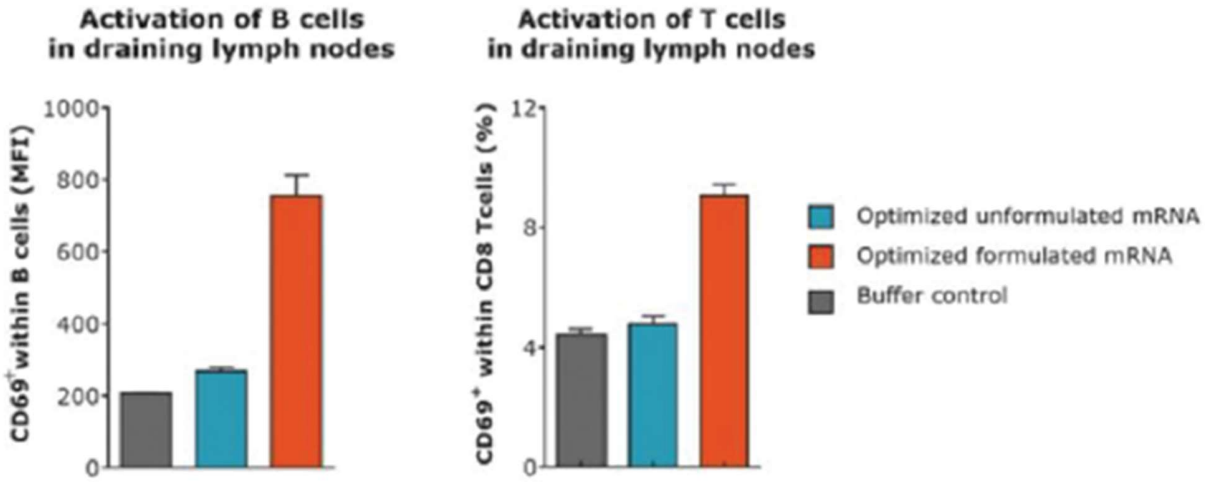
Our mRNA optimization process is designed to generate the most efficacious mRNA for any particular target and indication by optimizing translation, stability and immunogenicity. Each of these parameters can be modified by changing individual mRNA elements and their interplay guided by the envisaged application. Our mRNA molecule contains six elements that can be optimized to improve the potential efficacy of the mRNA construct. These elements include 5' cap, 5' UTR, ORF, 3' UTR, and 3' poly-A tail and 3' end.

Depending on the target and indication, the required pharmacokinetics of protein expression might be different. Some applications may require the highest possible protein expression but only for a limited time, as is the case for gene editing approaches. For other applications, for example some protein replacement therapies, long-lasting protein expression might be key. Peak level and duration of protein expression can be adjusted by the choice or design of enhancer and stabilizing elements in untranslated regions of mRNA. Each of the mRNA elements together in combination

with the overall sequence influence the degree of activation of the immune system by any particular mRNA. Therefore, our approach to RNA optimization always considers multiple factors as well as the whole construct to generate the optimal mRNA.

UTRs contribute decisively to the potential efficacy of therapeutic mRNAs. Natural mRNAs contain several different 5' and 3' UTRs, setting the individual level of translation and stability for each message. We have tapped this natural wealth of regulatory sequences and identified a large set of UTRs that confer translation or mRNA stability via diverse protein-RNA interactions.

Historically, one factor limiting the use of mRNA as a treatment has been the observation that *in vitro* produced synthetic mRNA activated the innate immune system, resulting in a fast shutdown of protein translation in cells. An effective mRNA therapy would need to evade recognition by the immune system to avoid shut down of protein translation. We have accumulated significant knowledge about the signatures recognized by the innate immune system over the past few years. With the insights we have gained, we are able to avoid signatures activating the immune system in elements at our disposal or eliminate them from mRNA constructs. This is demonstrated by the following example where formulated mRNA was injected intradermally in mice and both B cells and T cells were activated in the draining lymph node. In contrast, unformulated mRNA injected intradermally had limited immunostimulatory capacity.



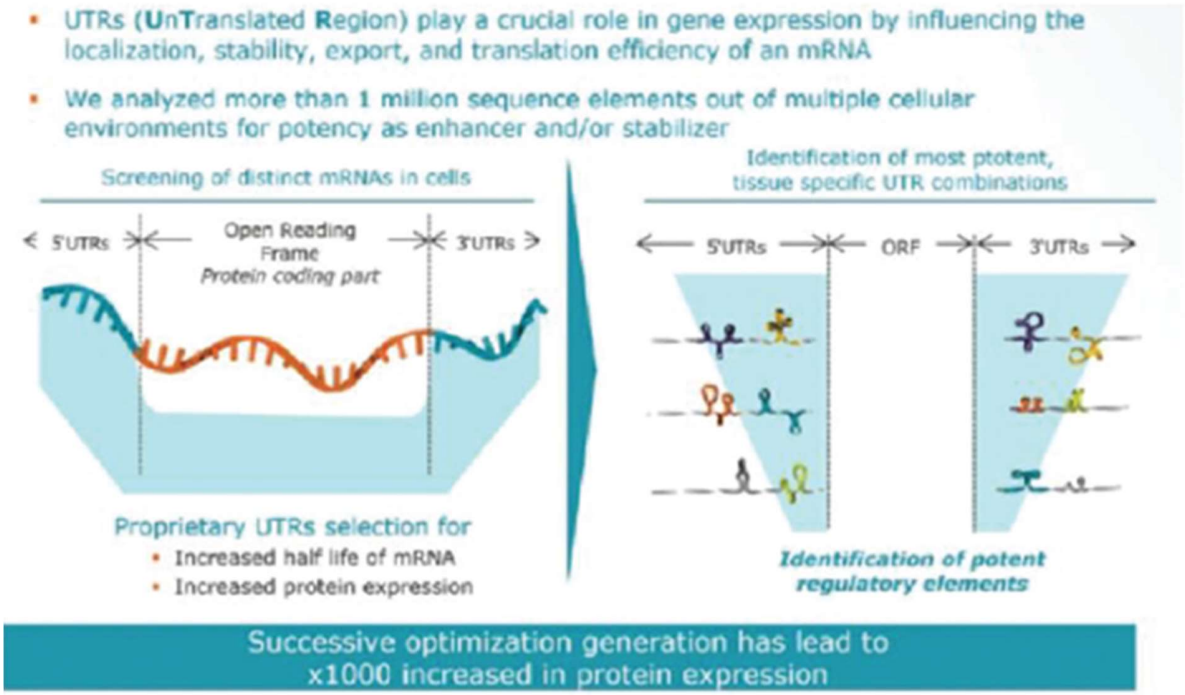
10 µg of mRNA, either free or formulated, was administered intradermally to the back of mice. Twenty-four hours post treatment, draining lymph nodes were isolated, and the activation status of immune cells was analyzed by flow cytometry. A higher CD69 signal indicates activation of the respective immune cells.

Cap Structure

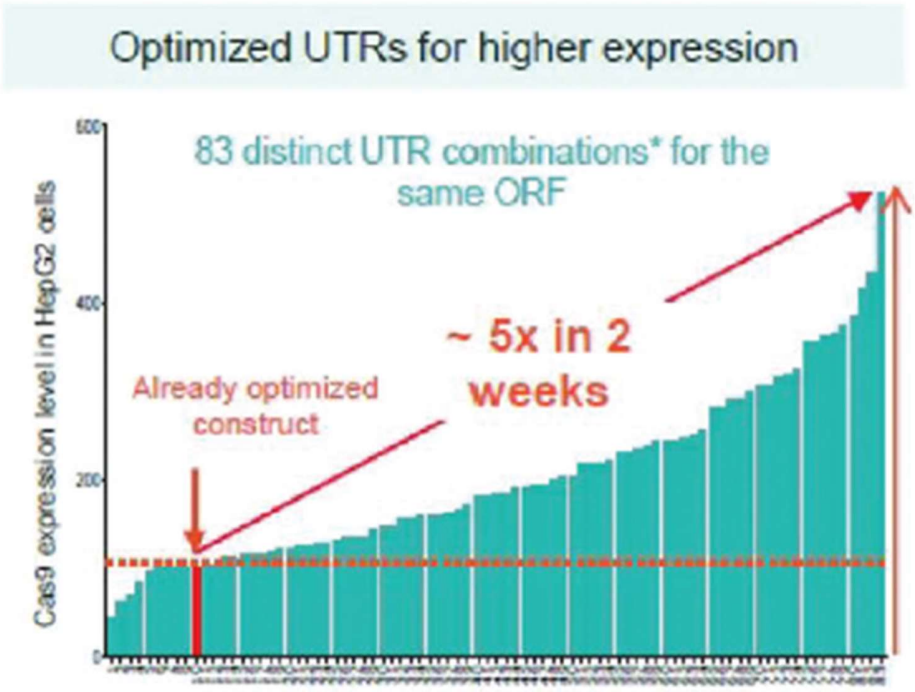
The cap structure influences translation as it recruits the translational machinery, including initiation factors and the ribosome. The cap structure also affects mRNA stability due to its influence on the various proteins recruited to mRNA. Further, the cap structure is a determinant of activation of the innate immune system as different cap structures are differentially recognized by several innate immune sensors. In addition, different cap structures are incorporated during *in vitro* production of mRNA with different capping efficiency, resulting in varying proportion of mRNA lacking a cap, which is an mRNA species which is recognized by yet other sensors of the innate immune system. Accordingly, there is great potential to improve protein expression and immunosilence in mRNA by optimizing the cap structure. We have access to several cap structures, including those we have developed and commercially available ones.

5' and 3' UTRs

We have identified high numbers of naturally occurring 5' and 3' UTRs. Using bioinformatics analysis to identify patterns of increased expression, duration of expression, and reduced immunogenicity, we have catalogued more than one million 5' and 3' UTRs. From these, we selected a large set of potential enhancer elements (improving the rate of protein expression) and stabilizer elements (improving half-life of protein expression). By running a high throughput combinatorial approach, we identify and create optimized UTR combinations for a specific construct. Further, we have created UTR sub-libraries because we discovered that different UTRs perform differently in various tissue types.



Below is an example of the effectiveness of our UTR library to optimize protein expression as part of our collaboration with CRISPR Therapeutics. An open reading frame coding for an optimized Cas9 protein was combined with 83 UTR combinations via automated cloning. This target-specific UTR screening increased Cas9 protein levels in HepG2 cells five-fold compared to an already optimized construct.

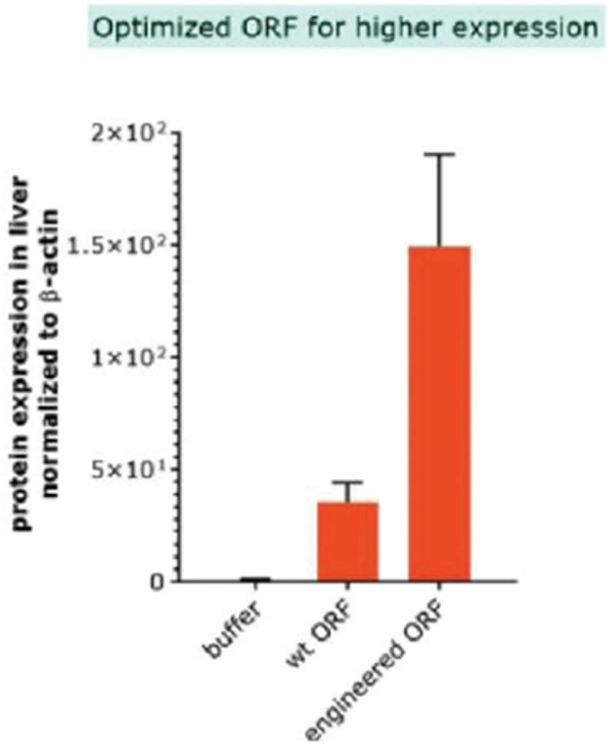


To maximize expression of the target protein a set of 83 combinations of untranslated regions (UTR) was selected from screens identifying stable or highly translated endogenous transcripts. These UTR combinations were combined with the target open reading frame (ORF) via automated cloning to enable facile screening and selection of the most potent product candidates. Target-specific UTR screening led to a five-fold increase in protein levels in HepG2 cells compared to an already optimized construct.

Open reading frame (ORF)

The ORF instructs the synthesis of the protein it encodes by the ribosome. The ORF is a continuous stretch of groups of three nucleotides called codons. Ribosomes decode each codon as an amino acid to be added to the nascent protein. Each codon specifies a particular amino acid, however, many amino acids are specified by more than one codon. Due to this multiplicity of codons that specify an amino acid, any protein can be encoded by a myriad of coding sequences differing in their codon composition. These various ORFs differ largely in their properties and for any particular protein a top-performing ORF needs to be identified or designed to make an efficacious mRNA-based medicine. We currently optimize the ORF in a broad, holistic approach that includes multiple parameters taking into account codon optimality. Our algorithms also take into account that, similar to UTRs, different codons are optimal for different tissues. Furthermore, these algorithms also analyze and consider secondary structure. For example, as certain elements are known to drive immune stimulation by secondary structure, our algorithms avoid generation of sequences that may give rise to such immune stimulations.

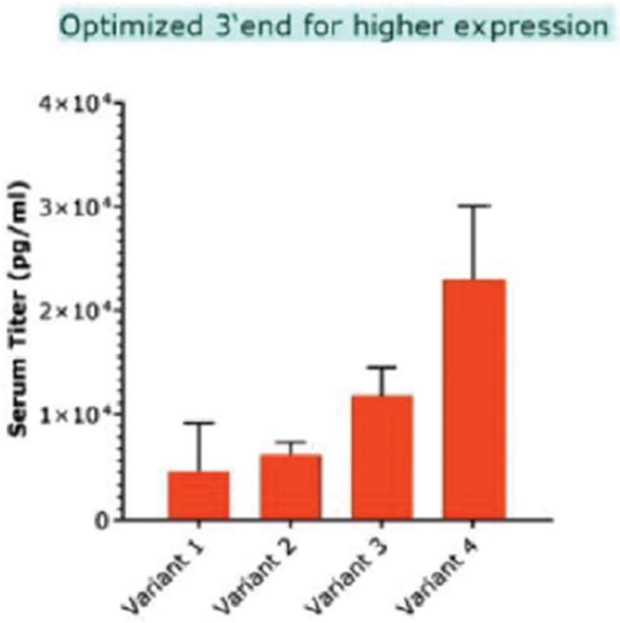
In the following example, protein expressed from our mRNA containing a wild-type coding sequence was abundant in the livers of mice injected intravenously with LNP-encapsulated mRNA. However, protein levels were higher from our mRNA containing a coding sequence engineered for maximal protein expression.



Abundance of a therapeutic protein in mouse liver expressed from an engineered open reading frame (ORF) in comparison to the wild ORF. mRNAs containing ORF variants were formulated in LNPs and injected intravenously into mice (called engineered ORF). Protein levels were determined by Western Blot analysis of liver lysates, followed by normalization to the signal from a loading control.

Poly(A) tail and 3' end

The 3' end of the mRNA molecule, prone to degradation by nucleases, is another form of optimization. The 3' end can be sealed using different stabilizing elements, including secondary structure or specific nucleotide sequences, to inhibit RNA nucleases degrading RNA from the 3' end.



Impact of different mRNA 3' end on serum levels of a therapeutic protein. mRNAs containing different vector-encoded 3' end variants were formulated in LNPs and injected intravenously at a dose of 20 µg into female Balb/c mice. Six hours after injection, serum levels of secreted protein were determined by an enzyme-linked immunosorbent assay test, also referred to as ELISA, to measure antibodies in blood.

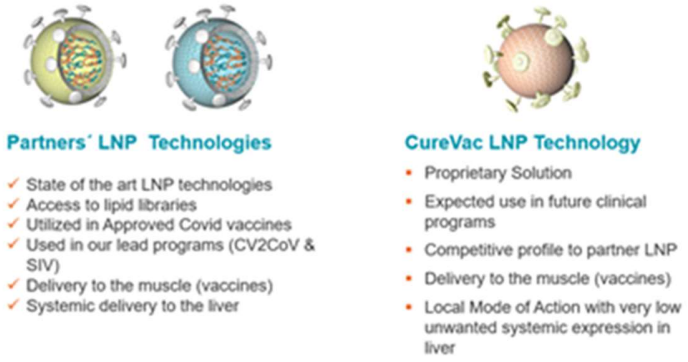
Finally, we analyze the structure of the optimized mRNA as a whole, including ORF and UTRs, to predict its recognition by RNA sensors and immune activating potential and modify any inappropriate elements.

Third Pillar: mRNA Delivery

The potency of the administered mRNA drug product is the combination of the potential efficacy of the mRNA that encodes the protein and the delivery system that transports the mRNA to the cells. Protein levels are highly correlated with the number of transfected cells which requires optimized delivery systems. While it is possible to deliver mRNA directly into the target tissue without delivery systems in certain cases, the presence of RNA degrading enzymes in blood and interstitial fluids rapidly regrade any extracellular mRNA. Additionally, cell membranes act as a significant barrier to entry of large molecules such as mRNA. These delivery technologies enable us to deliver large quantities of mRNA to the target cells.

We have access to a diverse portfolio of third-party and proprietary delivery systems that allow us to target a range of diseases. Access to this broad range of delivery technologies allows us to select the best-suited technology for development of each of our product candidates. We choose the most suited delivery system based on a number of factors, including immunogenicity, duration of treatment, dose levels, mode of administration and targeted tissue type.

The key delivery systems that we currently employ include lipid-based delivery systems. We employ lipid nanoparticles, or LNPs, to deliver our mRNA-based prophylactic and cancer vaccines locally. For protein and antibody therapeutic candidates, we apply LNP-formulated mRNA systemically. We have relied on third-party state-of-the-art LNP delivery systems for our initial clinical programs, and we are developing our proprietary LNP delivery systems for our future clinical programs. With these delivery modalities at hand, we are currently expanding our development pipeline and plan to bring new mRNA therapies to different organs and applications.



Lipid Nanoparticles (LNPs)

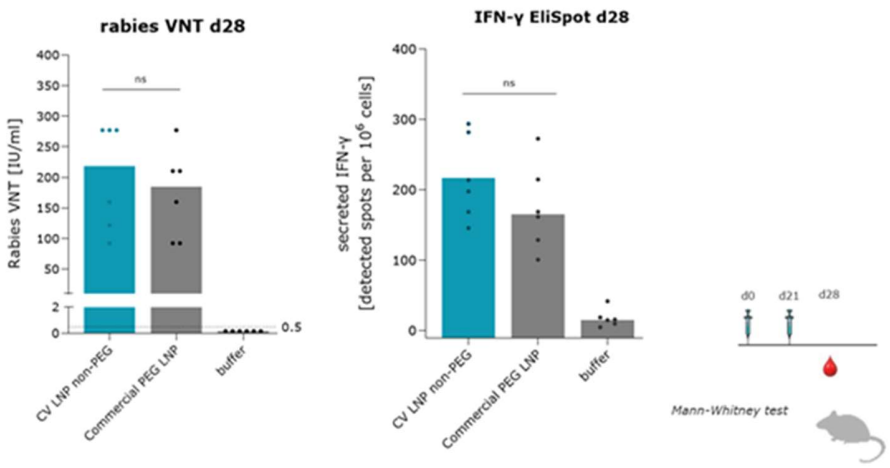
A variety of nanoparticles have been developed over the years for use in drug delivery. LNPs represent the most clinically advanced non-viral delivery systems. Encapsulation of the mRNA within LNPs enables delivery to the site of action within the cell. LNPs protect the mRNA from degradation, rapid excretion and liver clearance, enabling higher bioavailability and longer half-life.

LNPs consist of different lipids that form together a lipid nanoparticle with a solid core. The four primary LNP components include cationic lipids, pegylated lipids, phospholipids, and cholesterols. LNPs mimic low-density lipoproteins, which allows them to be taken up by an endogenous cellular transport pathway to deliver the mRNA cargo to cells. When LNPs are injected into biological systems, they attach to natural transport proteins, apolipoproteins, to facilitate the transport of lipids within the bloodstream and throughout the body. Following intravenous administration, the apolipoprotein binding enables efficient transport of the mRNA cargo to the liver. Once internalized in endosomes within cells, the LNPs are designed to escape the endosome and release their mRNA cargo into the cytoplasm, where the mRNA can be translated. Any mRNA and LNP components that do not escape the endosome are typically delivered to lysosomes where they are degraded by the natural process of cellular digestion.

The properties of each LNP system can be customized based on altering each component or overall composition. All of the LNPs we employ in our projects are designed to be biodegradable. We have extensively tested over 40 different delivery solutions and have selected the ones we use based on comparative data for the most efficient LNPs available from third parties for licensure. Having access to these technologies enables us to develop fast powerful solutions for vaccines and protein therapy.

Besides the licensed LNP technology from our partners, we are also developing our own LNP technology. We have established two ionizable lipid families and are developing those LNPs for application in local vaccination and systemic delivery to the liver. We conducted a systematic screening of LNP components and compositions for local vaccination in skin and muscle. Those optimized LNP formulations incorporating our own lipids helped to raise significant levels of immune response comparable with those of approved vaccine formulations.

The graphs below demonstrate comparable immunogenicity of CV LNP against a commercial PEG LNP in a vaccination trial with the rabies antigen in mice at same mRNA dose. On the left panel, the virus neutralization titer seven days post the second vaccination is shown, whereas on the right panel the induced T cell response is assessed by EliSpot of peptide library stimulated spleenocytes.



Our Approach to Disease Selection

Our approach seeks to mitigate risk across multiple levels to advance and expand our broad product portfolio. While mRNA is still an emerging treatment modality, we believe that we have made advances towards utilizing the potential of our technology platform through rational disease selection. Our approach for selecting new programs is based on the following key factors:

- Target diseases with high unmet medical needs that are not effectively addressed using the current standard of care.
- Target areas where the underlying mode of action of the disease is understood or hypothesized which allows us to identify the required protein(s) or antigen(s).
- Identify areas where mRNA therapies have potential to have differentiated profiles compared to the conventional treatment modalities.
- Assess the likelihood of being able to address the disease using our technology platform and seek to continuously improve and expand the capabilities of our platform to address an even broader range of diseases.
- Seek to build on our deep understanding of mRNA biology, data derived from our technology platform and previous clinical and preclinical studies to apply to new indications.

In building our product portfolio, we have considered a number of factors including immune response, duration of expression, dosing requirements, delivery technology, target tissue type, potential for responsiveness to mRNA-based medicine and target disease profile, among other factors. A disease indication may require an mRNA-based medicine that triggers an immune response, or that is immune active, or an mRNA-based medicine that requires no immune activation, or that is immune silent. Each of the disease indications that we are targeting require different levels of immune activation for the mRNA-based medicine to be effective. Our approach is to initially target indications that require an immune active approach (such as prophylactic vaccines or cancer vaccines), given the need for lower doses and transient expression of the antigen. These initial indications are amenable to localized delivery using an LNP delivery system. Based on the clinical validation of our prophylactic vaccines program and our advanced understanding of mRNA biology and immune stimulation modulation, we are also further expanding our product portfolio to target indications that require an immune silent approach (such as protein delivery). Targeting diseases amenable to the immune silent approach requires higher doses and longer expression of the protein, with potential for long-term repeat dosing for chronic diseases.

- ***Immune active.*** For indications that require immune stimulation such as prophylactic and therapeutic vaccines, our technology optimizes the combination of mRNA molecules encoding specific antigens and selected delivery modalities to provide the desired immunostimulatory capacity. This allows us to design vaccines with high immunogenic effect. The goal is to induce an immune response against the encoded antigen. The mRNA is taken up by cells, including dendritic cells, at the injection site. Expressed antigens are then presented to the adaptive immune system leading to selective activation of T cells and B cells that recognize these antigens. These activated adaptive immune cells can then recognize and attack similar antigens that are found on tumors or pathogens.

- ***Immune silent.*** For indications that require no immune stimulation such as protein delivery, our technology can also design product candidates to be immunosilent and to express encoded proteins over an extended period of time. These product candidates can be expressed either locally (eye, liver or lung) or systemically, using the liver as a bioreactor for production of the therapeutic proteins (enzymes and antibodies).

Prophylactic Vaccines

Infectious disease-related proteins, such as viral surface proteins, specific targets for the body's immune defense system, can be expressed by injected mRNA and then presented to B and differentiated T cells, activating a specific immune response. We believe that our mRNA technology offers a platform for the development and production of prophylactic vaccines against infectious diseases. We believe our mRNA vaccines offer many potential advantages over existing vaccine technologies, including:

- mRNA vaccines mimic several aspects of a natural viral infection and has the potential to offer improved and balanced immune response.

- mRNAs allow us to encode for specific protein antigens of choice, offering potential for the development against known and yet unidentified pathogenic threats.

- mRNAs allow production of multivalent vaccines with the potential to either demonstrate a broader efficacy by including additional target pathogens, or to strengthen potential efficacy by better targeting a specific pathogen, for example by adding of immunogenic epitopes, or by addressing different pathogen variants, or both.

- mRNA vaccines are generally expected to be safer than live or attenuated vaccines since no living virus is injected. As they do not interact with the host-cell DNA, they avoid the potential risk of genomic integration posed by DNA-based vaccines.

- mRNA binds to pattern recognition receptors and mRNA vaccines are thereby self-adjuvanting, a property which peptide- and protein-based vaccines lack.

- Rapid speed of development from knowing the sequence of the virus to progressing programs in clinical development given our ability to produce antigens without dedicated cell cultures and fermentation-based manufacturing processes.

- Commercial-scale production of mRNA is fast, cost-effective and, in contrast to traditional vaccine approaches, does not require cell culture or the use of live pathogens, and as a result, multiple vaccines can be produced in the same plant.

Our current approach to the development of potential prophylactic vaccines is focused on:

- ***CV0501 for SARS-CoV-2:*** Our second-generation mRNA vaccine candidate against SARS-CoV-2 is a monovalent construct, applying modified mRNA developed in collaboration with GSK. A Phase 1 study was initiated in August 2022. We reported positive preliminary data in early 2023. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant variants.

- ***Flu SV mRNA for influenza:*** Our second-generation mRNA vaccine candidate against influenza is a monovalent construct, applying modified mRNA developed in collaboration with GSK. A Phase 1 study was initiated in August 2022. We reported positive preliminary data in early 2023. The vaccine candidate for future clinical development is expected to target all four strains recommended by the WHO for influenza vaccines. A P½e 1/2 study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

Oncology

mRNA is a versatile platform for cancer vaccine development allowing to encode a wide range of antigens from full length tumor associated antigens to neoepitopes. We are taking multiple approaches in oncology to induce tumor-specific immune responses in patients:

- ***Novel cancer vaccines:*** We focus on building a meaningful portfolio of novel cancer vaccine candidates based on differentiated antigen discovery technologies and bioinformatics to target antigens that are overexpressed in tumor tissues with no or little expression on healthy tissues, using our LNP formulations. Within this strategy, we follow two approaches. The first approach assesses tumor antigens shared by different cancer patients for the development of off-the-shelf cancer vaccines. The second approach is tailored to the individual tumor setup of a patient for personalized therapy.

  We have demonstrated in a preclinical model that an optimized LNP formulated mRNA vaccine, encoding a TAA, that is also a self-antigen, can induce cellular and anti-tumoral immune responses and single-agent therapeutic activity. These immune responses led to single-agent therapeutic effect in the B16F10 tumor model that does not respond to anti-PD-1 antibodies alone. The therapeutic effect of the vaccine was further enhanced by concomitant systemic anti-PD-1 antibody treatment.
- ***Intratumoral therapy:*** Intratumoral injection of immunostimulating agents into tumors is an alternative to classic vaccination to induce a therapeutic immune response. High concentration of such agents can be achieved by local administration in the tumor tissue with little systemic side effects. Intratumoral immunotherapy activates antigen-presenting cells in the tumor environment and draining lymph nodes to present a broad panel of antigens expressed by the tumor to T and B cells and induce a systemic immune response against the injected tumor as well as non-injected metastatic lesions (abscopal effect).

Molecular Therapy: Deliver mRNA to express the right protein wherever needed

We are seeking to optimize mRNA molecules to trigger production of antibodies. Our antibody work has potential to protect against viruses, bacteria, and toxins and can be applied to many disease indications including cancer, cardiovascular diseases, infectious diseases and autoimmune diseases. In preclinical studies in non-human primates, we have demonstrated that antibodies encoded by mRNA can be produced in hepatocytes very rapidly and can reach the blood stream at relevant therapeutic levels.

With our technology, we can instruct human cells to produce or secrete specific proteins in the nucleus, cytoplasm, cellular organelles or cell membrane. Based on this "healthy" information delivered by mRNA, our cells are designed to produce proteins, which are required to treat the disease caused by missing or inactive proteins.

We believe there are several advantages of our technology applied to development of molecular therapy, including:

- mRNA encoded proteins can function within or outside of cells as well as inside cell membranes, allowing us to address intracellular protein deficiencies that are not addressed by recombinant proteins.

- mRNAs can enable production of complex proteins that are challenging to make using recombinant technologies due to their folding requirements and complexity.

- Administered mRNAs encode proteins using natural pathways allowing for post-translational modifications such as glycosylation whereas recombinant proteins use non-human post-translational modifications which may lead to lower effectiveness and increased immunogenicity.

- mRNA constructs can be optimized to produce proteins that offer desirable pharmacology relative to the wild-type protein, such as increased half-life.

- mRNA allows for dosing flexibility to meet patient needs without causing irreversible changes to the genome.

- mRNA can be delivered repeatedly, creating the opportunity to provide long-term benefit for treatment of chronic diseases.

We currently have collaborations focused on:

- ***Therapeutic antibodies:*** We are also developing mRNA therapies to produce antibodies systemically using the liver as a bioreactor for subsequent secretion and systemic distribution of the antibodies to primary organs affected by a disease. Our collaboration with Genmab, a global leader in antibody discovery and design, will allow us to work with novel antibodies produced using our mRNA technology. This partnership represents the first-ever publicly disclosed mRNA antibody-focused deal and will allow us to optimize and manufacture mRNA-encoded antibodies for Genmab.

- ***Liver diseases:*** We are working on mRNA therapies targeted for the liver, including designing and producing intracellular targets such as transcription factors. Our collaboration with the Hannover Medical School aims to design treatments for liver diseases such as NAFLD, NASH and liver cirrhosis, with the potential to treat or reverse liver fibrosis.

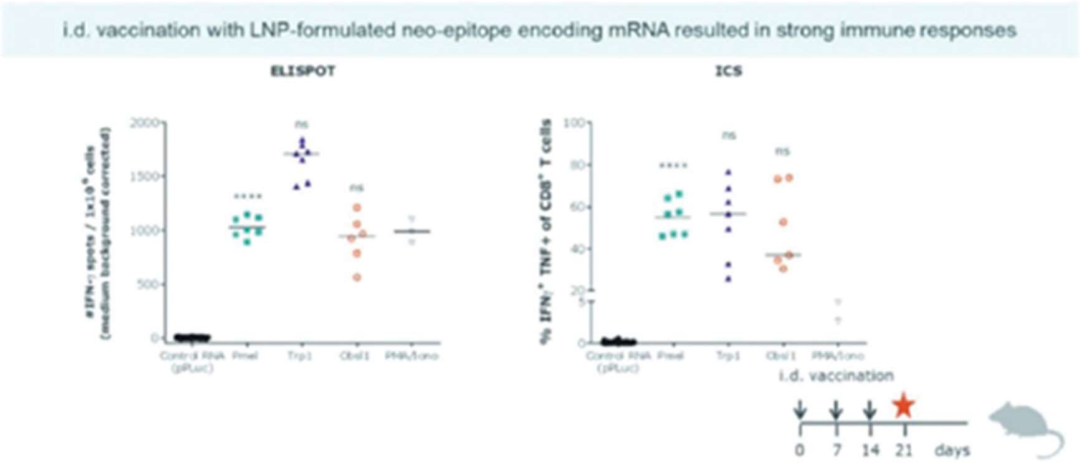
- ***Eye diseases:*** We are investigating development of mRNA-based treatments for undisclosed ophthalmic indications. We have a collaboration with SERI for our discovery efforts.

Our Key Pipeline Candidates

RNA-Based Therapeutics in Oncology

Discovery of new therapeutic cancer vaccine candidates

Our discovery efforts in oncology are focusing on novel mRNA-based therapeutic cancer vaccines candidates. In preclinical studies, we have demonstrated that LNP-formulated vaccines encoding mRNA are able to induce T cell responses against model neoantigens as well as tumor associated self-antigens.



The graphs above demonstrate the induction of antigen-specific T cell responses after intradermal vaccination of mice with LNP-formulated mRNA encoding for selected neoepitopes. Animals vaccinated with LNP-formulated mRNA encoding reporter protein served as negative controls. Stimulation of splenocytes harvested seven days post last vaccination with respective peptides demonstrated strong induction of antigen-specific T cells in Elispot (depicted in the left-hand graph) and FACs analysis (depicted in the right-hand graph).

A key component to the development of new therapeutic cancer vaccine candidates is the build-up of a powerful antigen discovery engine. To gain access to state-of-the-art antigen discovery technologies, we announced a partnership with Belgium-based company myNEO on May 25, 2022, and the acquisition of Netherland-based Frame Cancer Therapeutics on June 8, 2022.

Together with immunotherapy company myNEO, we aim to identify specific antigens found on the surface of tumors for the development of novel mRNA immunotherapies. myNEO utilizes a broad range of underlying genomic alterations to identify constantly emerging, novel classes of antigens of defined tumor types. Incorporating new ranking methodologies based on tumor cell antigen processing and presentation is expected to allow for selection of antigens with the highest confidence of success for potential clinical testing.

With the acquisition of Frame Cancer Therapeutics, a private company focused on advanced genomics and bioinformatics, to identify both shared and unique neoantigens across different cancer types, we complement existing in-house expertise to identify and validate promising antigens for mRNA cancer vaccine candidates. Our technology platform has the potential to identify a broad panel of neoantigens and tumor-associated antigens that go beyond conventional approaches and could strongly increase the likelihood of developing highly effective cancer vaccines that activate the human immune system against cancer.

The field of immuno-therapy has advanced with the progression of available technologies to extract data from patient samples, such as next-generation sequencing. Conventional approaches have so far focused on the exome, the protein-coding part of the genome, which represents only about 1.5% of the total genetic information. More recently, breakthrough developments in sequencing capacity have enabled the extraction of vastly larger amounts of data that allows us to utilize the remaining 98.5% of genetic information. The technologies brought in-house with the acquisition of Frame Cancer Therapeutics are based on whole-genome-sequencing for every patient sample and combine it with short as well as long-range RNA sequencing to map the full inventory of genomic changes. More specifically, downstream of the sequencing, a software package integrates all the data to retrieve the exact changes in the DNA of the tumor cells compared to healthy cells. Correlation of this data with changes in the RNA transcription of the tumor results in entirely new and potentially antigenic tumor antigens that we plan to test as targets for a portfolio of new cancer vaccine candidates. These new antigens are not only entirely foreign to the body but are also uniquely expressed in the tumor and not in healthy tissue. In their foreignness, these constructs are expected to raise stronger immune responses than antigens derived from exome-based conventional approaches.

The highly synergistic antigen discovery technologies of Frame Cancer Therapeutics and myNEO are expected to significantly accelerate CureVac's oncology strategy to build a meaningful portfolio of new cancer vaccine candidates. Within this strategy, we follow two approaches. The first approach assesses tumor antigens shared by different cancer patients for the development of off-the-shelf cancer vaccines. The second approach is tailored to the individual tumor setup of a patient for personalized therapy. We plan to advance new antigens for both approaches based on our second-generation mRNA backbone. To assess the safety and immunogenicity of our second-generation backbone in an oncology setting, we expect to initiate a proof-of-principle study in the second quarter of 2023, assessing an mRNA construct encoding eight epitopes from tumor-associated antigens in patients with surgically resected Glioblastoma Multiforme.

CV8102

CV8102 is the first compound we are developing for treatment of various solid tumors using an intratumoral approach. CV8102 is based on a complex of single stranded non-coding RNA with a polymeric peptide that binds and coats the RNA, protecting it from rapid degradation while also helping to stimulate the immune system.

CV8102 was shown to activate cellular receptors that normally detect viral pathogens entering the cells (such as TLR7, TLR8 and RIG-I pathways). By mimicking a viral infection at the injection site, CV8102 is designed to induce an inflammation that can activate the immune system to reject the tumor. CV8102 was initially developed as a vaccine adjuvant and was shown to enhance the induction of multifunctional CD8 T cell responses and therapeutic activity of peptide vaccines against cancer in preclinical models.

CV8102 is currently in a Phase 1 clinical trial for the intratumoral treatment of four types of solid tumors — cutaneous melanoma, or cMEL, adenoidcystic carcinoma, or ACC, and squamous cell carcinoma of skin, or SCC, as well as squamous cell carcinoma of head and neck, or HNSCC. Enrollment was completed in October 2021, and 98 patients were enrolled, 58 patients in the dose escalation part and 40 patients in a dose expansion part in Melanoma.

Accordingly, 58 patients were enrolled in the dose escalation part: 33 in the single-agent cohort and 25 in the combination cohort with anti-PD-1 antibodies. 40 patients were enrolled in the dose expansion part and treated at the recommended phase 2 dose of 600 µg (10 with single agent CV8102 and 30 in combination with PD-1 antibodies).

Intratumoral CV8102 was observed to be tolerated without dose limiting toxicities, or DLTs, at dose levels up to 600 µg (single-agent and combination). At the 900 µg dose level (single agent) one out of six patients experienced a DLT of Grade 3 increase in the liver enzymes ALT and AST, observed in the context of a Grade 2 cytokine release syndrome. Another patient in this cohort experienced a potentially related Grade 3 immune-mediated pneumonitis that occurred after DLT evaluation period set forth in the protocol.

As of the cutoff date we have observed preliminary evidence of activity with objective tumor responses according to RECIST 1.1:

- In the single-agent cohort 1 complete response (CR) in a melanoma patient
- 2 partial responses (PR) in a melanoma patient and a patient with squamous cell cancer of the skin (cSCC)

In the combination cohort:

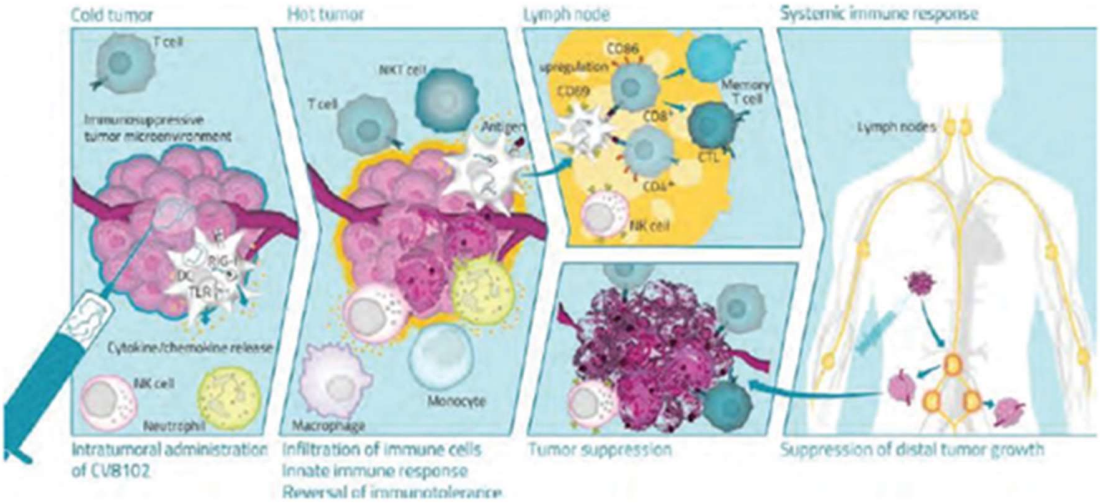
- 2 partial responses (PR) in two melanoma patients.

In February 2021, we initiated the expansion part of our Phase 1 study to confirm the safety, tolerability and efficacy of CV8102 at a 600 µg dose, the selected dose to be advanced in a Phase 2 clinical trial. The expansion part of the Phase 1 trial has enrolled 30 patients with PD-1 refractory melanoma, who receive intratumoral injections of CV8102 in combination with PD-1 antibodies, as well as 10 patients being treated with CV8102 only.

Initially, CV8102, with or without coadministration of anti-PD-1 treatment, was being injected weekly for five weeks, followed by three injections at two- or three-week intervals depending on the anti-PD-1 antibody schedule. Patients showing evidence of clinical benefit were eligible for further injections for up to 12 months.

Mechanism of Action

CV8102 is designed to activate cellular receptors that normally detect viral pathogens entering the cells (such as TLR7, TLR8 and RIG-I pathways) mimicking a viral infection of the tumor. CV8102 is designed to recruit and activate antigen-presenting cells at the site of injection to present tumor antigens released from tumor cells to T cells in the draining lymph node. This potentially leads to activation of tumor-specific T cells, which can kill tumor cells at the injected site, but also at distant non-injected tumor lesions or metastases. Activation of other immune cells like natural killer, or NK, cells at the site of injection may also contribute to the antitumor effect. This mechanism of action is illustrated in the figure below.



In preclinical models, CV8102 was shown to initially activate the innate immune system at the site of injection and the draining lymph node based on increase in number or activation of NK cells, monocytes and plasmacytoid dendritic cells. There was also an increased expression of genes associated with T cell mediated cytotoxicity. These effects were enhanced by concomitant treatment with anti-PD-1 antibodies which also led to increased tumor infiltration by CD8+-T cells.

Market Opportunity

CV8102 is currently being developed against four types of cancers, each frequently exhibiting easily accessible superficial tumor lesions:

- cMEL is an aggressive form of cancer that starts in the pigment-producing cells of the skin and can spread widely to other parts of the body. Cutaneous melanoma accounts for the majority of skin cancer-related deaths in the United States. In 2018, there were approximately 300,000 new cases of cutaneous melanoma and approximately 60,000 deaths worldwide. In the United States, the National Institute of Health, or NIH, estimates approximately 100,000 new diagnoses of cutaneous melanoma, and approximately 7,000 deaths in 2020. According to the National Comprehensive Cancer Network, or NCCN, guidelines, while surgical removal of the tumor is the primary treatment for localized melanoma, for patients with metastatic disease, chemotherapy and targeted therapies including the BRAF inhibitors are also recommended. Based on published literature, the majority of patients treated with BRAF inhibitors develop secondary resistance within a relatively short amount of time. Checkpoint inhibitors are recommended as the first-line treatment for advanced / unresectable metastatic melanoma, but their side effects are severe and a significant subset of patients (approximately 40% to 45%) do not respond to these drugs, and many of those who do respond (approximately 30% to 40%), develop secondary resistance. There are very limited therapeutic options for patients who have failed anti-PD-1 and targeted therapy (if eligible). Intralesional oncolytic virus therapy, or Tvec, is considered for selected cases, but its use is mostly limited to metastatic stage IIIc or M1A disease.

- HNSCC occurs in the outermost surface of the skin or certain tissues within the head and neck region including the throat, mouth, sinuses and nose. Squamous cell carcinoma makes up about 90% of all head and neck cancers. Consumption of tobacco products and alcohol and having a poor diet are important risk factors. HNSCC is the sixth most common cancer worldwide, with 890,000 new cases and 450,000 deaths in 2018. In the United States, according to American Society of Clinical Oncology, or ASCO, approximately 65,000 new cases are diagnosed annually, and more than 14,500 deaths are reported every year. Published literature indicates that more than two-thirds of patients with HNSCC initially present with locoregionally advanced disease (stage III-IV). HNSCC treatment typically involves a combination of chemotherapy, radiation and surgery. According to the Cancer Network and published literature, for patients with early-stage disease, these treatment approaches lead to approximately 60% to 80% response rate. The 5-year progression-free survival, or PFS, rate of advanced HNSCC has continued to remain at 40% to 50% and the average time to relapse is less than 2 years regardless of the combination of various treatment modalities. In patients with advanced disease, more than 50% develop local or regional recurrence and nearly 30% develop distant metastases. Based on the NCCN, the recommended first line treatment for recurrent/metastatic HNSCC include chemotherapy combinations with Cetuximab and anti-PD-1 antibody treatment with or without platinum-based chemotherapy. We believe, based on publications and our analysis, that the typical response rate to anti-PD-1 antibodies in patients with HNSCC is below 20%, and that there is still a significant unmet need.

- ACC is an uncommon form of malignant neoplasm that arises within secretory glands, most commonly the major and minor salivary glands of the head and neck. Other sites of origin include the trachea, lacrimal gland, breast, skin and vulva. ACC accounts for around 10% of all salivary gland neoplasms, 22% of all salivary gland malignancies and about 1% of all head and neck malignancies. The National Cancer Institute, or NCI, estimates that 1,200 patients are diagnosed annually in the United States with ACC and 15,000 patients are affected. Globally, ACC incidence rate is estimated between 0.4 to 13.5 cases per 100,000 annually. The primary treatment of ACC is surgery, which is usually followed by post-operative radiotherapy. According to the American Society of Clinical Oncology, or ASCO, while the 5-year survival of ACC is 89%, 15-year survival is only approximately 40%. For patients with recurrent or advanced/ metastatic disease not amenable to curative intent surgery there is no approved systemic standard treatment. There are minimal options for treatment of advanced ACC, traditional chemotherapy has been proven to be of minimal benefit, so patients often seek clinical trials as a second line option, leading to a high unmet medical need.

- SCC is the second most common form of skin cancer that develops in the squamous cells that make up the middle and outer layers of the skin. While not life-threatening, it can be aggressive and can spread to the other parts of the body, causing serious complications. According to ASCO, in the United States, keratinocyte carcinomas (KC) represent the two most common types of cancer in humans (basal cell carcinoma (BCC); and squamous cell carcinoma (SCC)). KCs are responsible for approximately 3,000 deaths per year in the United States, almost exclusively as a result of SCCs. According to published literature, global incidence varies widely with highest incidence reported in Australia and lowest rates reported in Africa. Given most countries do not have cancer registries for skin cancer, figures reported are likely underestimated. Although most SCC are localized and easily treated, approximately 5% of patients experience local recurrence, approximately 4% develop nodal metastases and approximately 2% die of the disease. According to NCCN, most SCC are managed through different surgical methods, along with topical therapy, cryotherapy and photodynamic therapy. Surgical methods usually lead to good prognosis and cure rates greater than 90%. In the rare case of metastases, radiation therapy, immunotherapy and/or chemotherapy are deployed. Despite the available treatments, 10-year survival rate is less than 20% in patients with locoregional lymph node metastases and less than 10% in the presence of distance metastases, leading to a significant clinical unmet need.

Phase 1 Clinical Trial of Intratumoral CV8102

We initiated a Phase 1 clinical trial of CV8102 for the treatment of various solid tumors in 2017. The Phase 1 clinical trial is evaluating intratumoral administration of CV8102 in patients with advanced melanoma, squamous cell carcinoma of the skin, squamous cell carcinoma of the head and neck, or adenoid cystic carcinoma. Patients receive CV8102 as single-agent or in combination with anti-PD-1 therapy. Patients with advanced inoperable melanoma, cutaneous or head and neck squamous cell or adenoid cystic carcinoma are eligible for single-agent CV8102, and patients with advanced inoperable melanoma and head and neck squamous cell carcinoma indicated for anti-PD-1 therapy or who did not respond or slowly progressed on anti-PD-1 therapy are eligible for the combination. CV8102 is administered for up to eight intratumoral injections into a single accessible tumor lesion over a 12-week period44abellobjectives of this clinical trial include to define the maximum tolerated dose and recommended dose for CV8102 alone and in combination with an anti-PD-1 therapy, and to evaluate safety and tolerability of CV8102 administered alone and in combination with an anti-PD-1 therapy. Secondary endpoints include anti-tumor activity analyses and tumor response assessment.

Key Inclusion Criteria:

- Patients enrolled into single-agent CV8102 dose escalation cohorts must have:
    - histologically confirmed advanced cMEL, SCC, HNSCC or ACC with documented disease progression;
    - not amenable to resection or locoregional radiation therapy with curative intent; and
    - at least 1 line of anti-cancer therapy for advanced disease (except adenoid cystic carcinoma).
- Patients enrolled into CV8102 anti-PD-1 combination cohort must have:
    - histologically confirmed advanced cMEL or HNSCC; and
    - indication for anti-PD-1 therapy or currently receiving anti-PD-1 therapy with stable of slowly progressing disease after at last eight-weeks (HNSCC) or 12 weeks (cMEL) of anti-PD-1.
- Patients enrolled into single-agent CV8102 expansion cohort must have:
    - histologically confirmed advanced cMEL with documented disease progression;
    - not amenable to resection or locoregional radiation therapy with curative intent;
    - progression on/after at least 1 line of anti-cancer therapy for advanced disease; and
    - willing to undergo baseline and post-baseline biopsy of the lesion which is to be injected.

- Patients enrolled into CV8102 anti-PD-1 combination expansion cohort must have:
    - histologically confirmed advanced Stage IIIB-IV cMEL refractory to anti-PD-1 therapy;
    - progression during or after anti-PD-1 therapy with progressive disease according to RECIST 1.1;
    - received a minimum dose of anti-PD-1 mAB (800mg for pembrolizumab or 1200 mg for nivolumab in monotherapy or at least two doses of nivolumab at a minimum dose of 1 mg/kg given every 3 weeks in combination with ipililumab);
    - last anti-PD-1 agent within 12 weeks prior to enrollment;
    - presence of measurable lesion(s) according to RECIST 1.1, not intended for injection; and
    - willing to undergo tumor biopsies at specific time points (baseline and post-baseline biopsy of the injected lesion at selected sites).
- Presence of at least one injectable lesion that is measurable according to RECIST 1.1 criteria.
- Recovered from prior relevant toxicities to grade ≤ 1.
- ECOG PS 0 or 1, 18 years of age or older.

Key Exclusion Criteria:

- Rapidly progressing multifocal metastatic or acutely life-threatening disease;
- Prior use of topical/local TLR-7/8 agonists within the past 6 months;
- Prior anti-cancer therapy administered 2-4 weeks prior to the first dose of the study drug depending on the indication;
- Lesions that are to be injected in previously irradiated areas unless progressive tumor growth has been demonstrated (no prior irradiation of injected lesions on patients with melanoma); or
- Treatment with any investigational anticancer agent within 30 days or 5 half–lives (whichever is longer)prior to the first dose of the study drug or planned during the study.

Primary Endpoints:

- Determine maximum tolerated dose, or MTD, based on occurrence of DLTs within 2 weeks after the first dose and recommended (combination) dose,naïve R(C)D, respectively, for CV8102 alone and with anti-PD-1 therapy.
- Tolerability and safety of CV8102 alone and in combination with anti-PD-1 therapy.

Secondary Endpoints:

- Evaluate anti-tumor activity of CV8102 alone and in combination with anti-PD-1 antibodies per RECIST 1.1 and irRECIST criteria.
- Evaluate duration of response, progression-free survival and disease control rate at 6 months.
- Evaluate tumor response of injected and non-injected lesions.
- Evaluate survival time.

Exploratory Endpoints:

- Evaluate effects on immune parameters and other biomarkers of interest in the peripheral blood.
- Evaluate effects on immune cell infiltration and other biomarkers of interest in tumor biopsy specimen (in selected cohorts during the expansion phase).

Patient Demographics Dose Escalation Part:

In total, 58 patients were enrolled in the dose escalation part: 33 in the single-agent cohort and 25 in the combination cohort with anti-PD-1 antibodies.

In the single-agent cohort, 42% of patients had melanoma, 12% HNSCC, 18% SCC and 27% ACC. 58% of patients were pretreated with anti-PD-1 antibodies and 9% with anti CTLA-4 antibodies.

In the combination cohort, 80% of patients had cMEL and 20% had HNSCC. 88% were pretreated with anti-PD-1 antibodies and 44% with anti CTLA-4 antibodies.

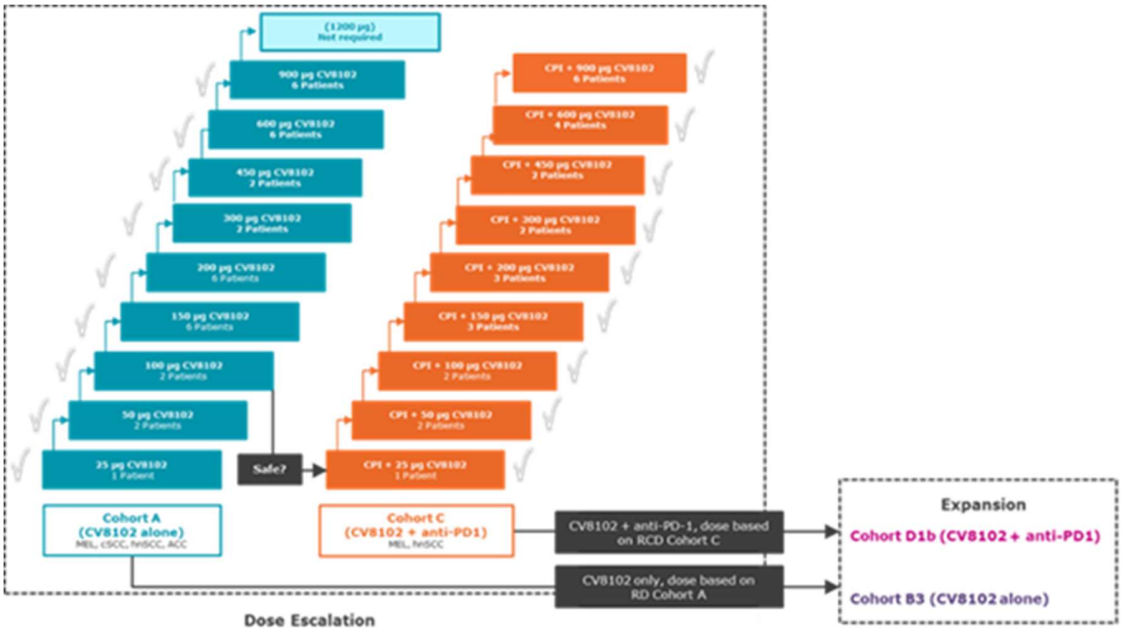
Characteristics	Number of patients (%)		
	Single agent (n=33)	anti-PD-1 combination (n=25)	All (n=58)
Age			
range (yrs)	35-91	36-90	35-91
median (yrs)	69	68	69
Gender			
Male	15 (45)	14 (56)	29 (50)
Female	18 (55)	11 (44)	29 (50)
cMEL			
Stage IIIB	1 (3)	0 (0)	1 (2)
Stage IIIC	4 (12)	5 (20)	9 (16)
Stage IV	9 (27)	15 (60)	24 (41)
HNSCC			
Stage IV	4 (12)	5 (20)	9 (16)
cSCC			
Stage III	1 (3)	0 (0)	1 (2)
Stage IV	5 (15)	0 (0)	5 (9)
ACC			
Stage IV	9 (27)	0 (0)	9 (16)
ECOG PS			
0	17 (52)	18 (72)	35 (60)
1	16 (48)	7 (28)	23 (40)
Pre-treatment with anti-PD-1	19 (58)	22 (88)	41 (71)
Pre-treatment with anti-CTLA4	3 (9)	11 (44)	14 (24)

Percentages presented above have been rounded to the nearest whole number.

CV8102 is administered weekly for the first five cycles and then every two to three weeks for the subsequent cycles for a total of eight injections or until disease progression or death of the patient. In the single-agent cohorts, more than eight injections may be administered should the patient experience a clinical benefit.

Dose escalation of single-agent CV8102 and the combination with anti-PD-1 are running in parallel, with the single-agent cohort being more advanced due to an earlier start of enrollment. We consider a dose level to be safe once it is cleared with monotherapy. This CV8102 dose level is then combined with an anti-PD-1. In parallel, the study continues with the next cohort of the dose escalation monotherapy. Once that higher monotherapy dose is considered safe, combination follows.

Phase 1 Dose Cohorts and Enrollment Status as of January 2022



Phase I trial updates as described above were presented at the ESMO conference in September 2021. Preliminary Biomarker Data were presented at SITC conference in November 2021.

Preliminary Safety Data Dose Escalation

Preliminary safety data:
Treatment emergent AEs occurring in ≥ 10% of patients

AE preferred term	Number of patients with ≥1 TEAE (%)*			
	Single agent (n= 33) DL 25-900 µg	anti-PD-1 combination (n= 25) DL 25-900 µg	All (n= 58)	
			G1/G2	≥ G3
Any Adverse Event	33 (100)	25 (100)	58 (100)	22 (38)
Pyrexia	17 (52)	11 (44)	28 (48)	0 (0)
Fatigue	12 (36)	8 (32)	20 (34)	0 (0)
Chills	6 (18)	10 (40)	16 (28)	0 (0)
Headache	9 (27)	3 (12)	12 (21)	0 (0)
Injection site pain	8 (24)	4 (16)	12 (21)	0 (0)
Nausea	8 (24)	3 (12)	11 (19)	0 (0)
Influenza like illness	7 (21)	2 (8)	9 (16)	0 (0)
Urinary tract infection	4 (12)	5 (20)	9 (16)	1 (2) §
C-reactive protein increased	5 (15)	2 (8)	7 (12)	0 (0)
Injection site erythema	2 (6)	5 (20)	7 (12)	0 (0)
Pain in extremity	4 (12)	3 (12)	7 (12)	0 (0)
Anaemia	5 (15)	2 (8)	6 (10)	2 (3) §
Arthralgia	4 (12)	2 (8)	6 (10)	0 (0)
Asthenia	3 (9)	3 (12)	6 (10)	0 (0)
Decreased appetite	3 (9)	3 (12)	6 (10)	0 (0)

The dose of CV8102 administered either alone or in combination with an anti-PD-1 antibody was escalated up to 900 µg. The MTD was not reached in either cohort, however, due to one DLT and a significant SAE (immune-mediated pneumonitis) after DLT period observed in the 900 µg DL for single agent, a recommended dose/recommended combination dose for the expansion (RD/RCD) of 600 µg was determined in agreement with the DMC for both single agent and combination with an anti-PD-1 antibody.

Adverse events were graded according to the NCI-Common Terminology Criteria for Adverse Events. Grades refer to the severity of the adverse events with unique clinical descriptions of the severity of each AE based on the following general guideline:

Grade 1: Mild; asymptomatic or mild symptoms or clinical or diagnostic observations only or intervention not indicated.

Grade 2: Moderate; minimal, local or non-invasive intervention indicated or limiting age appropriate instrumental activities of daily living.

Grade 3: Severe or medically significant but not immediately life-threatening or hospitalization or prolongation of hospitalization indicated or disabling or limiting self-care activities of daily life.

Grade 4: Life-threatening consequences or urgent intervention indicated.

Grade 5: Death related to adverse event.

- The most frequently reported adverse events occurring in more than 20% of patients were mild to moderate pyrexia, fatigue, chills, headache, injection site pain and nausea.

- 22 patients (38%) experienced treatment emergent ≥ Grade 3 AEs and 7 patients (12%) experienced Grade 3 AEs considered treatment related per investigator's judgment (one of the events fulfilled criteria for dose limiting toxicities per protocol). There were no Grade 4 or 5 AEs considered related to study treatment.

- In the single-agent CV8102 cohort, four patients experienced transient Grade 3 elevations of liver enzymes (1 at 150 µg dose level, 2 at 200 µg dose level and one at the 900 µg dose level, the latter fulfilled DLT criteria per protocol, because it occurred within one week after the second injection). One patient in the 900 µg cohort experienced an immune mediated Grade 3 pneumonitis and was recovering on steroid treatment approximately one week later. The patient had already experienced a previous episode of Grade 1 pneumonitis that may have been related to previous treatment with anti-PD-1 antibodies prior to study enrollment.

- In the combination cohort of CV8102 with anti-PD-1 antibodies, one patient (100 µg dose level) experienced Grade 3 hypertension, mild chills, fever and tachycardia on day of administration of CV8102 and anti-PD-1 requiring inpatient observation (SAE) and transient asymptomatic Grade 3 elevation of serum lipase. One patient (100 µg dose level) experienced transient asymptomatic Grade 3 elevation of serum amylase.

Treatment Related Serious Adverse Effects (SAEs)

- In the single agent CV8102 cohort one patient experienced Grade 2 CRP increase (150µg dose level), one patient experienced Grade 2 tumor pain (200 µg dose level), one patient experienced Grade 1 chills, pyrexia and vomiting and an episode of Grade 2 pyrexia (300 µg dose level), one patient experienced a Grade 2 cytokine release syndrome (900 µg dose level) and one patient a Grade 3 immune-mediated pneumonitis (900 µg dose level).

- In the combination cohort of CV8102 with anti-PD-1 antibodies, one patient required inpatient observation after Grade 3 hypertension, mild chills, fever and tachycardia (100 µg dose level), one patient experienced Grade 2 cytokine release syndrome (300 µg dose level), one patient a Grade 1 cytokine release syndrome (600 µg dose level) and one patient a Grade 1 cytokine release syndrome (900 µg dose level).

Preliminary Efficacy Data

Tumor responses were assessed according to Response Evaluation Criteria in Solid Tumors, or RECIST 1.1. The overall response evaluation according to RECIST 1.1 integrates changes in both measurable and non-measurable tumor lesions that can be assessed by radiographic imagining (CT or MRI) or clinical examination (documented by photographs). Assessment was performed by the investigators at baseline and at defined time points during the study period. Responses per RECIST 1.1 criteria are defined as follows:

- A CR is the disappearance of all tumor lesions that were present before start of treatment without appearance of new lesions.

- A PR is a ≥ 30% decrease in the sum of diameters of specified tumor lesions (called target lesions) taking as reference the baseline sum diameters without progression or disappearance of the other lesions and without appearance of new lesions or CR of target lesions without disappearance of other lesions but without progression or appearance of new lesions.

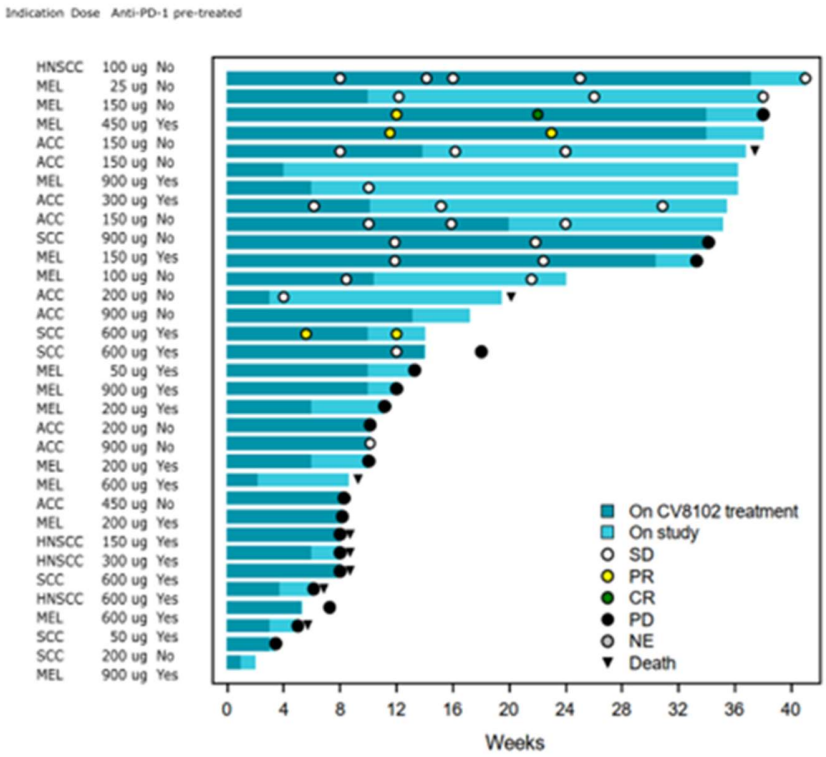
- Progressive disease, or PD, indicates a ≥ 20% increase in the sum of diameters of specified tumor lesions (called target lesions) (taking as reference the smallest sum of diameters while on study) and at least a 5 mm increase and/or an unequivocal progression of existing further lesions (called nontarget lesions) or appearance of new lesions.

- Stable disease indicates there is neither sufficient shrinkage nor increase in size of tumor lesions to declare PR or PD and no appearance of new lesions.

The tables below show duration of treatment, response and time to progression of individual patients enrolled in the trial.

Preliminary data on overall tumor response and duration according to RECIST 1.1

Preliminary efficacy data for single-agent CV8102

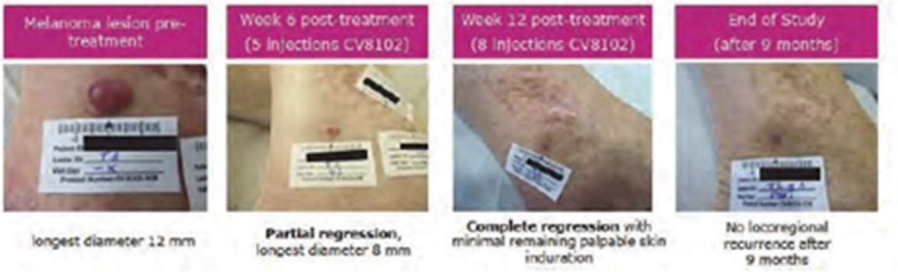


One patient showed a CR and two patients showed a PR according to RECIST 1.1 after single-agent CV8102. In addition, 12 patients experienced a best response of stable disease after eight weeks of treatment (associated with shrinkage of non-injected lesion in one patient, shrinkage of injected lesion in one patient and shrinkage of both the non-injected and injected lesions in one patient). Nine of the 33 (27%) patients treated with single-agent CV8102 remained free of progression for more than six months.

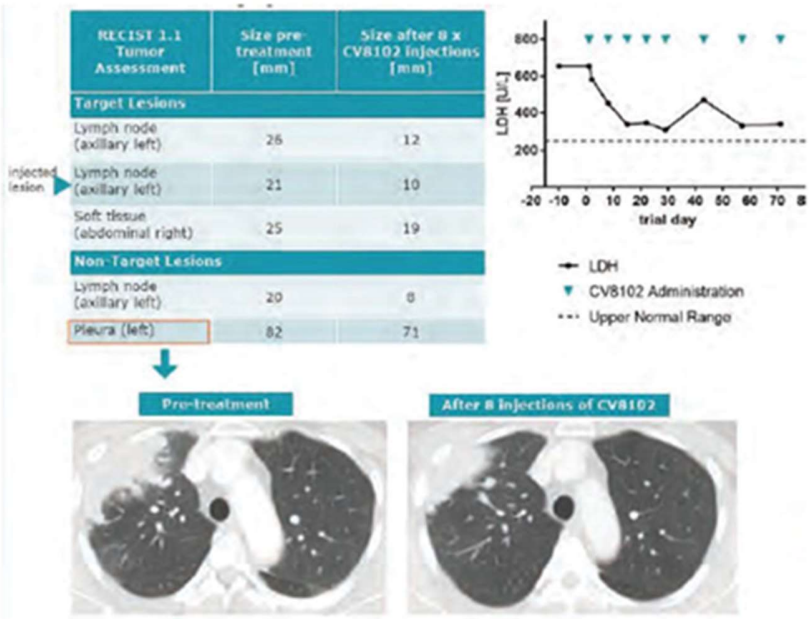
Single-agent Response Data

Case reports of patients with observed tumor shrinkage after single-agent CV8102:

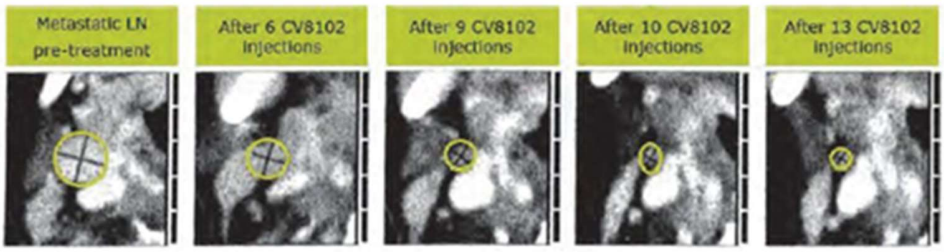
- A 74-year-old female patient with Stage IIIc melanoma and multifocal in-transit metastases was treated with single-agent CV8102 (150 µg). The pictures below show the injected primary tumor before treatment, after first five weekly injections, and after eight injections at 12 weeks. After the first five injections, a partial regression of the injected lesion became apparent, which turned into a complete regression after eight injections (12 weeks). An MRI scan showed a complete regression of all non-injected in-transit metastases. The response data together represent a confirmed complete response based on RECIST 1.1 criteria. The patient continued to receive injections at monthly intervals for up to nine months without locoregional recurrence but there was occurrence of a new intra-abdominal soft tissue lesion.



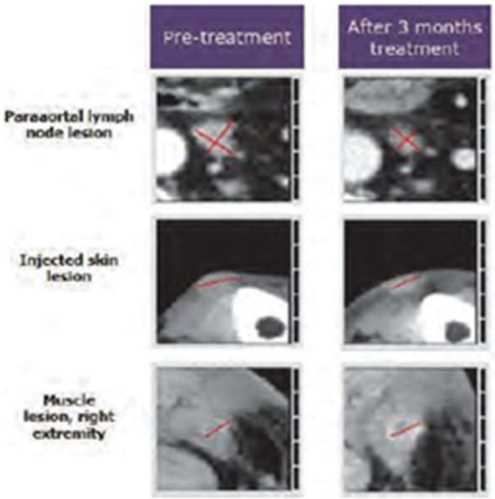
- A 50-year-old female patient with Stage IV melanoma, metastases in ipsilateral supraclavicular lymph nodes and distant detectable metastases at study entry was treated with single-agent CV8102 (450 µg). The patient previously experienced early tumor progression on adjuvant treatment with Nivolumab and subsequently underwent multiple resections of cutaneous and lymph node metastases and radiation prior to study entry. The patient received eight intratumoral injections of CV8102 into an axillary lymph node metastasis. After an early decrease in serum LDH she developed a partial response. Treatment with CV8102 was ongoing as of April 2020. The table below shows the decrease in the size of measurable tumor lesions after eight intratumoral injections of CV8102. The CT scan shows the decrease in size of the non-injected metastatic pleural lesion. The graph shows the decrease in serum LDH over time during the treatment period.



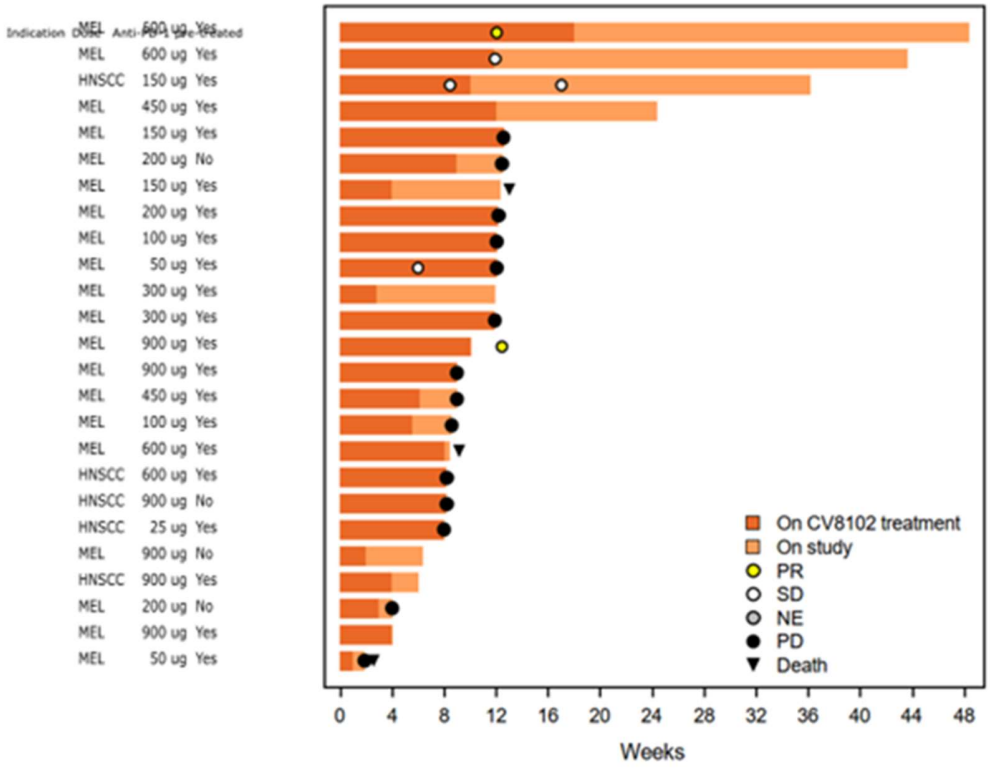
- A 91-year-old male patient with Stage IV HNSCC with large buccal and small lip lesion and a contralateral metastatic cervical lymph node was treated with single-agent CV8102 (100 µg) after pretreatments with cetuximab, external beam radiation and multiple surgeries. The patient experienced prolonged stable disease according to RECIST 1.1 until the end of study after nine months. Whereas the injected buccal lesion remained stable in size, the non-injected contralateral metastatic lymph node showed ongoing regression.



- A 64-year-old male patient with Stage IV melanoma (150 µg dose level, single-agent CV8102) who had progressed on previous anti-PD-1 antibody treatment experienced stable disease according to RECIST 1.1 for six months, with shrinkage of the injected lesion in the skin, and shrinkage of a non-injected contralateral paraaortic lymph node lesion.



Preliminary efficacy data in combination with PD-1 antibodies



As of June 21, 2021, two patients with PD-1 refractory melanoma showed a partial response according to RECIST 1.1 in the combination cohort.

One PD-1 refractory HNSCC patient experienced stable disease according to RECIST 1.1. The following salvage tumor resection due to persistent tumor hemorrhage 11 weeks after last dose which included the area of injected lesion showed a complete response within the histopathological results with no tumor cells detected.

One PD-1 refractory melanoma patient experienced stable disease after the eight-week treatment period with regression of the injected and some non-injected lesions, while other non-injected lesions showed progression.

The number of treated patients and follow-up time in this cohort were more limited as compared to the single-agent cohort. The patient population was also more heavily pretreated compared to the patients enrolled in the single-agent cohort (88% vs. 58% were pretreated with anti-PD-1 antibodies and 44% vs. 9% with anti-CTLA-4 antibodies).

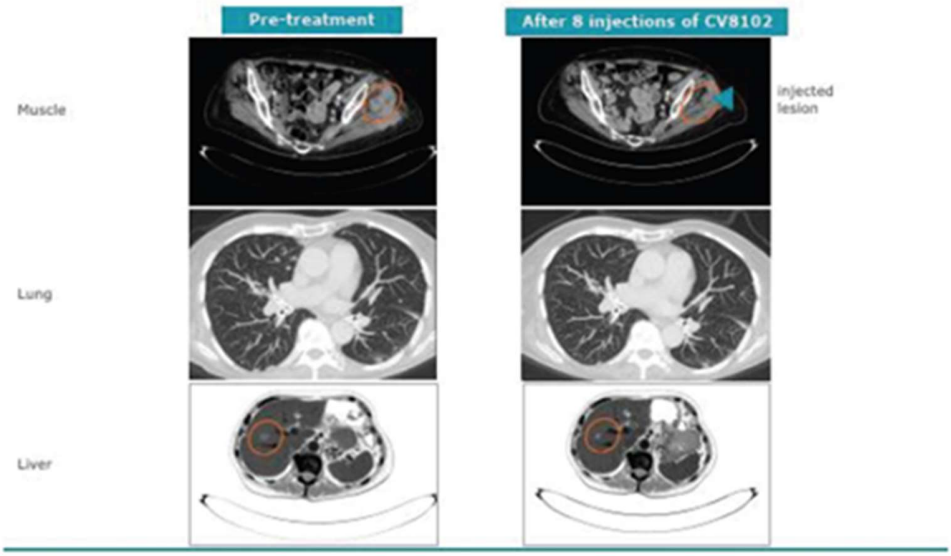
Combination response data:

- A 90-year-old female patient with Stage IVc melanoma and metastatic lesions in the lung and liver was treated with eight intratumoral injections of CV8102 (600 µg) in combination with the anti-PD-1 antibody Pembrolizumab.

- The patient was pretreated with Nivolumab in combination with Ipilimumab followed by Nivolumab monotherapy that resulted in progressive disease four months prior to study entry.

- After eight injections, the patient showed a partial response according to RECIST 1.1 with regression of the injected lesion in a muscle and multiple non-injected lung and liver lesions.

RECIST 1.1 Tumor Assessment	Size pre-treatment [mm]	Size after 8 x CV8102 injections [mm]
Target Lesions		
Muscle	31.4	19.8
Lung	6.4	4
Lung	6.8	0
Liver	18.4	10.1



- An 84-year old male patient with stage IV melanoma was treated with eight intratumoral injections of CV8102 (900 µg) in combination with the anti-PD-1 antibody Nivolumab. The patient was pretreated with Nivolumab resulting in progressive disease prior to study entry. After eight injections, the patient showed a partial response according to RECIST 1.1 with regression of injected and non-injected lesions.

Expanded Phase 1 Clinical Trial of Intratumoral CV8102

In February 2021, we initiated the expansion of our Phase 1 study to confirm the safety, tolerability and efficacy of CV8102 at a 600 µg dose, the selected dose to be advanced in a Phase 2 clinical trial. Furthermore, the expansion part of the Phase 1 trial evaluated the effects of CV8102 on systemic and intratumoral immune markers, which will provide additional clinical insights on CV8102's mode of action.

The expansion part of the Phase 1 trial enrolled 30 patients with PD-1 refractory melanoma, who received intratumoral injections of CV8102 in combination with PD-1 antibodies, as well as 10 patients being treated with CV8102 only. Initially, CV8102, with or without coadministration of anti-PD-1 treatment was injected weekly for five weeks, followed by three injections at two- or three-week intervals depending on the anti-PD-1 antibody schedule. Patients showing evidence of clinical benefit were eligible for further injections for up to 12 months.

Patient Demographics Dose Expansion Part as of June 15, 2022

Characteristics	Number of patients (%)		
	Single agent (n=10)	anti-PD-1 combination (n=30)	All (n=40)
Age			
range (yrs)	34 - 83	35 - 86	34 - 86
median (yrs)	73	61	63
Gender			
Male	7 (70)	18 (60)	25 (63)
Female	3 (30)	12 (40)	15 (38)
Melanoma Stage			
IIIC	0 (0)	4 (13)	4 (10)
IIID	1 (10)	1 (3)	2 (5)
IV	9 (90)	25 (83)	34 (85)
ECOG PS			
0	7 (70)	19 (63)	26 (65)
1	3 (30)	11 (37)	14 (35)
Pre-treatment with anti-PD-1	10 (100)	30 (100)	40 (100)
Pre-treatment with anti-CTLA-4	5 (50)	12 (40)	17 (43)

Due to rounding, percentages presented above may not add up precisely to 100%.

As of June 15, 2022:

- In the single-agent cohort: 100% of patients were pretreated with anti-PD-1 antibodies and 50% with anti-CTLA-4 antibodies.

- In the combination cohort: 100 % of patients were pretreated with anti-PD-1 antibodies and 40% with anti-CTLA-4 antibodies.

Preliminary Safety Data Dose Expansion

Preliminary safety data:

Treatment emergent AEs occurring in ≥ 10% of patients, as of August 18, 2022

AE preferred term	Number of patients with ≥1 TEAE (%)*			
	Single agent (n= 10)	anti-PD-1 combination (n= 30)	All (n= 40)	
			G1/G2	≥ G3
Any Adverse Event	10 (100)	21 (70)	31 (78)	10 (25)
Pyrexia	7 (70)	13 (43)	20 (50)	1 (3)
Chills	6 (60)	11 (37)	17 (43)	0 (0)
Asthenia	1 (10)	6 (20)	7 (18)	0 (0)
Nausea	1 (10)	6 (20)	7 (18)	0 (0)
Anaemia	2 (20)	3 (10)	5 (13)	1 (3) §
Headache	0 (0)	5 (17)	5 (13)	0 (0)
Influenza like illness	0 (0)	5 (17)	5 (13)	0 (0)
Tumour pain	4 (40)	1 (3)	5 (13)	1 (3)
Diarrhoea	1 (10)	3 (10)	4 (10)	0 (0)
Injection site pain	1 (10)	3 (10)	4 (10)	0 (0)

§ assessed as unrelated by investigator

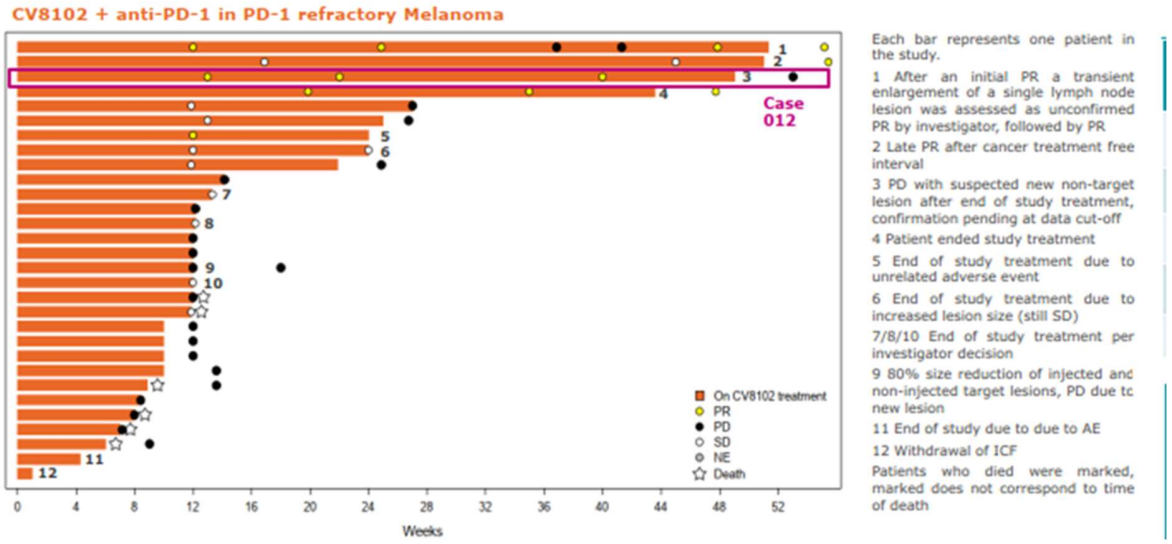
- **≥ Grade 3 AEs considered treatment related per investigator's judgement occurred in 3 (8%) patients (no G4 and G5 AEs):**
  - **Single agent:** Two G3 episodes of worsening of tumor pain were reported in one patient
  - **Combination with anti-PD-1:** Three episodes of fever G3 (1 patient) and G3 elevation of blood pressure (1 patient, not shown in the table)
- **Treatment related SAEs per investigator's judgement** (these events required inpatient observation):
  - **Single agent:** Chills G1, Chills G2, G1 Fever, G2 Fever and worsening of tumor pain (one episode G2 and two episodes of G3) – all occurred in one patient
  - **Combination with anti-PD-1:** G1 CRS (2 patients), G1 chills (1 patient), G1 Fever (1 patient)

Adverse events were graded according to the NCI-Common Terminology Criteria for Adverse Events. Grades refer to the severity of the adverse events with unique clinical descriptions of the severity of each AE.

As of August 18, 2022:

- The most frequently reported adverse events occurring in more than 20% of patients were mild to moderate pyrexia and chills.
- 10 patients (25%) experienced treatment emergent ≥ Grade 3 AEs and 3 patients (8%) experienced Grade 3 AEs considered treatment related per investigator's judgment (G3 worsening tumor pain (1 patient) in the single agent cohort, G3 fever (1 patient) and G3 elevation in blood pressure (1 patient) in the combination cohort.
- There were no Grade 4 or Grade 5 AEs considered related to study treatment.
- In the single agent cohort: 1 patient experienced multiple AEs requiring inpatient observation (G2 chills, G2 fever and worsening tumor pain G3).
- In the combination cohort: 2 patients experienced SAEs of G1 CRS, 1 patient G1 chills and 1 patient G1 Fever, all requiring inpatient observation.

- **Preliminary efficacy data dose expansion**



Best Overall Response per RECIST 1.1 in patients with PD-1 refractory Melanoma

Response	Single agent (n=10) (%)	anti-PD-1 combination (n=30) (%)
CR	0 (0)	0 (0)
PR	0 (0)	5 (17)
SD	2 (20)	8 (27)
PD	8 (80)	15 (50)
NE	0 (0)	2 (7)

As of August 18, 2022, five (17%) patients with PD-1 refractory melanoma showed a partial response according to RECIST 1.1 in the combination cohort and 8 patients (27%) stable disease. In the single agent cohort, no objective responses were observed and 2 patients (20%) experienced stable disease.

Safety data in the expansion cohort confirmed the acceptable safety profile of CV8102 at the recommended dose as single agent and in combination with anti-PD1 antibodies. CV8102 showed preliminary efficacy in combination with anti-PD-1 antibodies in patients with PD-1 refractory melanoma.

mRNA-Based Prophylactic Vaccine Programs Jointly Developed With GSK: Second-Generation mRNA Backbone

COVID-19: Disease Overview

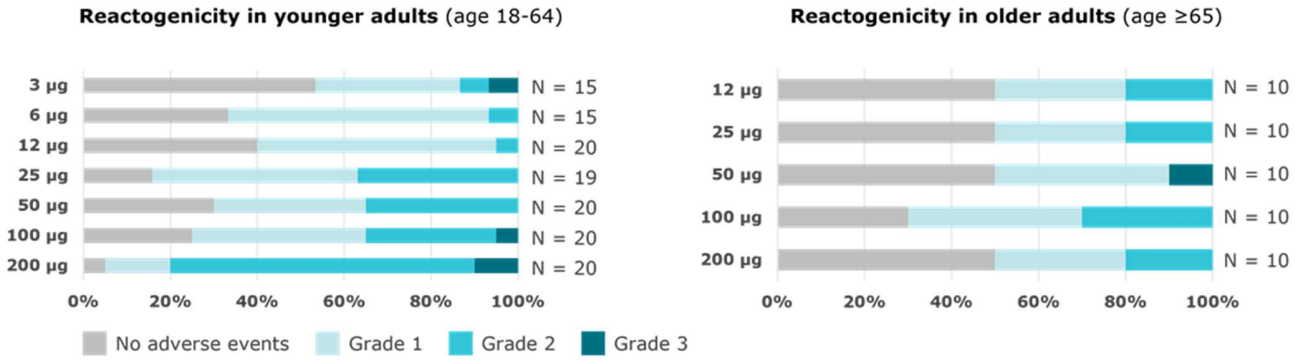
Coronaviruses are a family of viruses that can lead to respiratory illness, including Middle East Respiratory Syndrome, or MERS-CoV, and Severe Acute Respiratory Syndrome, or SARS-CoV. Coronaviruses are transmitted between animals and people and can evolve into strains not previously identified in humans. On January 7, 2020, a novel coronavirus (2019-nCoV) was identified as the cause of pneumonia cases and deaths in Wuhan, China and an exponentially increasing number of cases have since then been found worldwide. On March 11, 2020, the World Health Organization ("WHO") designated COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, an international pandemic. As of April 12, 2023 there have been 762,791,152 confirmed cases of COVID-19 globally, including 6,897,025 deaths, reported to WHO.

Clinical COVID-19 Vaccines Program (second-generation mRNA backbone)

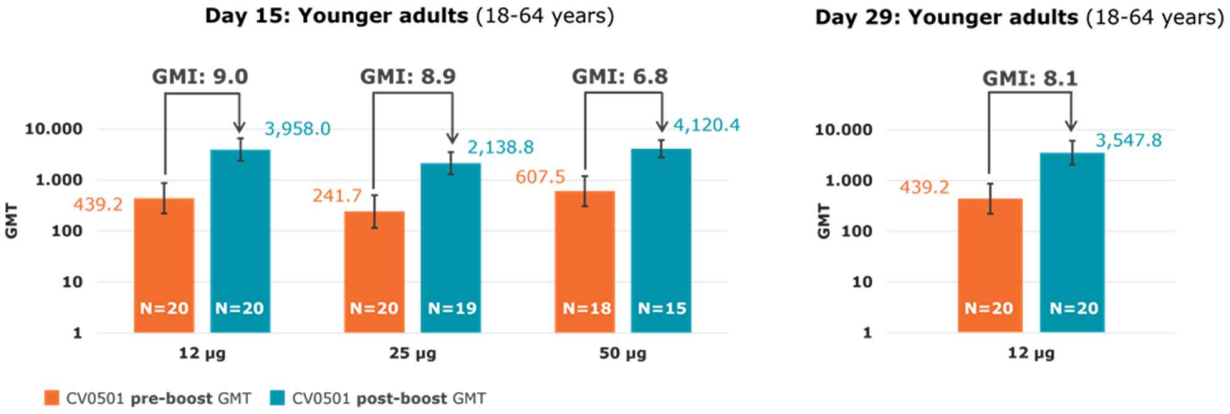
In February 2021, we announced a new collaboration with GSK for our COVID-19 vaccine program, which went into effect in April 2021 pursuant to which we are collaborating with GSK to research, develop and manufacture mRNA vaccines based on our second-generation mRNA backbone targeting the original SARS-CoV-2 strain as well as emerging variants. The second-generation mRNA backbone can flexibly encode for different COVID-19 variants and features targeted optimizations designed to improve intracellular mRNA stability and translation for increased and extended protein expression. The optimizations potentially allow for strong and early immune responses at low doses, which will also support the development of multivalent vaccines to target rapidly spreading COVID-19 variants as well as combination vaccine approaches. The second-generation mRNA backbone differs significantly from the mRNA backbone for our first-generation. The first candidate from the second-generation backbone COVID-19 program was the non-chemically modified mRNA construct CV2CoV. The start of a Phase 1 clinical trial with CV2CoV was announced on March 30, 2022. The Phase 1 dose-escalation study is being conducted at clinical sites in the United States and evaluates the safety, reactogenicity and immunogenicity of a single booster dose of CV2CoV in the dose range of 2µg to 20µg. Within the jointly developed COVID-19 vaccine program, we also extended our technology platform to chemically modified mRNA constructs to allow for data-driven selection of the best candidate. The first chemically modified construct from the second-generation backbone COVID-19 program is CV0501. We announced the start of a Phase 1 clinical trial with CV0501 on August 18, 2022. CV0501 specifically targets the Omicron BA.1 variant. The study is being conducted at clinical sites in the United States, Australia and the Philippines and evaluates the safety, reactogenicity and immunogenicity of a single booster dose of CV0501 in the dose range of 3µg to 200µg. On January 6, 2023 we announced that the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the COVID-19 program.

CV0501: Preliminary Phase 1 Data of the Chemically Modified Construct Encoding the BA.1 Variant

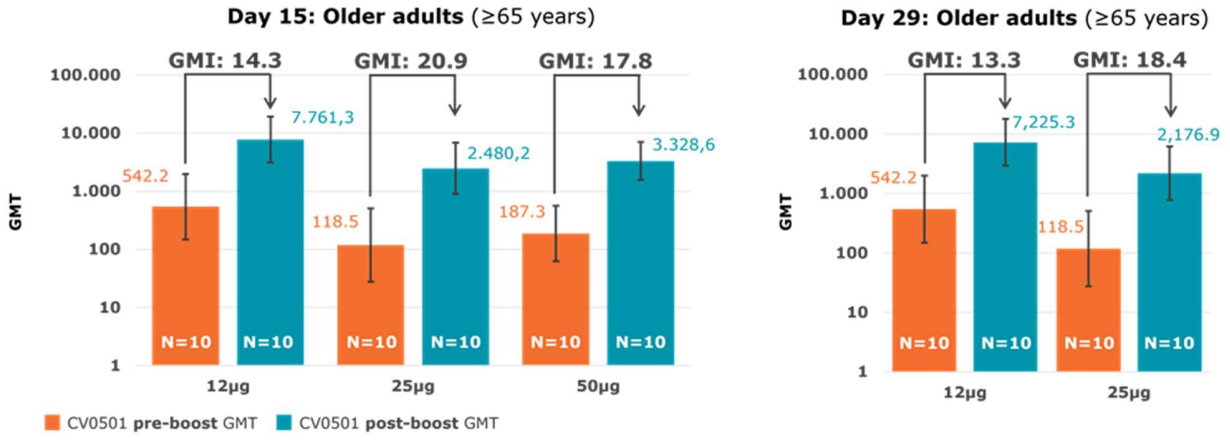
In January and April 2023, we announced positive preliminary data from the CV0501 Phase 1 trial. The data are based on cohort sizes of up to 20 participants in the younger adults age group (age 18-64) and 10 participants in the older adults age group (age ≥65). Reported preliminary safety data cover the fully recruited dose groups of 3, 6, 12, 25, 50, 100 and 200µg in the younger adult age group and 12, 25, 50, 100 and 200µg in the older adult age group. The data illustrated below show solicited adverse events in younger and older adults within seven days after booster vaccination ranging in severity from no adverse events (grey bars) to grade 3 or severe adverse events (dark blue bars) from left to right. The data demonstrate that for younger adults CV0501 reactogenicity remains acceptable from 3 to 100µg with one systemic grade 3 adverse event at 3µg, which was reported as fatigue and one systemic grade 3 adverse event at 100µg, which was reported as a headache. At the highest dose of 200µg, two local grade 3 adverse events occurred, both reported as redness at the injection site. In older adults, one systemic grade three adverse event occurred, reported as a headache in the 50µg dose group. The preliminary data confirm that CV0501 was generally well tolerated across both age groups and all dose levels.



Preliminary immunogenicity data in both age groups showed relevant titers of neutralizing antibodies beginning at the lowest tested dose. Shown below are the available geometric mean titers (GMT) of neutralizing antibodies induced by CV0501 in younger adults as a function of dose against the Omicron BA.1 variant. The orange bars represent antibody titers before the booster vaccination and the blue bars represent antibody titers either on day 15 or on day 29 after the booster vaccination. All GMTs were measured with a pseudo-virus neutralization assay. Across the displayed dose levels of 12, 25 and 50µg on day 15 and at 12µg on day 29, CV0501 induced a substantial antibody increase from pre- to post-boost titers. This antibody boost is further quantified for each dose group as the ratio of post- to pre-boost titers. This so-called geometric mean increase (GMI) is indicated above the orange and blue bars. It represents the most meaningful metric to assess the potential of CV0501 as a booster vaccine against a tested variant. Depending on the dose and day, the GMI ranges between a 6.8- and a 9-fold increase of antibody titers.



Neutralizing antibody titers induced by CV0501 in older adults led to even higher GMIs as illustrated in the graph below. Comparison of the lowest 12µg dose groups in younger and older adults demonstrates a ratio of post-boost to pre-boost serum neutralizing titers against the Omicron BA.1 variant of 8.1. in younger adults and 13.3 in older adults.



Preliminary immunogenicity data for additional dose groups are summarized in the table below.

GMI against BA.1, both age groups, Day 15 and 29
(Younger adults 18-64, older adults ≥65)

Dose	Day 15	Day 29
3 µg (only YA)	4.8 (n=15)	n/a
6 µg (only YA)	3.3 (n=14)	n/a
12 µg	10.5 (n=30)	9.5 (n=30)
25 µg	11.1 (n=29)	10.5 (n=28)
50 µg	12.1 (n=30)	10.6 (n=30)
100 µg	12.4 (n=29)	11.4 (n=26)
200 µg	21.8 (n=26)	14.6 (n=18)

The data read-out for both age groups are currently being finalized. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant variants. A pivotal Phase 3 trial may be initiated in 2024, contingent on discussion with regulatory authorities.

Influenza: Disease Overview

Influenza is a highly contagious virus that causes mild to severe respiratory virus that can lead to death. According to the CDC, since the emergence of SARS-CoV-2, influenza activity has been lower than observed before the pandemic. During the 2021-2022 influenza season influenza was associated with 9 million illnesses, 4 million medical visits, 10,000 hospitalizations and 5,000 deaths in the United States. Preliminary in-season burden estimates for the U.S. in the 2022-2023 flu season showed 26-51 million flu illnesses, 12-24 million flu medical visits, 290,000-630,000 flu hospitalizations and 19,000-56,000 flu deaths. The WHO reports that globally there are as many as five million severe influenza cases annually, leading to as many as 290,000 to 650,000 deaths.

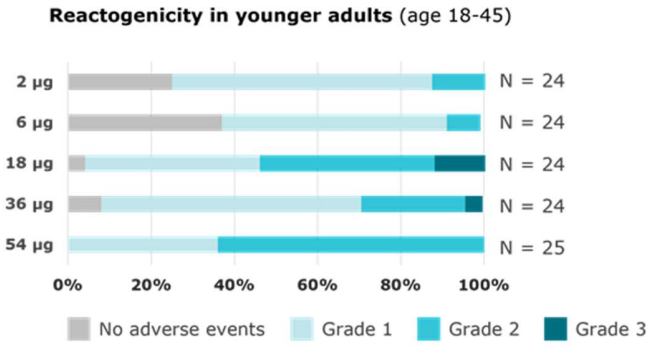
Influenza viral infections can be prevented by vaccination although there are several limitations associated with current flu vaccines. Flu vaccines are not always effective, primarily because the influenza virus and its associated antigens undergo mutations or changes in its sequence over short periods of time, which is called antigenic drift. Vaccines that are developed for the predominant strain infecting people can be rendered ineffective as the virus mutates as it passes from person to person. The process of developing a standard traditional vaccine typically takes approximately eight months from strain identification to doctor’s office availability, increasing the likelihood that a significant pool of viruses circulating will be poorly recognized by antibodies in vaccinated individuals. Additionally, vaccine efficacy tends to wane over time. For these reasons, vaccination of the target population needs to be repeated every year before the start of the next influenza season, putting a significant burden on the health system. Furthermore, only a part of the population targeted to get the yearly shot is vaccinated each year, leaving many individuals unprotected.

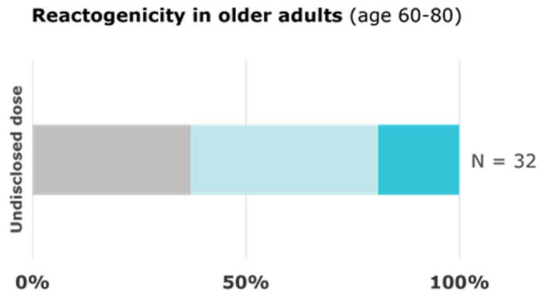
Clinical Influenza Vaccines Program (second-generation mRNA backbone)

Influenza is the first indication from the initial collaboration we started with GSK in July 2020, which focuses on the development of new products for different targets in the field of infectious diseases. The jointly developed influenza vaccine candidates are based on our second-generation mRNA backbone, which can flexibly encode for different influenza strains and which features targeted optimizations designed to improve intracellular mRNA stability and translation for increased and extended protein expression. The optimizations potentially allow for strong and early immune responses at low doses, which will also support the state-of-the-art multivalent format of influenza vaccines as well as combination vaccine approaches. The second-generation mRNA backbone differs significantly from the mRNA backbone for our first-generation. The first candidate from the second-generation backbone influenza program was the non-chemically modified mRNA construct CVSQIV, a differentiated multivalent vaccine candidate featuring multiple non-chemically modified mRNA constructs to induce immune responses against relevant targets of four different influenza strains. On February 10, 2022, we announced the start of a Phase 1 dose-escalation study in Panama evaluating the safety, reactogenicity and immunogenicity of CVSQIV in the dose range of 3µg to 28µg. Preliminary safety data reported on April 28, 2022, showed a benign reactogenicity profile across the tested dose groups. Within the jointly developed COVID-19 vaccine program, we also extended our technology platform to chemically modified mRNA constructs to allow for data-driven selection of the best candidate. We announced the start of a Phase 1 dose-escalation study with a chemically modified influenza vaccine candidate, Flu SV mRNA, on August 18, 2022. The candidate is a monovalent candidate. The Phase 1 dose-escalation study is being conducted in Canada, Spain and Belgium to evaluate the safety, reactogenicity and immunogenicity of Flu SV mRNA. On January 6, 2023 we announced that the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the influenza program.

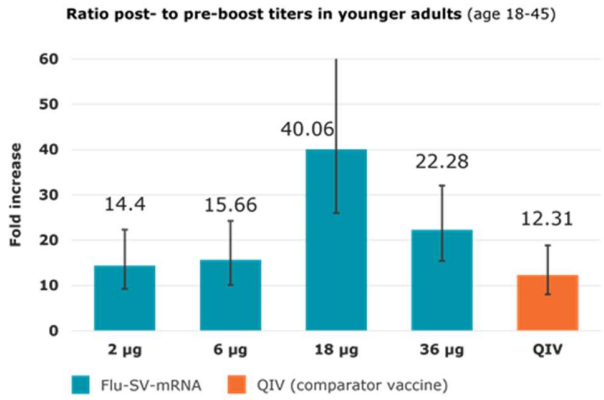
Flu SV mRNA: Preliminary Phase 1 Data of the Chemically Modified Construct Expressing an H1N1 hemagglutinin antigen

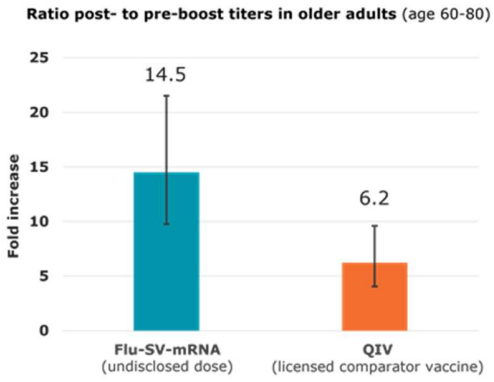
On January 6, 2023, the second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the seasonal flu vaccine program. In the Phase 1 study of the monovalent Flu-SV-mRNA, expressing an H1N1 hemagglutinin antigen (subtype of influenza A), five doses ranging from 2 to 54µg with up to 25 subjects per dose cohort were evaluated in younger adults (age 18-45). This dose range takes into account that the candidate is a monovalent construct. Correspondingly, the applied doses reflect doses for a single mRNA construct, which would later be multiplied for a state-of-the-art multivalent flu vaccine. In the younger adult age group, the preliminary safety and reactogenicity data shown below demonstrate that the monovalent Flu-SV-mRNA candidate was generally well tolerated with no safety concerns observed to date across all tested dose levels. A single dose of Flu-SV-mRNA (dose level undisclosed) was assessed for safety and reactogenicity in older adults (age 60-80) and was also observed to be safe and well tolerated with no grade 3 adverse events in the 32 subjects who were administered the mRNA construct.



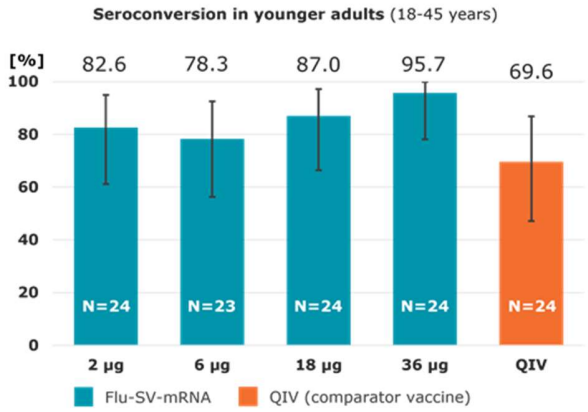


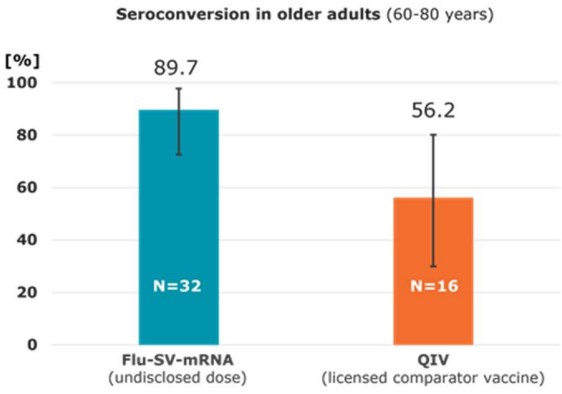
Immunogenicity of the monovalent Flu-SV-mRNA construct was assessed in parallel with a licensed seasonal flu vaccine comparator in both age groups, shown as the orange bar to the right in the figures below. The data illustrate the ratio of post- to pre-boost geometric mean hemagglutinin inhibition antibody titers. In younger adults, Flu-SV-mRNA achieved comparable antibody increases to the licensed vaccine, boosting geometric mean titers at least about 14-fold beginning at the lowest dose of 2µg. In older adults a comparable ratio of post- to pre-boost titers of 14.5 was achieved at the undisclosed dose, which compares to a ratio of 6.2 for the flu vaccine comparator.





The robust preliminary ratios of post- to pre-boost geometric mean hemagglutinin inhibition antibody titers were shown to result in seroconversion rates that are substantially higher for the modified mRNA candidate. Specifically in the older adults age group, the percentage of subjects achieving seroconversion was 89.7% for Flu-SV-mRNA and 56.2% for the licensed flu vaccine comparator.





Interim data support the progression of the modified second-generation mRNA technology for the development of a multivalent mRNA flu vaccine. The vaccine candidate for future clinical development is expected to target all four strains recommended by the WHO for influenza vaccines. ½hase 1/2 study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

Preclinical COVID-19 Vaccines Program (second-generation mRNA backbone)

CV2CoV: Preclinical Data of the Non-Chemically Modified Construct Encoding the Original Virus

CV2CoV encodes the prefusion stabilized full-length spike protein of the original SARS-CoV-2 virus formulated within Lipid Nanoparticles, or LNPs. On May 13, 2021, we announced that CV2CoV is able to induce high levels of antigen production in an *in vitro* setup as well as strong and dose-dependent immune responses in a preclinical study in rats. These data were complemented in June, 2021, by preclinical data published in Nature Communications demonstrating full protection by CV2CoV and CVnCoV from lethal infection caused by SARS-CoV-2 ancestral strain BavPat1 or the Beta variant (B.1.351) in a transgenic mouse model. On August 16, 2021, we announced availability of a preprint manuscript with preclinical data investigating immune responses as well as the protective efficacy of CV2CoV in comparison to first-generation vaccine candidate, CVnCoV, against SARS-CoV-2 challenge in non-human primates. The study, conducted in collaboration with Dan Barouch, MD, Ph.D., of Beth Israel Deaconess Medical Center, assessed cynomolgus macaques vaccinated with 12µg of either the first or second-generation vaccine candidate. Better activation of innate and adaptive immune responses was achieved with CV2CoV, resulting in faster response onset, higher titers of antibodies and stronger memory B and T cell activation as compared to our first-generation candidate, CVnCoV. Higher antibody neutralizing capacity was observed with CV2CoV across a broad range of variants, including the Beta, Delta and Lambda variants. During challenge with the original SARS-CoV-2 virus, animals vaccinated with CV2CoV were found to be better protected compared to CVnCoV based on effective clearance of the virus in the lungs and nasal passages. A direct comparison of CV2CoV with a licensed mRNA vaccine in non-human primates was able to show that neutralizing antibody levels measured following full vaccination of animals with either 12µg of CV2CoV or a 30µg standard dose of the licensed mRNA vaccine were highly comparable. Full data was published in Nature on November 18, 2021. Following these preclinical data, we announced the start of a Phase 1 clinical trial with CV2CoV on March 30, 2022. On April 21, 2022, the preclinical data for the second-generation mRNA backbone was extended by a study conducted in collaboration with the Friedrich-Loeffler-Institut, comparing immune responses and protective efficacy of monovalent and bivalent mRNA vaccines encoding Beta and/or Delta variants, primarily in a transgenic mouse model and a Wistar rat model. The preclinical data from the highlighted CV2CoV publications are detailed in the following chapters.

CV2CoV-based Bivalent Beta/Delta Candidate: Mice Challenge Studies with SARS-CoV-2 Beta and Delta Variant

On April 21, 2022, data of a preclinical study conducted in collaboration with the Friedrich-Loeffler-Institut comparing monovalent and bivalent mRNA vaccines encoding B.1.351 (Beta) and/or B.1.617.2 (Delta) SARS-CoV-2 Spike protein, primarily in a transgenic mouse model and a Wistar rat model was uploaded to the bioRxiv preprint server.

For the preclinical study, we designed unmodified mRNA vaccines encoding the Spike protein sequences from the Beta and Delta variants, which are distant variants with non-overlapping mutations in the RBD domain, as well as the ancestral strain, CV2CoV.351, CV2CoV.617 and CV2CoV, respectively. The vaccines containing a total of 0.5 µg mRNA per dose were administered intramuscularly; the bivalent vaccine (CV2CoV.351 and CV2CoV.617 together) contained 0.25 µg mRNA of each variant, i.e., half the dose of the monovalent vaccines. K18-hACE2 transgenic mice received 20 µL of a low dose monovalent CV2CoV, CV2CoV.351, CV2CoV.617 or bivalent vaccine (CV2CoV.351 and CV2CoV.617) containing a total of 0.5 µg mRNA or NaCl (sham) on Day 0 and Day 28. Following challenge with Beta and Delta variants ($10^{4,4}$ $TCID_{50}$) on Day 56, all vaccinated mice were protected from SARS-CoV-2-induced lethality and virus spread, while all Beta-challenged and 67% of Delta-challenged sham-vaccinated animals succumbed to infection.

Neither SARS-CoV-2 genomic RNA or sub-genomic RNA (sgRNA) were detectable in oral swabs collected on Day 4, or in lung, cerebellum and cerebrum samples taken on Day 10 in all but one of the Beta-challenged, bivalent-vaccinated animals, indicating that productive infection was prevented. The suppression of viral replication in the upper respiratory tract by the monovalent vaccines differed depending on the challenge virus. While the bivalent vaccine reduced viral load in the conchae equivalent to that observed with the matched monovalent vaccine after Beta challenge, replication of the Delta variant in the conchae was abolished (no detectable sgRNA) in all vaccinated groups.

Monovalent and bivalent mRNA vaccines encoding ancestral, Beta and Delta derived Spike protein sequences protect against SARS-CoV-2 variants

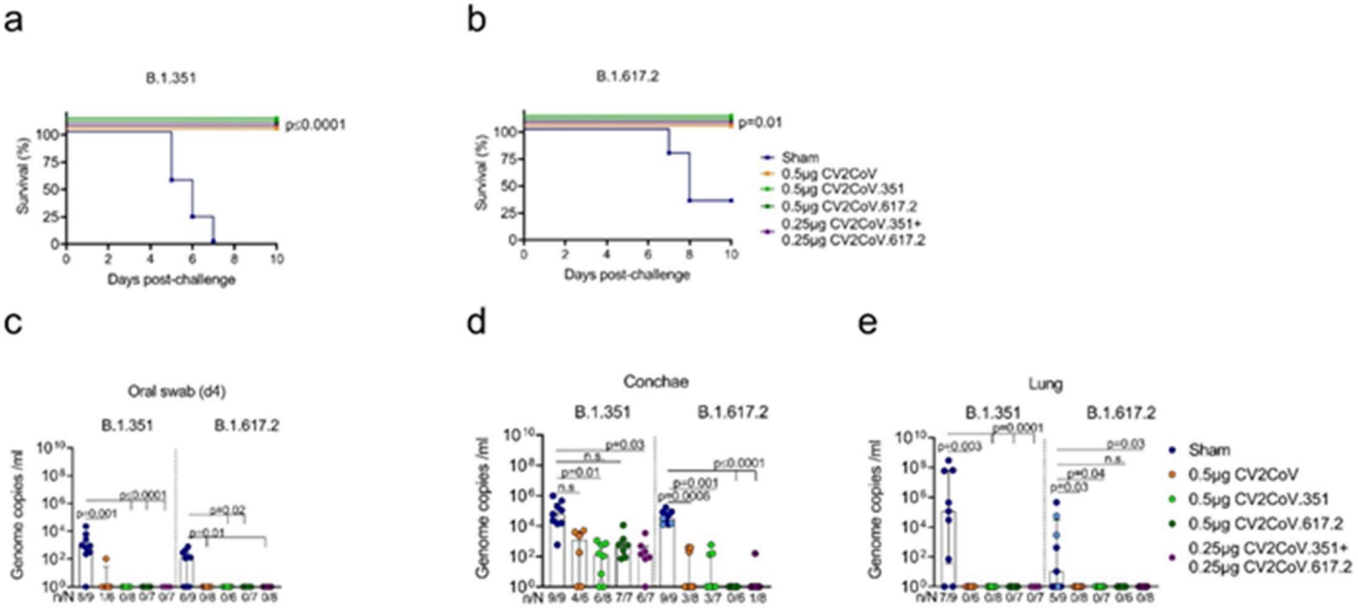


Figure: K18-hACE2 mice vaccinated on day 0 and 28 with a total of 0.5 µg CV2CoV (ancestral, orange), 0.5 µg CV2CoV.351 (Beta, light green), 0.5 µg CV2CoV.617.2 (Delta, dark green), CV2CoV.351 + CV2CoV.617.2 (0.25 µg of each; purple) or NaCl (sham; blue) were challenged i.n. with $10^{4,4}$ $TCID_{50}$ SARS-CoV-2 variant B.1.351 (Beta) or B.1.617.2 (Delta) at day 56. (a,b) Survival curves (Kaplan-Meier) for K18-hACE2 mice challenged with B.1.351 (Beta) (a) or B.1.617.2 (Delta) (b) with follow-up for 10 days post challenge. (c-g) RT-qPCR results from Day 4 oral swabs (c) or Day 10 conchae (d) anaïvelung (e). Sham group samples were obtained at Day 10 (light blue) or at the humane endpoint (dark blue). Number of RT-qPCR positive and total number of animal sample are shown on the x-axis. Each dot represents one individual mouse.

Scatter plots are labelled with median and interquartile range. p-values were determined by two-sided log-rank (Mantel-Cox) test (a,b) or one-way ANOVA and Dunn's multiple comparison test (c-e). Differences were considered significant at $p < 0.05$ with exact p values shown.

It was shown that the bivalent mRNA vaccine induced similarly high neutralizing antibody titers as the Beta and Delta monovalent vaccines with their respective homologous challenges, despite the bivalent vaccine containing half the mRNA dose of each monovalent vaccine (0.25 µg vs. 0.5 µg). Irrespective of the challenge, the bivalent mRNA vaccine-induced neutralizing antibody titers were statistically significantly higher than those induced by CV2CoV, whereas with the monovalent mRNA vaccines the neutralizing antibody titers were statistically significantly higher with the respective homologous challenges only.

In separate experiments, serum from Wistar rats vaccinated with CV2CoV or CV2CoV.617.2 mRNA vaccines (monovalent; 8 µg), or vaccines combining CV2CoV617.2 with either CV2CoV or CV2CoV.351 (bivalent; 4 µg of each) on Day 0 and Day 21 contained high level nAb titers against Delta. Neutralizing antibody titers were notably diminished against Omicron BA.1 in all but the bivalent vaccine group containing Beta and Delta Spike protein sequences. Including the Beta Spike protein sequence in the vaccine resulted in nAb titers that were 2× higher against Omicron BA.1 than those induced by Delta alone, whereas the nAb titers induced by vaccines without Beta Spike protein were 3–9 times lower against Omicron BA.1 than those induced by Delta. The bivalent formulation contained a half dose of each mRNA compared with the monovalent vaccines with better antigen coverage; this strategy may be advantageous in case of the emergence of additional antigenic distant variants.

Bivalent SARS-CoV-2 mRNA vaccines induce abundant virus neutralizing titers and robust lung T cell responses

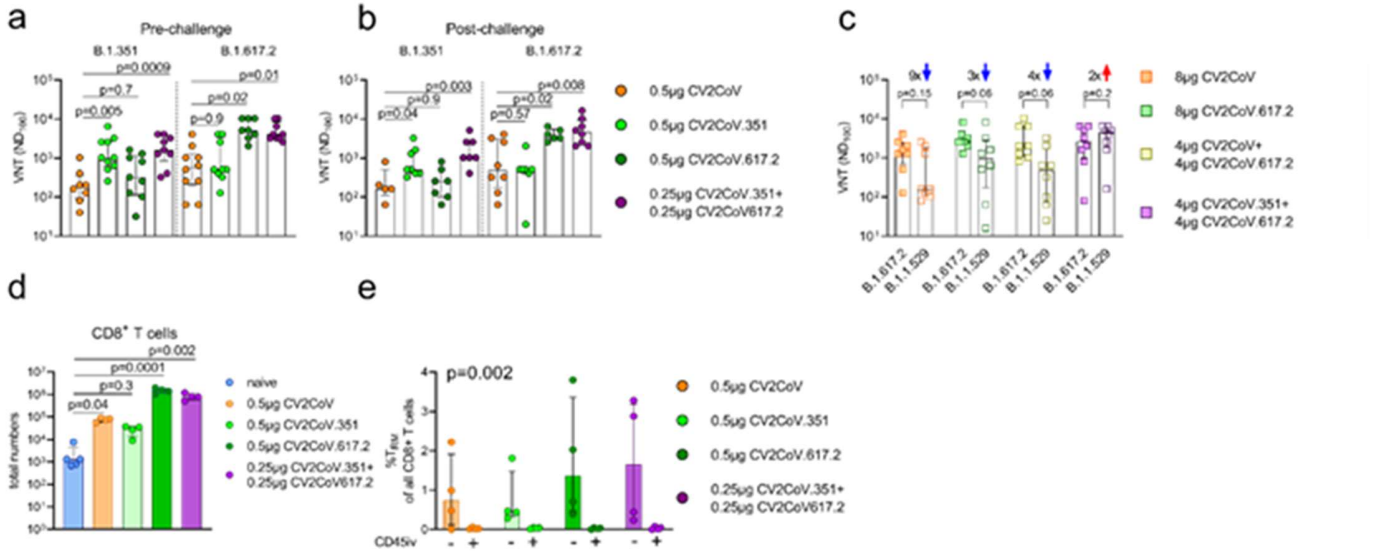


Figure: (a,b) Neutralizing antibody (nAb) titers (at Day 56 (Pre-challenge, a) and Day 66 (Post-challenge, b). Mice were vaccinated as described in fignaïve above. (c) nAb titers at Day 42 (pre-challenge; Wistar rats), the numbers above the bars indicate the fold-differences. Rats were vaccinated on day 0 and 21 and nAb titers against B.1.617.2 (Delta) or B.1.1.529 (Omicron, BA. 1) were tested. Each dot represents an individual animal. (d-e) Induction of low-dose mRNA vaccine induced T cell responses. Lung parenchyma T cells at Day 56 post vaccination were investigated by in vivo injection of 3 µg anti-mouse CD45 antibodies (CD45iv) for 3 minutes before harvesting of lung tissue. (d) Total number of CD45iv$^-$ CD8$^+$ CD3$^+$ T cells in all vaccine groups compared tnaïveaïve mice. (e) Frequency of CD8$^+$ TRM cells after vaccination and defined as CD45iv$^-$CD3$^+$ γδTCR$^-$CD8$^+$ CD44^{high}CD62L$^-$CD103$^+$ CD69$^+$ T cells.

Scatter plots are labelled with median and interquartile range. p-values were determined by one-way ANOVA and Dunn's multiple comparison test against CV2CoV (orange) (a-c) or against a group of nanaïve animals (d). (e) p-values were determined by two-way ANOVA and Dunn's multiple comparison test comparing CD45iv$^-$ versus CD45iv$^+$. Differences were considered significant at $p < 0.05$ with exact p values displayed in the figure.

In summary, SARS-CoV-2 evolution is a challenge for vaccine-based strategies for disease control. Our study demonstrates that a low-dose, bivalent, unmodified mRNA vaccine is highly efficacious in pre-clinical mouse and rat models and suggests that dose-sparing, multivalent vaccines combining mRNA encoding the Spike protein from the variants with unrelated lineages may induce heterologous protection and thus increase the breadth of immune responses. Given their exceptional flexibility in antigen formulation, mRNA vaccine platforms offer advantages regarding adaptability to circulating *Variants of Concern* and opportunities to design improved vaccines.

CV2CoV and CVnCoV: Non-human Primate Challenge and SARS-CoV-2 Variant Studies

On November 18, 2021, full data of a study assessing cynomolgus macaques vaccinated with 12µg of either the second-generation COVID-19 vaccine candidate, CV2CoV, or first-generation vaccine candidate, CVnCoV, conducted in collaboration with Dan Barouch, MD, Ph.D., of Beth Israel Deaconess Medical Center, was published in Nature.

To assess humoral immune responses, induction of binding antibodies following vaccination with either candidate was investigated by performing receptor-binding domain (RBD)-specific enzyme-linked immunosorbent assays (ELISAs) at multiple time points following immunization. At week 2, binding antibody titers were detected only with Cv2CoV and not with CVnCoV while one week after the second vaccination at week 4, the antibody titers were increased in both groups. By week 8, the binding antibody titers had increased in the CVnCoV group but were still >50 times lower than those in the CV2CoV group. Induction of neutralizing antibody titers were shown to follow a trend similar to that of the binding antibody titers. Neutralizing antibody responses were assessed by pseudovirus neutralization assay using the vaccine-matched SARS-CoV-2 wild-type strain. At week 2, neutralizing antibodies were detected only with Cv2CoV and not with CVnCoV, while week after the week 4 second vaccination, the neutralizing antibody titers were increased, for CVnCoV and CV2CoV, respectively. By week 8, the neutralizing antibody titers had increased in the CVnCoV group but were still >20 times lower than those in the CV2CoV group.

Neutralization capacity of both vaccine candidates against a range of relevant COVID-19 variants was investigated at week 6. The median pseudovirus neutralizing antibody titers were measured against the D614G, Alpha (B.1.1.7) and Beta (B.1.351) variants and amounted to 121, 101 and 189, respectively, for CVnCoV while they were 4,962, 1,813 and 755 for CV2CoV.

CV2CoV elicits high levels of binding and neutralizing antibody responses in macaques

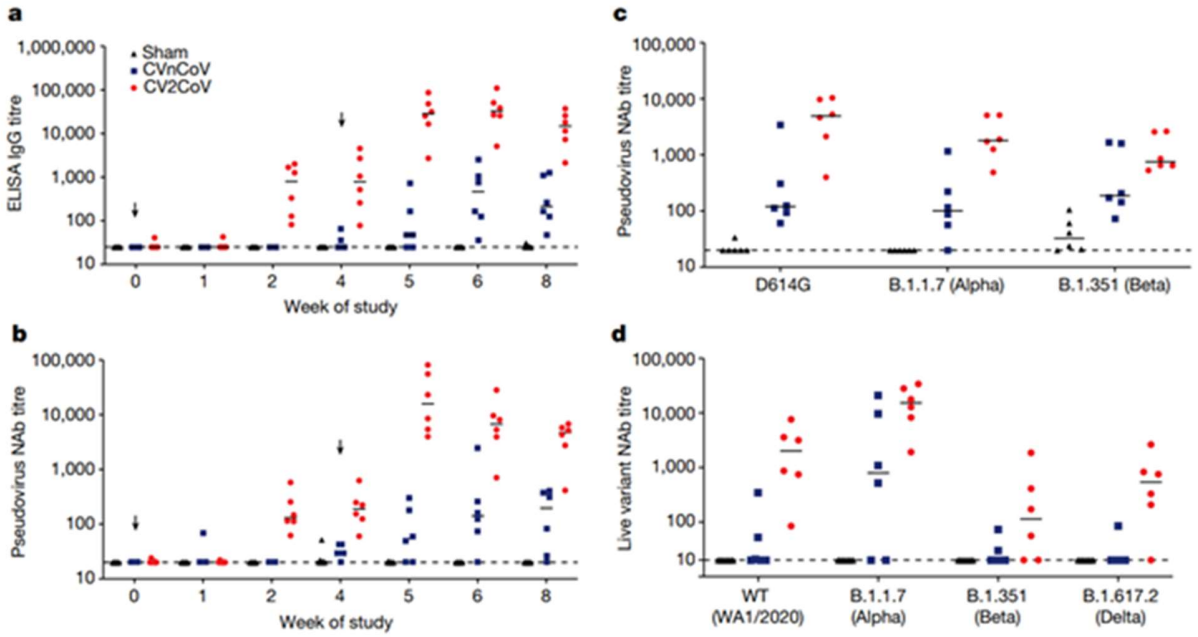


Figure: Animals (n = 6 per group) were vaccinated twice with 12 µg of CVnCoV or CV2CoV on day 0 and on day 28 or remained untreated as negative controls (sham). (A, B) Titers of RBD-binding antibodies (A) and pseudovirus neutralizing antibodies (NAb) against the ancestral SARS-CoV-2 strain (B) were evaluated at different time points after the first (weeks 0, 1, 2 and 4) and second (weeks 5, 6 and 8) vaccinations. (C, D) Sera collected on day 42 (week 6) were analyzed for pseudovirus (C) and live-virus (D) neutralizing antibody titers against virus with the D614G mutation and the Alpha (B.1.1.7), Beta (B.1.351) and Delta (B.1.617.2) variants. Each dot represents an individual animal, bars depict the median and the dotted line shows limit of detection.

Further testing of neutralizing capacity against an extended range of variants including the Lambda (C.37), Kappa (B.1.617.1) and Delta (B.1.617.2) variants showed median pseudovirus neutralizing antibody titers of 516, 158 and 36, respectively, for CVnCoV, while they were 1,195, 541 and 568 for CV2CoV. Taken together, these data show that CV2CoV induces substantially higher pseudovirus neutralizing antibody titers against SARS-CoV-2 variants than CVnCoV. Additionally assessed live-virus neutralizing antibody titers were largely consistent with those for the pseudovirus: the live-virus neutralizing antibody responses elicited by CV2CoV were higher than those elicited by CVnCoV against the wild-type and Delta (B.1.617.2) strains, with similar trends for Alpha (B.1.1.7) and Beta (B.1.351).

CV2CoV elicits high levels of neutralizing antibody titers against further variants

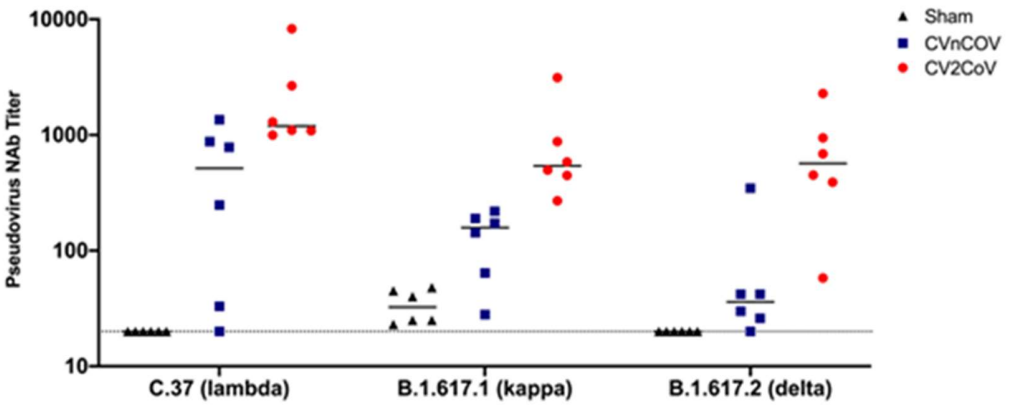


Figure: Animals (n = 6 per group) were vaccinated twice with 12µg of CVnCoV or CV2CoV on day 0 and day 28 or remained untreated as negative controls (sham). Sera isolated on day 42 (week 6) were analyzed for pseudovirus neutralizing antibody titers against Lambda (C.37), Kappa (B.1.617.1) and Delta (B.1.617.2) variants. Each dot represents an individual animal, bars depict the median and the dotted line shows limit of detection.

Within the study, we also compared the pseudovirus neutralizing antibody titers induced in macaques by two immunizations with 12 µg of CV2CoV to those induced by two immunizations with 30 µg of a licensed clinical mRNA vaccine obtained as leftover product from pharmacies. At peak immunity at week 5, the neutralizing antibody responses induced by CV2CoV were comparable to those induced by the licensed mRNA vaccine.

CV2CoV elicits comparable levels of neutralizing antibody titers to licensed mRNA vaccine

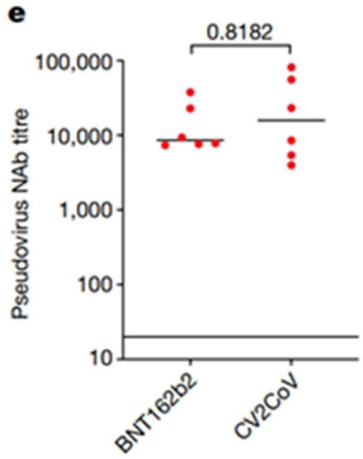


Figure: Sera collected from non-human primates immunized with 12 µg of CVnCoV or 30 µg of a licensed clinical mRNA vaccine on day 35 (week 5) after boosting were analyzed for pseudovirus neutralizing antibody titers against the ancestral WA/2020 (WT) strain. Each dot represents an individual animal and bars depict the median; the lower line shows the limit of detection.

The study also included assessment of cellular immune responses. Most SARS-CoV-2 RBD-specific B cells reside within the memory B cell pool. We used flow cytometry to assess memory B cell responses in the blood of non-human primates vaccinated with CVnCoV, CV2CoV or sham. Higher numbers of RBD-specific and spike-specific memory B cells were detected in the CV2CoV-vaccinated animals as compared with those vaccinated with CVnCoV at week 6. T cell responses were assessed by interferon γ (IFNγ) and interleukin (IL)-4 enzyme-linked immunosorbent spot (ELISPOT) assay using pooled spike peptides at week 6. IFNγ responses were detected in both groups but were higher in the CV2CoV group. IL-4 responses were not detectable, suggesting that CVnCoV and CV2CoV induce T helper type 1-biased responses.

Memory B and T cell Immune responses following immunization with either CV2CoV or CVnCoV

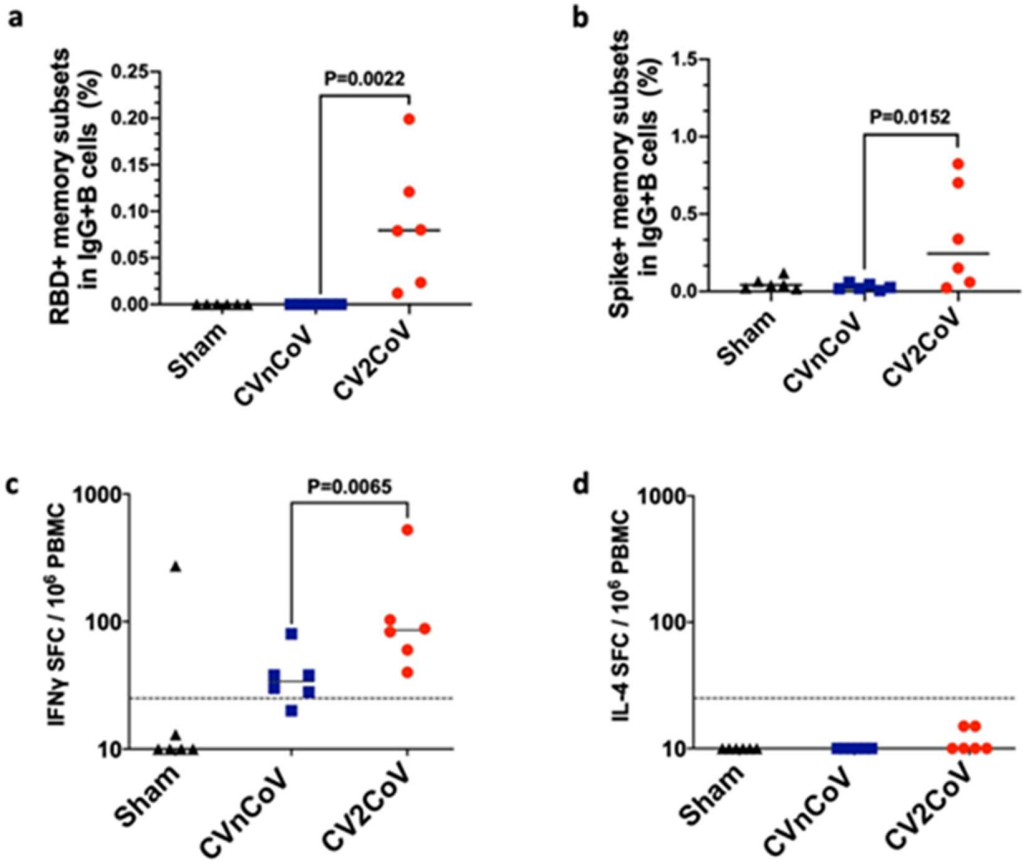


Figure: Peripheral blood mononuclear cells (PBMCs) from negative control (sham), CVnCoV or CV2CoV vaccinated animals (n = 6 per group) isolated on day 42 were stained for (A) RBD and (B) Spike-specific activated memory B cells and analyzed by high-parameter flow cytometry. IFNγ responses to pooled spike peptides were analyzed via ELISPOT (C). IL-4 responses (D) were not detectable. Each dot represents an individual animal, bars depict the median and the dotted line shows limit of detection. Statistical analysis was performed using two-tailed nonparametric Mann-Whitney test. SFC = spot forming cells.

All animals were challenged at week 8 with 1.0×10^5 median tissue culture infectious doses (TCID50) of the SARS-CoV-2 WA1/2020 strain via the intranasal and intratracheal routes. Viral loads were assessed in bronchoalveolar lavage (BAL) and nasal swab samples collected on days 1, 2, 4, 7 and 10 following challenge by quantitative PCR with reverse transcription specific for subgenomic RNA (sgRNA). The sgRNA levels in the BAL and nasal swab samples in the sham group peaked on day 2 and largely resolved by day 10. The sham controls had peak medians of 6.02 $\log^{10}$-transformed sgRNA copies per ml in the BAL and 7.35 log10-transformed sgRNA copies per swab in the nasal swab samples on day 2. The CVnCoV-immunized animals showed peak medians of 4.92 $\log^{10}$-transformed sgRNA copies per ml in the BAL and 6.42 $\log^{10}$-transformed sgRNA copies per swab in the nasal swab samples. The CV2CoV-immunized animals exhibited peak medians of 2.90 log10-transformed sgRNA copies per ml in the BAL and 3.17 $\log^{10}$-transformed

sgRNA copies per swab in the nasal swab samples, with resolution of sgRNA levels in the BAL samples by day 2 in most animals and by day 4 in all animals. Overall, CV2CoV resulted in significantly lower peak viral loads than CVnCoV in both the BAL and nasal swab samples.

Assessment of protective efficacy following challenge infection with SARS-CoV-2

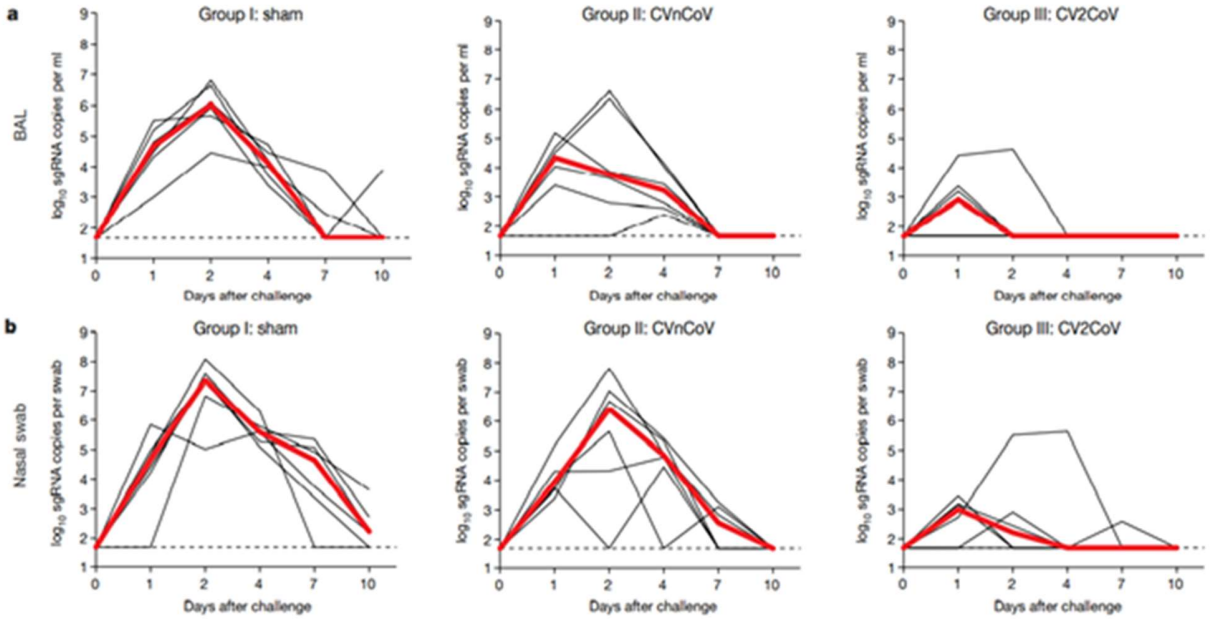


Figure: Negative-control animals (sham) and animals (n = 6 per group) vaccinated on day 0 and day 28 with 12 µg of CVnCoV or CV2CoV were challenged with 1.0 × 105 $TCID^{50}$ of SARS-CoV-2 (USA-WA1/2020) via the intranasal and intratracheal routes. (A B) BAL (A) and nasal swab (B) samples collected on days 1, 2, 4, 7 and 10 after challenge were analyzed for levels of replicating virus by RT–PCR specific for sgRNA. Thin black lines represent individual animals and thick red lines depict the median; the dashed line shows the limit of detection.

We next evaluated the immune correlates of protection. The log^{10}-transformed ELISA and neutralizing antibody titers at week 6 were inversely correlated with the peak log^{10}-transformed sgRNA copies per ml in the BAL samples and with the peak sgRNA copies per nasal swab in the nasal swab samples. Consistent with prior observations from our laboratory and others these findings suggest that binding and neutralizing antibody titers are important correlates of protection for these SARS-CoV-2 vaccines in non-human primates.

Titers of binding and neutralizing antibodies elicited following CVnCoV and CV2CoV vaccination

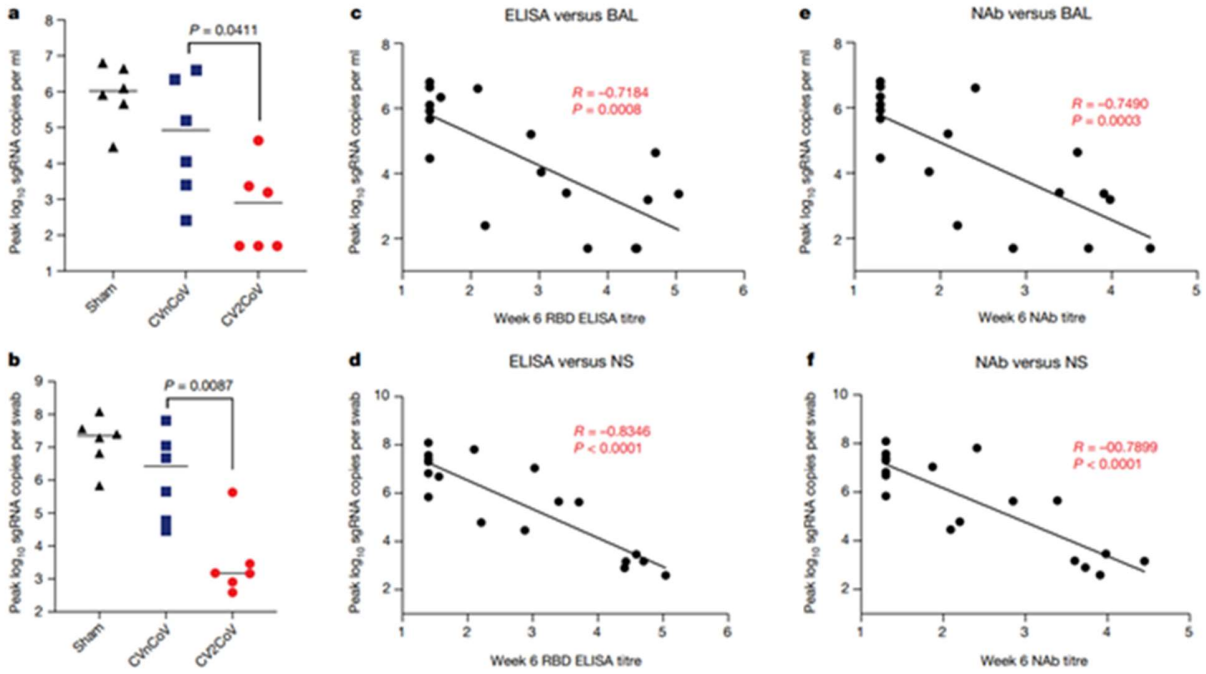


Figure: Titers of binding and neutralizing antibodies elicited following CVnCoV and CV2CoV vaccination (n = 6 per group) correlate with protection against SARS-CoV-2. (A, B) Summary of peak viral loads following SARS-CoV-2 challenge in BAL and nasal swab (NS) samples. Animals were challenged with 1.0×10^5 $TCID^{50}$ of SARS-CoV-2 derived from strain USA-WA1/2020. (C-F) Antibody correlates of protection for binding antibodies (C, D) and neutralizing antibodies (E, F). Statistical analysis was performed using the two-tailed non-parametric Mann–Whitney test, and correlation was analyzed by two-sided Spearman rank-correlation test. The bars indicate median values.

In summary, the data show that optimization of non-coding regions of the mRNA backbone in a SARS-CoV-2 mRNA vaccine can substantially improve its immunogenicity against multiple viral variants and can enhance its protective efficacy against SARS-CoV-2 challenge in macaques. CV2CoV elicited substantially greater humoral and cellular immune responses and provided significantly improved protective efficacy against SARS-CoV-2 challenge as compared with CVnCoV in macaques. Prime immunization with CV2CoV induced binding and neutralizing antibodies in all macaques by week 2, and these responses had increased substantially by 1 week after the boost immunization. As previously reported for other vaccines, the neutralizing antibody titers against certain SARS-CoV-2 variants, such as the Beta (B.1.351) and Delta (B.1.617.2) variants, were lower than those against the parental strain WA1/2020. Although our challenge virus in this study was SARS-CoV-2 WA1/2020, the neutralizing antibody titers elicited by CV2CoV to viral variants exceeded the values we previously reported as threshold titers for protection (50–100). However, future studies will be required to directly assess the protective efficacy of CV2CoV against SARS-CoV-2 variants of concern in non-human primates. CV2CoV also induced both antigen-specific memory B cell responses and T cell responses. Although the correlates of protection in this study were binding and neutralizing antibody titers, it is likely that $CD8^+$ T cells contribute to viral clearance in tissues. Memory B cells might contribute to the durability of antibody responses; B cell germinal center responses and the durability of protective efficacy following CV2CoV vaccination remain to be determined. Previous studies with rodents and non-human primates have demonstrated protection by CVnCoV. However, protection in macaques was primarily observed in the lower respiratory tract. In the present study, CVnCoV provided only modest viral load reductions in BAL and nasal swab samples compared with sham controls. In contrast to CVnCoV, CV2CoV induced >10-fold-higher neutralizing antibody responses against multiple viral variants and provided >3 log reductions in sgRNA copies per ml in BAL and >4 log reductions in sgRNA copies per swab in nasal swab samples compared with sham controls.

CV2CoV and CVnCoV: Human ACE2 Transgenic Mice Challenge Studies with SARS-CoV-2 Beta Variant

On June 30, 2021, preclinical data demonstrating the protection efficiency of CV2CoV and CVnCoV from the SARS-CoV-2 ancestral strain BavPat1 and the Beta variant (B.1.351) was published by Nature Communications. The study was carried out in a transgenic mouse model, expressing the human ACE2 receptor, the receptor through which SARS-CoV-2 enters human cells. For immunization of the mice, 8µg of the CVnCoV vaccine candidate was administered. For CV2CoV, a dose titration ranging from 0.5µg to 8µg was performed. Both vaccine candidates were administered following a two-dose schedule on days 0 and 28. Mice were challenged 4 weeks after the second vaccination with more than 10^5 $TCID^{50}$ of SARS-CoV-2 BavPat1 or B.1.351. Overall, CVnCoV and CV2CoV vaccinations were shown to induce robust antibody titers with variant neutralizing capacity and to provide full protection against infection and mortality during challenge infection.

For the analysis of antibody titers, sera from all mRNA-vaccinated mice were collected on days 28 and 55. Analysis showed strong induction of RBD binding antibodies irrespective of the mRNA amount. Robust RBD binding antibody titers were reflected by high virus neutralization titers (VNT). Even a low dose of 0.5µg of CV2CoV elicited high levels of humoral responses in K18-hACE2 transgenic mice. However, consistent with other available variant studies, neutralization capacity of VNT titers was significantly lower for the Beta variant (B.1.351, mean titer = 525) compared to BavPat1 (mean titer = 10,151) for both vaccine candidates.

To analyze the potential of CVnCoV and CV2CoV to protect from SARS-CoV-2 challenge infection despite impacted VNT titers, immunized K18-hACE2 mice were studied applying a high-dose challenge model, which induces severe clinical disease resembling COVID-19 in humans. On day 4 following the challenge infection, non-vaccinated control animals (sham group) started succumbing to the BavPat1 infection. B.1.351 infection led to a delayed onset of severe disease compared to BavPat1, with 20% survival on day 10 after inoculation. By contrast, vaccination with 8µg CVnCoV or 0.5µg to 8µg of CV2CoV resulted in complete protection (100% survival) against the lethal challenge infection with BavPat1 and B.1.351, with no significant weight loss or disease symptoms throughout the course of the challenge infection.

CVnCoV and CV2CoV protect K18-hACE2 mice against SARS-CoV-2 variants BavPat1 and B1.351

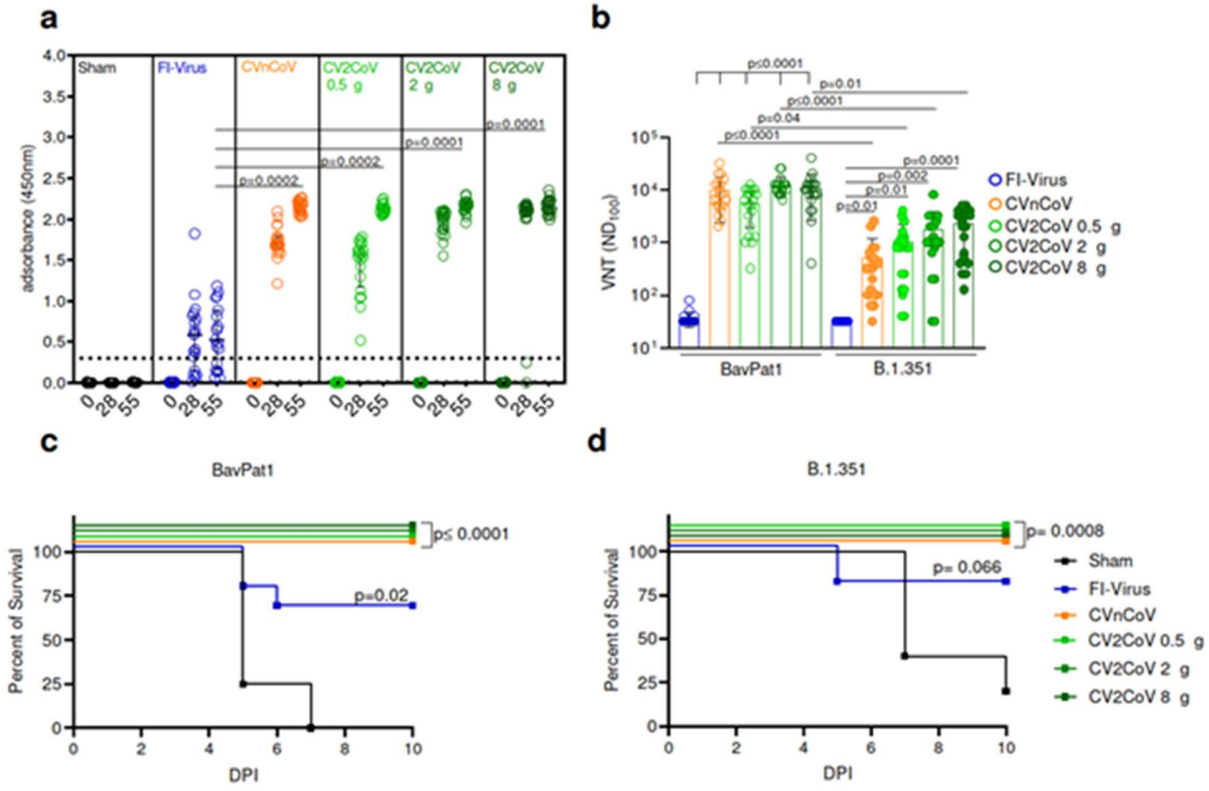


Figure: K18-hACE2 mice vaccinated with 8µg CVnCoV (orange) or 0.5µg (light green), 2µg (green) or 8µg (dark green) CV2CoV received 10^6 FI-Virus (blue, formalin-inactivated and adjuvanted SARS-CoV-2-preparation) or NaCl (black, SHAM group) on day 0 and day 28 followed by i.n. challenge with $^{105.9}$ TCID^{50} of SARS-CoV-2 variants BavPat1 or $10^{5,5}$ TCID^{50} B1.351. (A) RBD-Elisa with sera from K18-hACE2 mice on day 0, 28 and 55 of respective groups: median and interquartile range are presented. Dashed line indicates threshold for positive anti-RBD antibody level. (B) Virus neutralization assay using day 55 sera from all groups. Bars indicate mean with SD. (C and D) Survival curves (Kaplan-Meyer) for K18-hACE2 mice from all groups challenged either with BavPat1 (C) or B.1.351 (D) and followed up for 10 days post-infection (DPI). (A and B) Each dot represents one individual mouse sample. Each sample was tested once (RBD-Elisa) or in triplicates (VNT), and assays were repeated at least once. (C and D) Each line represents a groups of mice as shown in A and B from a single experiment (n=5 Sham, n=10 all other groups). (A and B) Scatter plots are labeled with median (height of the bar) and interquartile range. P-values were determined by non-parametric one-way ANOVA and Dunn's multiple comparisons test (A and B) or two-sided log-rank (Mantel-Cox) test (C and D). Differences were considered significant at p<0.05 with exact p-values displayed in the figure.

Viral replication and hence viral RNA load following challenge infection was determined via RT-qPCR in saliva, the upper respiratory tract (URT) (conchae), the lower respiratory tract (LRT) (trachea, caudal lung and cranial lung) and the central nervous system (brain, cerebellum/cerebrum). In saliva, non-vaccinated control animals showed 4/4 and 4/5 positive samples after infection with BavPat1 or B.1.351, respectively. in contrast, after CVnCoV or CV2CoV vaccination, no viral genomes were detected in the saliva of either challenge group irrespective of the vaccine or vaccine dose. Similarly, the URT provided a niche for viral replication in non-CVnCoV or CV2CoV treated animals. In the CVnCoV and CV2CoV-vaccinated group challenged with BavPat1, we observed a significant reduction of detectable viral replication in all groups with a maximum of 5/10 animals showing low genome copy numbers in the conchae. No animal in the LRT and only one sample from the brain was positive at a low level for SARS-CoV-2 genomic RNA, indicating complete protection from infection by BavPat1 in all groups.

For B.1.351, 5-7/10 CVnCoV or CV2CoV-vaccinated animals exhibited residual viral replication in the conchae. Here, viral levels were reduced without reaching statistical significance. In contrast, both CVnCoV and CV2CoV almost completely prevented replication of this variant in the LRT and the brain, with low viral copy numbers close to the limit of detection in the lung of 7/80 animals, and only 1/40 and 2/40 animals in the cerebellum and cerebrum, respectively.

CVnCoV prevents replication of SARS-CoV-2 variants BavPat1 and B.1.351 in K18-hACE2 mice

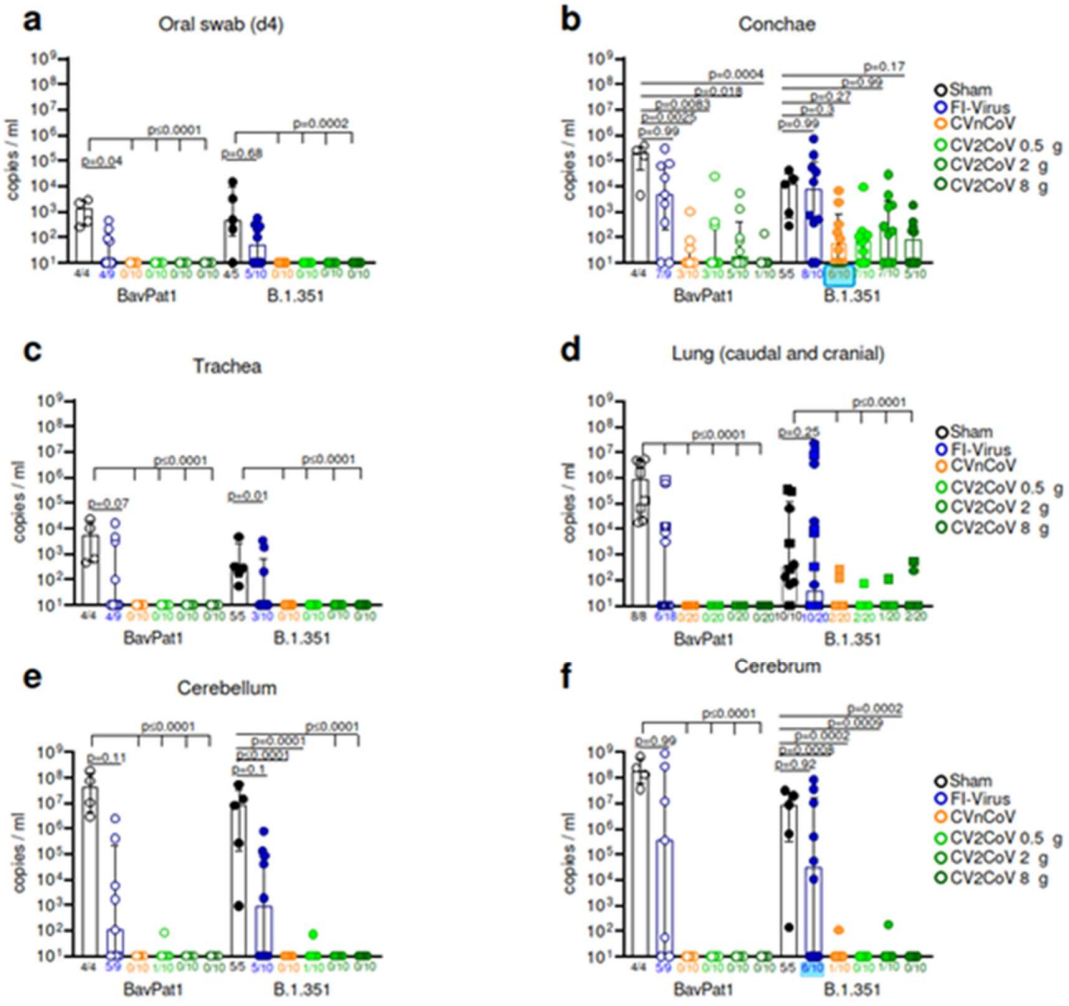


Figure: K18-hACE2 mice vaccinated with 8µg CVnCoV (orange) or 0.5µg (light green), 2µg (green) or 8µg (dark green) CV2CoV received 10^6 FI-Virus (blue, formalin-inactivated and adjuvanted SARS-CoV-2-preparation) or NaCl (black, SHAM group) on day 0 and day 28 followed by i.n. challenge with $10^{5.9}$ $TCID^{50}$ of SARS-CoV-2 variants BavPat1 or $10^{5,5}$ $TCID^{50}$ B1.351. RT-qPCR for genomic RNA of SARS-CoV-2 was performed with either (A) oral swab samples at day 4 or from organ samples of (B) the upper respiratory tract, (C and D) the lower respiratory tract (caudal lung = circle; cranial lung = squares) and (E and F) the brain at day 10 or at the humane endpoint. Each dot represents one individual mouse. Each sample was tested once, and assays were repeated at least once. P-values were determined by nonparametric one-way ANOVA and Dunn's multiple comparisons test. Scatter plots are labeled with median (height of the bar) and interquartile range. Differences were considered significant at $p<0.05$ with exact p-values displayed in the figure. Source data are provided as a Source Data file.

In summary, we believe the preclinical data collected for second-generation vaccine candidate CV2CoV and CVnCoV in human transgenic ACE2 mice is important complementary data to assess the impact of Variants of Concern. The emergence of new strains with immune escape potential pose a threat to global vaccination efforts, since currently licensed COVID-19 vaccines were developed based on the ancestral SARS-CoV-2 strains. The described challenge study in a human transgenic mouse model contributes to our preclinical studies with SARS-CoV-2 variants specific data and provides evidence on the protection efficiency of CV2CoV. Our data demonstrate that 8µg of CV2CoV and 0.5 to 8 µg of CVnCoV fully protects mice from lethal infection caused by BavPat1 and B.1.351. Both CV2CoV and CVnCoV immunization resulted in abundant RBD binding and virus neutralizing antibodies, and conferred a complete and robust protection, including protection from viral replication in the lung and the brain. Only very limited viral replication was observed in the URT of mRNA-vaccinated animals challenged with B.1.351. The reduced neutralizing capacity of sera from CV2CoV and CVnCoV-vaccinated transgenic mice against B.1.351, and the insufficient prevention of replication in the conchae, might reflect the detected transmission rates of this variant in human populations previously exposed to the ancestral strain. Nevertheless, this study provided the first evidence for the efficacy of a vaccine to prevent disease and viral dissemination from the site of infection against an emerging SARS-CoV-2 variant in a sensitive, well-established and accepted *in vivo* model.

CV2CoV in Wistar Rats

On May 13, 2021, we announced first preclinical data in a rat model showing that our second-generation COVID-19 vaccine candidate, CV2CoV, induced high levels of antigen production in an *in vitro* setup as well as strong and dose-dependent immune responses in vaccinated rats. CV2CoV is designed to exhibit improved intracellular mRNA stability and translation for increased and extended protein expression on the basis of a new mRNA backbone. These improvements aims to increase vaccine-induced immune responses to compensate for potentially reduced virus neutralization responses and efficacy against different virus variants. In addition, emerging immune escape variants might necessitate multivalent vaccines, in which each component needs to be efficacious at a lower dose.

In vitro, we were able to show that CV2CoV supports higher levels of protein expression in cell culture than first-generation vaccine candidate, CVnCoV. Flow cytometry-based analysis of protein expression levels of the mRNA components in cV2CoV compared to CVnCoV in HeLa cells transfected with identical amounts of mRNA demonstrated a significant increase of protein expression upon transfection with cV2CoV compared to CVnCoV. This effect was evident in both intracellular and cell surface expression of the S protein. CV2CoV displayed a 3.3 fold increase in the geometric mean in intracellular and a 1.8 fold increase in the geometric mean in cell surface expression compared to CVnCoV analyzed by flow cytometry.

CV2CoV mRNA enhances protein expression

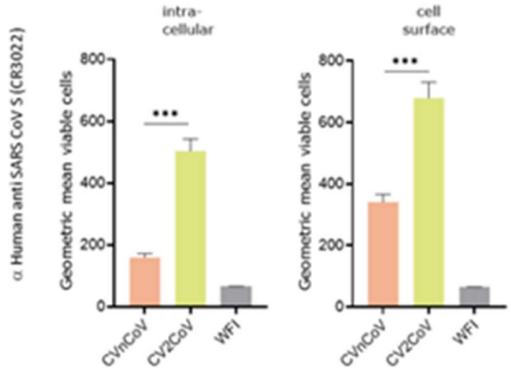


Figure: Flow cytometric analysis using an S-specific antibody either with or without membrane permeabilization allowing detection of intracellular or cell surface bound S protein. Geometric mean fluorescence intensity (GMFI) of transfected HeLa cells are expressed as mean + standard deviation (SD) of duplicate samples of two independent experiments. T-test was used to compare groups.

We next characterized the immunogenicity of CV2CoV in a small animal model. Wistar rats were vaccinated twice on day 0 and day 21 with five different doses ranging from 0.5µg to 40µg of CV2CoV. NaCl vaccinated animals served as negative controls. Rats vaccinated with 0.5µg, 2µg or 8µg of CV2CoV elicited a strong dose dependent binding antibody response directed against the S receptor binding domain (RBD). High values of RBD reactive antibodies without a clear dose response were detectable upon vaccination with 20µg and 40µg of CV2CoV possibly due to saturating dose levels employed. RBD binding antibodies developed rapidly and were detectable two weeks after a single vaccination in all dose groups. Both IgG1 and IgG2a titers increased over time and a clear boost effect was detectable upon a second vaccination.

CV2CoV triggers high levels of binding antibody responses in rats

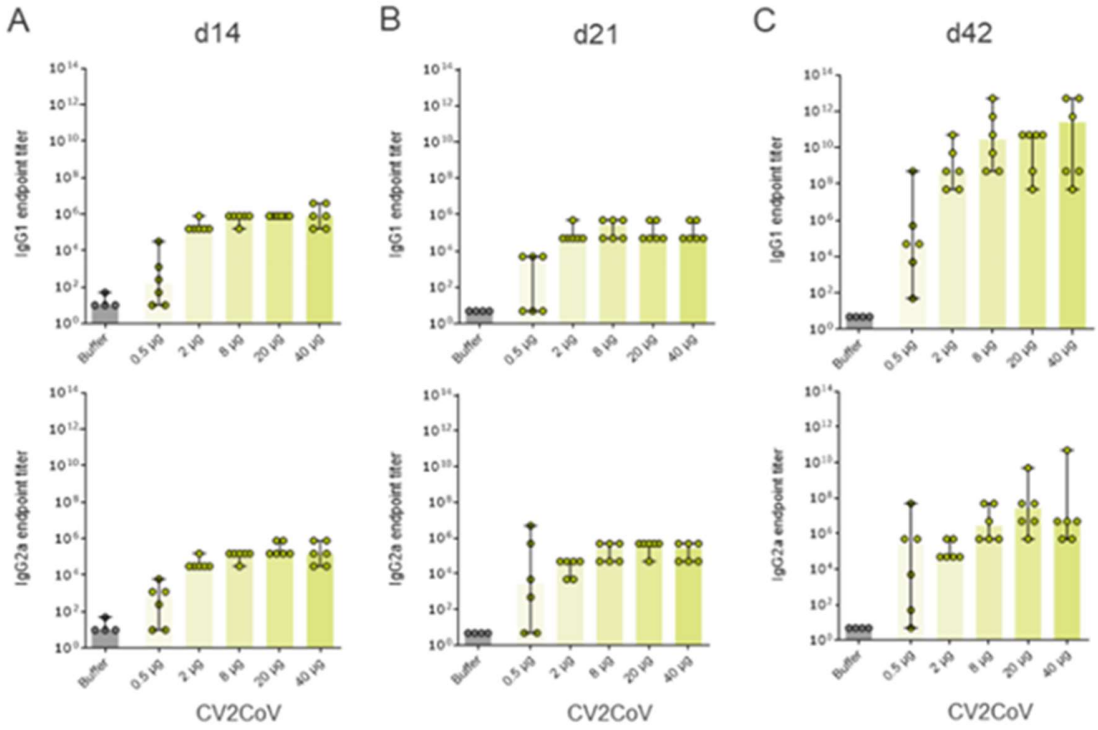


Figure: Female and male Wistar rats (n=6 per group) were vaccinated IM on day 0 and day 21 with five different doses ranging from 0.5µg to 40 µg of CV2CoV. Wistar rats (n=4) vaccinated with 0.9% NaCl (Buffer) on day 0 and day 21 served as negative control. SRBD protein specific binding antibodies, displayed as endpoint titers for IgG1 and IgG2a in serum upon one vaccination ((A) day 14 and (B) day 21) or two vaccinations ((C) day 42). Each dot represents an individual animal, bars depict the median.

Induction of virus neutralizing titers in rat sera was assessed in a cytopathic effect-based assay and showed that CV2CoV induced significant, dose dependent neutralizing titers two weeks after a single vaccination in all animals vaccinated with a dose of 2µg or higher. On day 14, CV2CoV induced homologous titers ranging from 1:42 in the 2µg group to 1:193 in the 40µg group. Neutralizing titers increased over time and the second vaccination led to a substantial increase in neutralizing titers in all dose groups except for two animals in the 0.5µg group. On day 42 post vaccination, neutralizing titers in animals that had received ≥2µg exceeded the upper range of detection in the assay, i.e. a dilution of 1:5120.

CV2CoV induces high titers of virus neutralizing antibodies (VNT) against SARS-CoV2 in rats

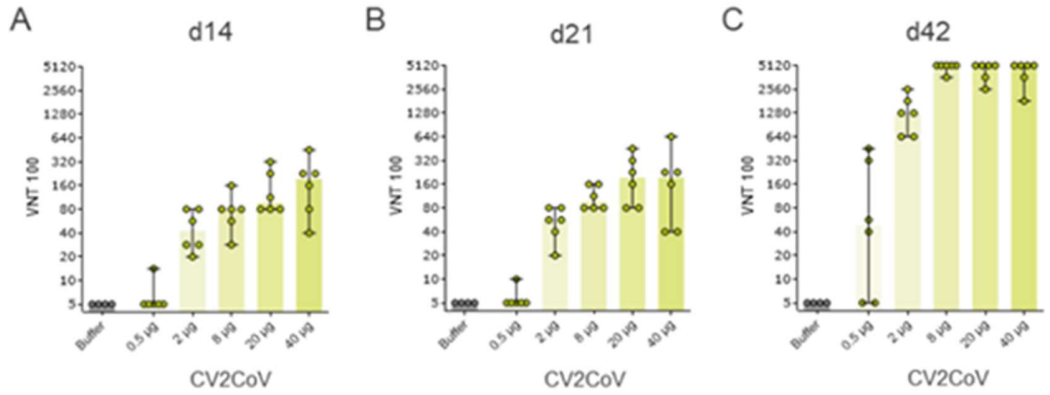


Figure: Female and male Wistar rats (n=6 per group) were vaccinated IM with five different doses ranging from 0.5µg to 40 µg of CV2CoV on day 0 and day 21. Animals (n=4) vaccinated with NaCl (Buffer) served as negative controls. SARS-CoV-2 100% neutralization titers (VNT100) in serum samples taken on day 14, day 21 and day 42 were analyzed. Highest dilution step was 1:5120. Each dot represents an individual animal, bars depict the median.

CV2CoV's ability to induce robust levels of neutralizing antibodies was highlighted by its ability to cross-neutralize three different SARS-CoV-2 variants. Neutralizing titers in the day 42 sera against heterologous SARS-CoV-2 variants B.1.1.298, Alpha (B.1.1.7) and Beta (B.1.351) originating from Denmark, the UK and South Africa, respectively, compared to ancestral SARS-CoV-2 (B.1) were analyzed. In the 8µg dose group, CV2CoV induced median titers of 1:2438 (B.1), 1:4096 (B.1.1.298), 1:1935 (B1.1.7) and 1:806 (B.1.351). Overall, sera from CV2CoV-vaccinated animals were able to neutralize B.1.1.298 without detectable decrease. A reduction of neutralizing titers were measured against B.1.1.7 and B.1.351, where a median decrease across dose groups 0.5µg, 2µg, 8µg and 20µg of 1.4 fold (B.1.1.7) and 3.3 fold (B.1.351) was detected.

CV2CoV induces high titers of cross neutralizing antibodies (VNT) against SARS-CoV-2 variants in rats

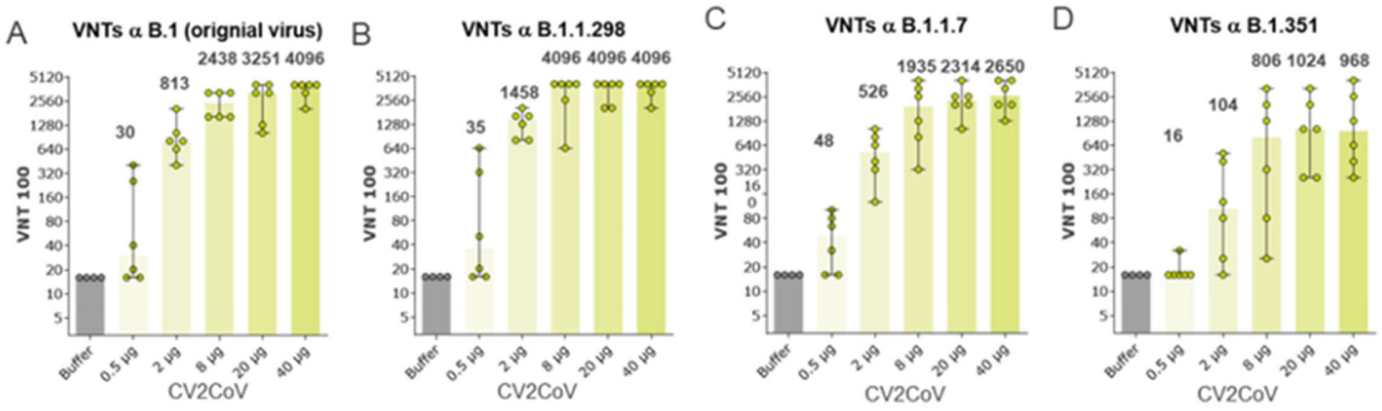


Figure: Female and male Wistar rats (n=6 per group) were vaccinated IM with five different doses ranging from 0.5µg to 40µg of CV2CoV on day 0 and day 21. Animals (n=4) vaccinated with NaCl (Buffer) served as negative controls. SARS-CoV-2 100% neutralization titers (VNT100) in serum samples taken on day 42 against distinct SARS-CoV-2 variants were analyzed as indicated. Highest dilution step was 1:4096. Each dot represents an individual animal, bars depict the median.

In summary, vaccination with CV2CoV induced high, dose-dependent levels of RBD binding and virus neutralizing antibodies in outbred rats. Antibody responses were detectable in doses as low as 0.5µg and doses of ≥2µg resulted in robust antibody levels. Importantly, a single vaccination of ≥2µg was sufficient to induce neutralizing titers two weeks

post injection. In comparison, preclinical studies in rats, hamsters and NHPs have shown that two vaccinations of CVnCoV are required to induce significant levels of VNTs, providing proof for the enhanced characteristics of CV2CoV. In addition, the serum of vaccinated rats showed significant cross-neutralization against certain *Variants of Concern*, including the B.1.1.298, Alpha (B.1.1.7) and Beta (B.1.351) variants. These abilities further support CV2CoV's application in the context of multivalent vaccines that might become necessary as the virus mutates further.

mRNA-Based Prophylactic Vaccine Programs Applying First-Generation mRNA Backbone

Clinical COVID-19 Vaccines Program (first-generation mRNA backbone): CVnCoV

Upon publication of the sequence of the novel Coronavirus (SARS-CoV-2) in early 2020, we designed and optimized potential antigenic constructs based on the spike protein to elicit high immunogenicity. Our initial approach was based on encoding a stabilized spike protein and we successfully conducted several preclinical studies that we started in January 2020. The results of our preclinical studies enabled us to identify a first-generation vaccine candidate against SARS-CoV-2, CVnCoV, to advance to clinical testing. We initiated a Phase 1 clinical trial in healthy volunteers in June 2020, a Phase 2a clinical trial in older adults above 60 years old in September 2020 and a pivotal Phase 2b/3 clinical trial in December 2020. Our pivotal Phase 2b/3 trial for CVnCoV, which included approximately 40,000 participants, reported interim analysis outcomes following a first interim analysis on May 28, 2021, based on 59 adjudicated COVID-19 cases and a second interim analysis on June 16, 2021, based on 134 adjudicated COVID-19 cases in the unprecedented context of at least 13 variants circulating within the assessed study population subset**.** Primary data was published in The Lancet on November 23, 2021. Overall, CVnCoV demonstrated a vaccine efficacy of 48% against COVID-19 disease of any severity. In the highly dynamic variant environment, the HERALD trial met the prespecified success criteria for efficacy against symptomatic COVID-19 of any severity and for efficacy against moderate-to-severe COVID-19, as defined in the protocol. The primary efficacy analysis included 12,851 participants in the CVnCoV group and 12,211 in the placebo group. The mean observation period, starting 15 days after administration of the second dose, was 48.2 days. Vaccine efficacy against COVID-19 of any severity was 48.2% in the overall primary efficacy analysinaïve of SARS-CoV-2-naive participants, and 52.5% in those aged 18–60 years. Vaccine efficacy against moderate-to-severe COVID-19 was 70.7% overall and 77.2% in participants aged 18–60 years. There were too few participants aged 61 years or older who developed COVID-19 to allow a meaningful estimate of efficacy in this age group.

On October 12, 2021, we announced the strategic decision to withdraw our first-generation COVId-19 vaccine candidate, CVnCoV, from the approval process with the European Medicines Agency, or EMA, and to focus our COVID-19 vaccine program on the development of mRNA vaccine candidates based on our second-generation backbone in collaboration with GSK. The decision was aligned with the evolving dynamics of the pandemic response toward greater need for more differentiated vaccines. The rolling submission with the EMA was originally initiated in february 2021 to assess CVnCoV's compliance with standards for vaccine efficacy, safety and pharmaceutical quality as a prerequisite for a formal market authorization application. Later in 2021, the EMA informed us that it would not start reviewing the provided CVnCoV data packages before 2022. As a result, we estimated that the earliest possible approval of CVnCoV would come in the second quarter of 2022. By this time, we expected candidates featuring the second-generation backbone to be progressing through clinical development. Consequently, CVnCoV was also withdrawn from a rolling submission with Swissmedic, Switzerland's authority responsible for the authorization and supervision of therapeutic products, initiated in April 2021, to review the safety, efficacy and pharmaceutical quality of CVnCoV as a prerequisite for market authorization.

Two clinical studies with our first-generation candidate, CVnCoV, are still ongoing with the scheduled safety follow-up times for all trial participants as per the respective trial protocols, i.e. the Phase 2b/3 (HERALD) study in Europe and Latin America (initiated in December 2020) and a Phase 3 study in healthcare workers in Germany (initiated in December 2020). Primary data of the Phase 2b/3 (HERALD) trial was published in The Lancet on November 23, 2021.

For a Phase 1 study in Germany (initiated in June 2020), a Phase 2a study in Peru and Panama (initiated in September 2020) and a Phase 3 study in participants with comorbidities in Belgium (initiated in April 2021) all subject follow-up times have been completed as per the respective trial protocols. Data of an interim analysis of the Phase 1 trial was published in Wiener klinische Wochenschrift on August 10, 2021. The first clinical data readout of the Phase 2a clinical trial in Peru and Panama was uploaded to the SSRN preprint server on December 10, 2021.

Previously announced studies to be initiated with CVnCoV, including a Phase 2 clinical trial, focusing on immunogenicity in older adults above the age of 65 years old compared to younger adults and a flu-coadministration

study, planned to be initiated together with Bayer AG to assess compatibility with established seasonal vaccines in an older population, were cancelled.

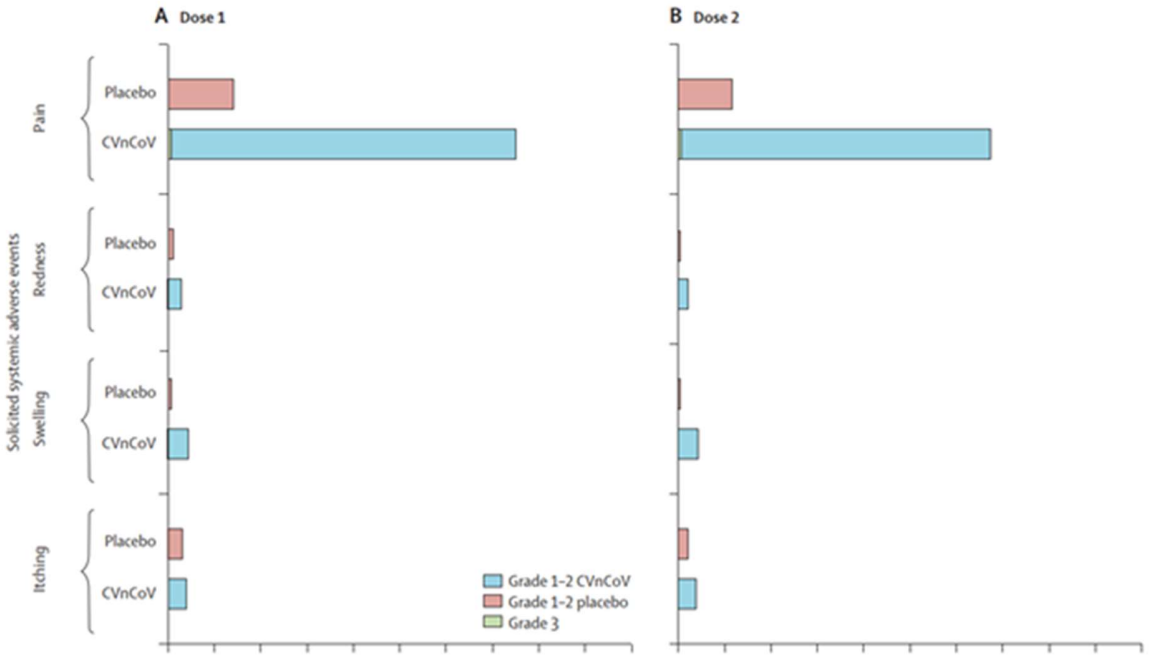
CVnCoV Phase 2b/3 Clinical Trial (Pivotal Trial for CVnCoV Safety and Efficacy)

We initiated a Phase 2b/3 clinical trial for CVnCoV, called HERALD, in December 2020. The study is still ongoing with the scheduled safety follow-up times for all trial participants as per the trial protocol. Primary data of the Phase 2b/3 (HERALD) trial was published in The Lancet on November 23, 2021.

The study is a randomized, observer blind, placebo-controlled trial on a two-dose 12µg schedule. The initial phase 2b part of the trial was designed to characterize the safety, reactogenicity and immunogenicity of CVnCoV, and the phase 3 part of the trial was designed to evaluate its efficacy and safety. An independent data and safety monitoring board (DSMB) conducted interim safety reviews of the phase 2b part of the trial before enrollment for the phase 3 part of the trial and will continue to monitor safety until study end. The trial has a primary safety objective and a primary efficacy objective: the demonstration of the efficacy of preventing first episodes of confirmed cases of COVID-19 of any severity in participants who have never been infected with SARS-CoV-2. Altogether, 39,680 participants were enrolled in the predefined age groups of 18 to 60 and above 60 years old and randomly assigned in the phase 2b and phase 3 parts of the trial.

Solicited and unsolicited adverse events were analyzed in the reactogenicity analysis set, which comprised participants in the phase 2b trial who received at least one dose of CVnCoV or placebo. Although the prevalence of solicited and unsolicited adverse events was higher in CVnCoV recipients than in placebo recipients, these events were transient and mostly mild-to-moderate (grade 1–2). The proportion of CVnCoV recipients reporting solicited local and systemic adverse events in the 7 days following any dose was similar to that seen in other mRNA vaccine phase 3 trials. No increase in solicited reactions was seen between the first and second CVnCoV doses. Serious adverse events and adverse events of special interest were uncommon and similar in frequency between the CVnCoV and placebo groups, although the short follow-up duration needs to be considered when interpreting these findings. The safety of the CVnCoV vaccine candidate will continue to be monitored for the duration of the trial. Taken together the findings observed in this trial provide further support for the safety of the RNActive mRNA vaccine platform.

Solicited local and systemic adverse events in the phase 2b reactogenicity analysis set



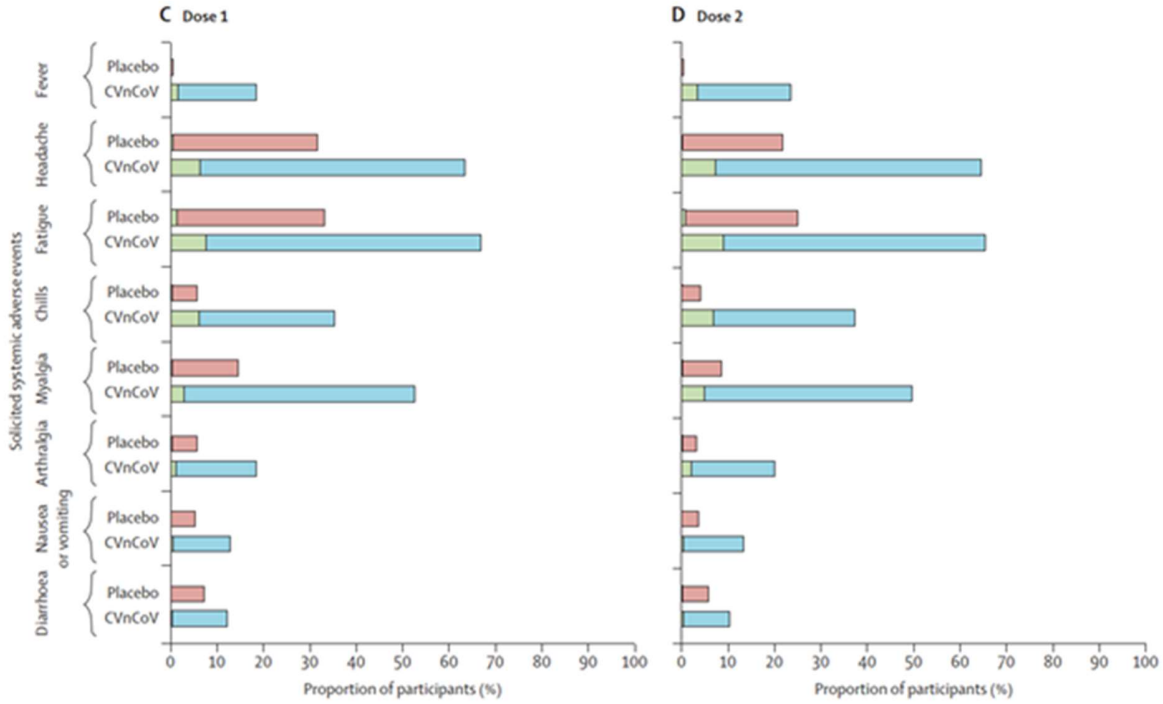


Figure. Solicited local adverse events occurring within 7 days of the first dose (A) and the second dose (B) and solicited systemic adverse events occurring within 7 days of the first dose (C) and the second dose (D).

First Interim Analysis

On May 28, 2021, we announced that the Data Safety Monitoring Board confirmed that we passed a first interim analysis in the pivotal Phase 2b/3 trial at 59 adjudicated COVID-19 cases. The DSMB confirmed that there were no safety concerns for CVnCoV. As a standard procedure within a blinded trial, we had no access to trial data. The study was recommended to continue to the next interim analysis to collect sufficient data in order to conduct a statistically significant efficacy analysis.

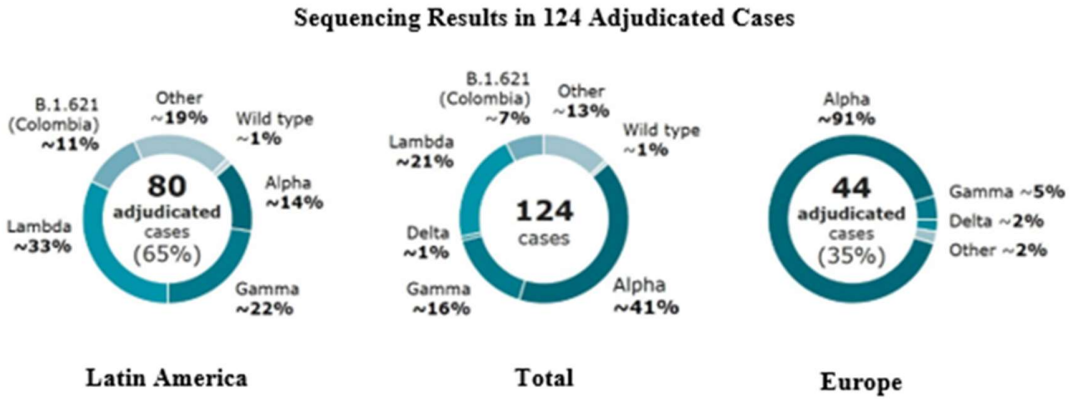
Second Interim Analysis

On June 16, 2021, we announced results of the second interim analysis of the pivotal Phase 2b/3 study at 134 adjudicated cases. In the unprecedented context of 13 variants circulating within the study population subset assessed at this interim analysis, CVnCoV demonstrated an interim vaccine efficacy of 47% against COVID-19 disease of any severity. It thereby did not meet the prespecified statistical success criteria. Initial analyses suggested age and strain dependent efficacy. The study was continued to the final analysis in order to provide more data in the complex variant-rich environment.

The efficacy readout from this trial needs to be viewed against the background of sequencing data, acquired in parallel to the accrual of COVID-19 cases within the trial to identify the virus strains responsible for the detected COVID-19 cases. 124 of the 134 adjudicated cases were sequenced. 10 adjudicated cases could not be sequenced due to insufficient sample material. The strain distribution illustrated below provides the variant context around the preliminary CVnCoV efficacy of 47% against any severity of disease, according to the primary study objective. Of the 124 sequenced adjudicated cases, variants of concern, including the Alpha and the Gamma strain, represented approximately 57%. This was mainly supplemented by 21% of the Lambda strain, originating from Peru, and 7% of the B.1.621 strain, originating from Colombia.

Overall, 13 variants were shown to provide direct context for the preliminary efficacy calculation. As shown in the geographic breakdown of the total number of sequenced cases, the broad variety of variants originated primarily in

Latin America, which contributed about 80 cases to the 124 sequenced cases. In Europe, the 44 observed cases were strongly dominated by the Alpha strain in accordance with the general virus distribution in Europe.



(i)

Figure. Breakdown of different variants in a total of 124 adjudicated COVID-19 cases following sequencing-based strain identification (middle). Adjudicated and sequenced cases from Latin America (left) represent 80 out of the 124 cases while adjudicated and sequenced cases from Europe (right) represent 44 out of 124 cases.

Primary Data (data cut-off from June 18, 2021)

Primary data was published in The Lancet on November 23, 2021. Overall, CVnCoV demonstrated a vaccine efficacy of 48% against COVID-19 disease of any severity. In the highly dynamic variant environment, the HERALD trial met the prespecified success criteria for efficacy against symptomatic COVID-19 of any severity and for efficacy against moderate-to-severe COVID-19, as defined in the protocol.

The primary efficacy analysis included 12,851 participants in the CVnCoV group and 12,211 in the placebo group. The mean observation period, starting 15 days after administration of the second dose, was 48.2 days. Vaccine efficacy against COVID-19 of any severity was 48.2% in the overall primary efficacy annaïves set of SARS-CoV-2-naive participants, and 52.5% in those aged 18–60 years. Vaccine efficacy against moderate-to-severe COVID-19 was 70.7% overall and 77.2% in participants aged 18–60 years. There were too few participants aged 61 years or older who developed COVID-19 to allow a meaningful estimate of efficacy in this age group.

HERALD was conducted in an unprecedented evolving landscape that reflects the changing reality of the global COVID-19 pandemic, with an increasing number of SARS-CoV-2 variants adding additional challenges to the assessment of COVID-19 vaccine candidates. Sequence data were available for 184 of 207 adjudicated cases in people aged 18–60 years. About 50% of cases of COVID-19 in our trial were caused by variants of concern, 35% were caused by variants of interest, as classified by WHO in September 2021, and about 3% were caused by wild-type, with the remaining 11% caused by other variants. Although we were only able to evaluate vaccine efficacy against these variants in participants aged 18–60 years, the results indicate that the vaccine had similar efficacies against Alpha, Gamma and Lambda variants. Many newly emerged strains have shown increased transmissibility, and differences in neutralizing antibody activity against these strains might alter vaccine efficacy.

Efficacy of CVnCoV against virologically confirmed COVID-19 occurring 15 days or more after the second dose in the primary efficacy analysis set

	CVnCoV		Placebo		Vaccine efficacy (95% CI)
	n/N	Person-years	n/N	Person-years	
COVID-19 of any severity					
Overall	83/12 851	1735·29	145/12 211	1569·87	48·2% (31·0–61·4)*
18–60 years	71/11 532	1591·47	136/11 031	1449·23	52·5% (36·2–64·8)
≥61 years	12/1319	143·82	9/1180	120·64	–†
COVID-19 of any severity by region‡					
Europe	21/4091	684·22	33/3919	604·83	43·7% (–0·2 to 69·1)
Latin America	62/8760	1051·07	112/8292	965·03	49·2% (30·1–63·3)
COVID-19 of any severity by strain§					
Alpha variant (B.1.1.7/501Y.V2)	20/11 532	1591·47	42/11 031	1449·23	55·1% (23·5–73·6)
Gamma variant (P.1/501Y.V3)	9/11 532	1591·47	26/11 031	1449·23	67·1% (29·8–84·6)
Lambda variant (C.37)	13/11 532	1591·47	26/11 031	1449·23	52·8% (8·2–75·8)
Mu variant (B.1.621)	11/11 532	1591·47	17/11 031	1449·23	–†
Other	7/11 532	1591·47	13/11 031	1449·23	–†
Moderate-to-severe COVID-19					
Overall	12/12 851	1735·29	37/12 211	1569·87	70·7% (42·5–86·1)
18–60 years	9/11 532	1591·47	36/11 031	1449·23	77·2% (51·8–90·4)
≥61 years	3/1319	143·82	1/1180	120·64	–†
Severe COVID-19					
Overall	4/12 851	1735·29	10/12 211	1569·87	–†
18–60 years	2/11 532	1591·47	9/11 031	1449·23	–†
≥61 years	2/1319	143·82	1/1180	120·64	–†

*Table. *For COVID-19 of any severity, the 95.826% CI is provided (due to adjustment for multiplicity across interim analyses). †Not reported; the number of cases was too low to be statistically meaningful. ‡Vaccine efficacy by region was evaluated post-hoc. §Efficacy against strains was evaluated in adjudicated and sequenced cases in participants aged 18–60 years; other strains include B.1 lineage SARS-CoV-2.*

Overall, the two-dose regimen of CVnCoV had an acceptable safety profile and was efficacious in the prevention of symptomatic COVID-19 in adults. the clinical implications of CVnCoV's 70.7% efficacy against moderate-to-severe COVID-19, nearly all cases of which were caused by variants of concern or variants of interest, suggest a high potential for a positive impact on public health. Access to vaccines protecting against moderate-to-severe disease, and thus preventing disruption to the normal functioning of hospitals and intensive care units, is essential to prevent non-COVID-19-associated morbidity and mortality.

CVnCoV Phase 2a Clinical Trial

We initiated a Phase 2a clinical trial for CVnCoV in September 2020 for which all subject follow-up times have been completed as per trial protocol. The first clinical data readout was published in Vaccines on March 25, 2022.

The Phase 2a clinical trial is a partially observer-blind, multi-centered, controlled, dose-confirmation trial, and enrolled 674 participants. In this trial, we assessed the reactogenicity and immunogenicity in younger (18–60 years of age) and older (>60 years of age) adults after two or three 12 µg CVnCoV doses. The third dose was administered as per protocol either four weeks (>60 years of age) or five months (18–60 and >60 years of age) after the second dose in a subset of subjects to assess the age-related need for a booster vaccination. Neutralizing antibody responses were measured against the SARS-CoV-2 wild-type and Delta variant after the administration of a third dose of the CVnCoV vaccine in a subset of the phase 2a trial participants. Participants' SARS-CoV-2 serostatus was det82abellingtrospectively after enrollment in the trial and only data from either SARS-CoV-2-naïve participants (on all time points) or pre-exposed participants at baseline were included in the analysis.

We compared the neutralizing antibody responses to the wild-type and Delta variant induced after a third dose of CVnCoV. Four weeks after the third dose administered on day 57 or day 180, neutralizing antibody geometric mean titers (GMTs) increased against both the wild-type and Delta variant in SARS-CoV-2-naïve participants above the levels observed on day 43 after the first two doses. This demonstrates that the first two doses of CVnCoV induced immune memory. The neutralizing antibody GMTs against Delta were lower than those against wild-type on day 43 after the two doses, but reached similar levels, or higher as those for the wild-type after the third dose, demonstrating that a robust immune response against Delta variant was induced. These findings are consistent with other studies showing that homologous and heterologous mRNA booster vaccines increased immune responses against SARS-CoV-2 variants. In participants aged >60 years, the day 180 dose induced higher GMTs and seroconversion rates for Delta than the day 57 dose. The results suggest that a third dose administered at a later time-point is potentially more immunogenic than the earlier third dose, at least in individuals aged >60 years. We compared the immune responses to CVnCoV by age, because older individuals are at a higher risk of serious SARS-CoV-2 disease. In younger participants, GMTs for wild-type and Delta were about 2-fold higher than those in adults aged >60 years after 2 doses of CVnCoV and about 2.5-fold higher after the day 180 dose. However, the GMTs were higher after three doses than after two in both younger and older individuals, suggesting all participants benefitted from the third dose on day 180.

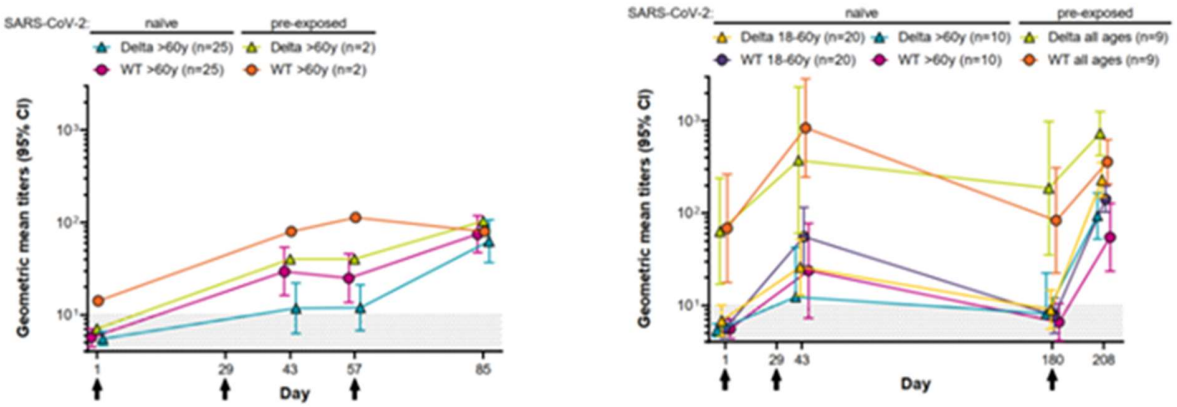


Figure. Neutralizing antibody response against wild-type SARS-CoV-2 virus and Delta variant after CVnCoV vaccination. The geometric mean titers (GMTs) of neutralizing antibodies with 95% confidence intervals (CIs) to wild-type (WT; filled circles) and Delta (filled triangles) are shown. (Left) Participants aged >60 years with a third dose on Day (D)57 and (right) participants aged 18–60 years and >60 years with a third dose on D180. SARS-CoV-2-naïve (seronegative for N protein throughout the trial period) and SARS-CoV-2-pre-exposed (seropositive for N protein at baseline) participants are indicated by color. The black arrows indicate the days of vaccinations: day 1 (baseline), day 29 (left, right) and day 57 (left) or day 180 (right)). n = number of participants with available data per group for all time points. Values above the black-dotted region (≥10) were considered positive.

We previously reported that two doses of CVnCoV-induced seroconversion in more than 60% of individuals who were immunologically naïve for SARS-CoV-2, although GMTs waned to baseline levels on day 180 in our phase 1 and 2a studies. Here, we observed that SARS-CoV-2-pre-exposed individuals still had measurable neutralizing antibodies against both wild-type and Delta up to six months after the first two doses. This indicates that two doses of CVnCoV induced a more potent and longer-lasting immune response against the wild-type and Delta variant in pre-exposed individuals, compared with SARS-CoV-2-naïve individuals. The participants who were naturally pre-exposed by a SARS-CoV-2 infection and who received the day 180 booster had the highest day 208 wild-type and Delta neutralizing response compared to those who were naïve at baseline.

	D57 Dose >60 Years		D180 Dose >60 Years		D180 Dose 18–60 Years	
	Wild-Type	Delta	Wild-Type	Delta	Wild-Type	Delta
GMT (95% CI)						
D43	29.5 (16.3–53.5)	11.8 (6.3–22.1)	23.8 (7.3–77.5)	12.3 (3.6–42.6)	55.6 (26.8–115.2)	25.9 (12.8–52.5)
D85	74.6 (46.9–118.9)	62.8 (36.8–107.2)	-	-	-	-
D208	-	-	54.6 (23.3–128.4)	93.5 (52.4–167.0)	141.7 (101.9–197.1)	230.2 (148.8–356.1)
Seroconversion [a], *n*/N (%)						
D43	16/25 (64%)	5/25 (20%)	5/10 (50%)	2/10 (20%)	15/20 (75%)	10/20 (50%)
D85	23/25 (92%)	20/25 (80%)	-	-	-	-
D208	-	-	9/10 (90%)	10/10 (100%)	20/20 (100%)	20/20 (100%)
GMFR [b]						
D43	5.2	2.1	4.3	2.3	9.8	3.8
D85	13.2	11.4	-	-	-	-
D208	-	-	9.8	17.4	25.1	33.7

In conclusion, a third CVnCoV dose induced strong neutralizing antibody responses against the SARS-CoV-2 wild-type virus in adults aged 18–60 and >60 years, demonstrating that the first two doses induced immune memory. The third dose induced similar levels of neutralizing responses against the wild-type virus and the Delta variant in both naïve and pre-exposed participants. This is in alignment with the current knowledge from licensed COVID-19 vaccines that a third dose is beneficial against SARS-CoV-2 variants. Although the development of CVnCoV has stopped, these cross-neutralizing immune responses against SARS-CoV-2 variants are promising for the next-generation SARS-CoV-2 vaccines, which are based on the same mRNA platform and are being optimized for variants.

CVnCoV Phase 1 Clinical Trial

We initiated a Phase 1 clinical trial for CVnCoV in June 2020 for which all subject follow-up times have been completed as per trial protocol. Data from an interim analysis of the Phase 1 trial was published in Wiener klinische Wochenschrift on August 10, 2021.

The Phase 1 trial was conducted as a partially blinded, placebo-controlled, dose-escalation, first in human, clinical trial to evaluate the safety, reactogenicity and immunogenicity after 1 and 2 doses of the investigational SARS-CoV-2 mRNA vaccine, CVnCoV, administered intramuscularly in healthy adults 18 to 60 years of age. The Phase 1 trial was conducted at three clinical sites in Germany and one clinical site in Belgium. The Phase 1 trial data featured below is based on an interim analysis with 245 adults assigned to five dose groups between 2µg and 12µg of CVnCoV. The dose groups included 2µg (n=47), 4µg (n=48), 6µg (n=46), 8µg (n=44), 12µ (n=28) or placebo (n=32). The majority of the participants recruited in each dose group were seronegative, with several seropositive participants (i.e., participants that were previously infected with SARS-CoV-2). All of the subjects received two doses of CVnCoV on days 1 and 29.

The primary objective of the Phase 1 study was the assessment of safety and reactogenicity at all tested doses. The vaccine candidate appeared safe and to have an acceptable reactogenicity profile at all doses from 2µg to 12µg, including participants known to be SARS-CoV-2 seropositive at baseline. There were no vaccine-related serious adverse events.

In SARS-CoV-2-naïve participants there was a dose-dependent increase in incidence and severity of local solicited adverse events. Local reactions were almost exclusively cases of transient mild to moderate injection site pain with a median duration of 1 day; only 3 first doses of the 415 total administered doses of CVnCoV resulted in severe local pain. The frequency and severity of solicited systemic adverse events also increased with dosage level and were generally of higher intensity after the second dose than the first. Systemic adverse events mainly consisted of transient mild or moderate headache and fatigue, and to a lesser extent myalgia and chills, with fever being observed less frequently. Severe solicited adverse events decreased or rapidly disappeared, mostly within 24–48 h of onset. Overall, the same reactogenicity profile has been reported for other mRNA SARS-CoV-2 vaccines.

In participants who were SARS-CoV-2 seropositive at the time of vaccination the local and systemic reactogenicity profiles were similar to the SARS-CoV-2- naïve participants.

First-generation SARS-CoV-2 mRNA vaccine candidate, CVnCoV, was generally well tolerated

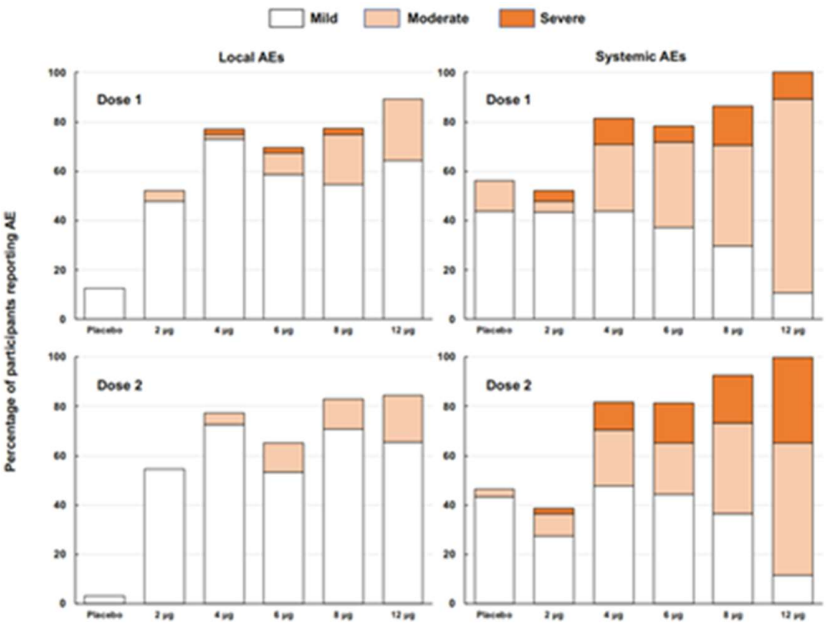


Figure. Overall incidence rates (%) of solicited local and systemic adverse events (AEs) per dose group after the first and second doses with severity classified as mild (Grade 1, white columns), moderate (Grade 2, light orange columns) or severe (Grade 3, orange columns).

Main secondary objectives were evaluations of humoral immune responses including SARS-CoV-2 spike protein-specific IgG and receptor-binding domain (RBD) IgG antibodies as well as SARS-CoV-2 virus neutralizing antibodies. The subset of seropositive participants was also included to assess whether the baseline serostatus impacted any of the assessed parameters.

Robust immune responses were observed in all groups of initially seronegative participants, with median titers comparable with those in sera from patients convalescing after COVID-19 infection. At day 29, 4 weeks after the first dose, there were small dose-dependent increases with seroconversion rates of 6–26% across vaccine groups, with more marked increases in all groups on day 36, with 50–74% seroconverting. The seroconversion rate continued to increase to 69–95% at day 43 when median titers were 1738 (IQR: 725–3094), 2239 (2175–3079), 2818 (12–6086), 3135 (56–5349) and 5118 (485–6319), in 2, 4, 6, 8 and 12µg groups, respectively. Notably, the 12µg group value at day 43 was comparable to the median titer of 6381 (5400–12432) in convalescent sera.

The applied human convalescent patient sera panel consisted of 67 convalescent patients, who exhibited multiple symptoms and of which 16 patients (24%) were hospitalized. Binding and neutralizing antibody titers of these

convalescent patients are based on blood samples collected mainly at the peak time of humoral response, between four to eight weeks after diagnostic confirmation of a SARS-CoV-2 infection.

The ELISA IgG antibody titers against RBD generally reflect the same dose-dependent profile as IgG titers against the spike protein, with substantial increases in titers 7 days (day 36) after the second dose when seroconversion rates were 17–65%. There was a further increase by day 43 when the seroconversion rates were 82% and 91% in the 8 and 12μg groups with median titers of 1228 (1325–2542) and 1572 (535–2971), respectively, comparable to the median of 1448 (726–5391) observed in convalescent sera.

First-generation SARS-CoV-2 mRNA vaccine candidate, CVnCoV, elicited humoral immune responses

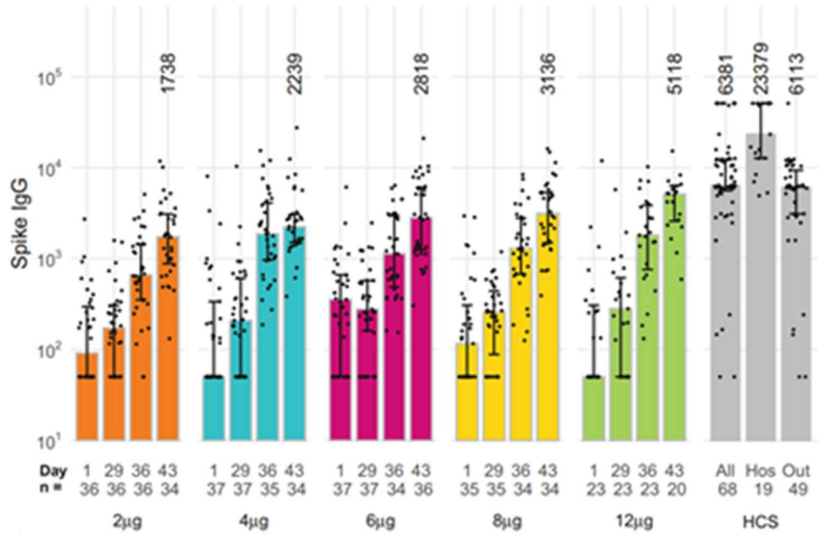


Figure. Anti-Spike protein IgGs in the different study groups and convalescent sera measured by ELISA. Bars show median values per group at each study time point, individual GMT values for each sample are shown as diamonds. Numbers show median values at day 43, two weeks after the second vaccination, for each group and the convalescent sera panel.

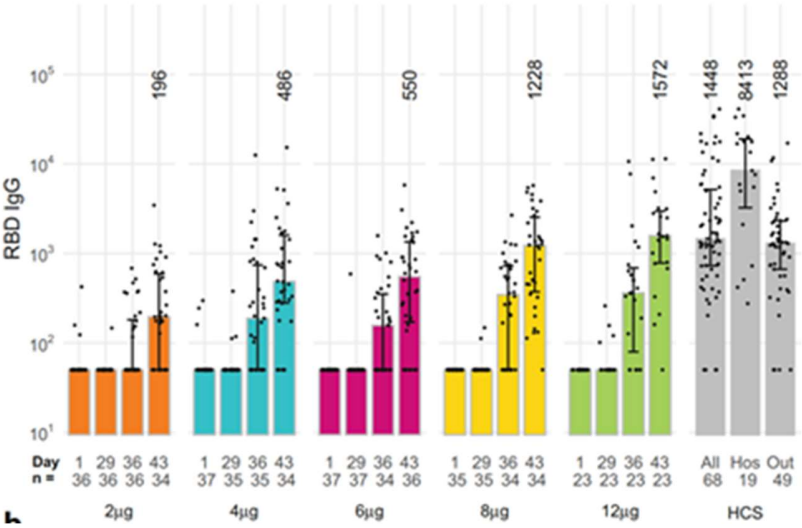


Figure. Anti-RBD IgGs in the different study groups and convalescent sera measured by ELISA. Bars show median values per group at each study time point, individual GMT values for each sample are shown as diamonds. Numbers show median values at day 43, two weeks after the second vaccination, for each group and the convalescent sera panel.

The observations of IgG antibody responses to the spike protein and RBD correlated with SARS-CoV-2 neutralizing titers. This response was less obviously dose-dependent from the available samples, but across the groups 31–59% had seroconverted at day 36 from baseline, increasing to 56–83% at day 43. At day 43 median MN_{50} in the 8 µg and 12 µg groups (57 MN_{50}, 7–113 and 57 MN_{50}, 28–113) overlapped with the range observed in convalescent sera which had a median titer of 113 MN_{50}, 57–453.

Since an imbalance between neutralizing versus binding antibodies could hypothetically lead to immune-mediated disease enhancement, we calculated the ratios of neutralizing and IgG antibodies to spike protein and RBD in 12µg vaccinees at day 43 and convalescent sera. As the ratios in vaccinees were very close to those in convalescent sera after natural infection we hypothesized that the CVnCoV mechanism of action mimics the natural immune response to RNA viruses.

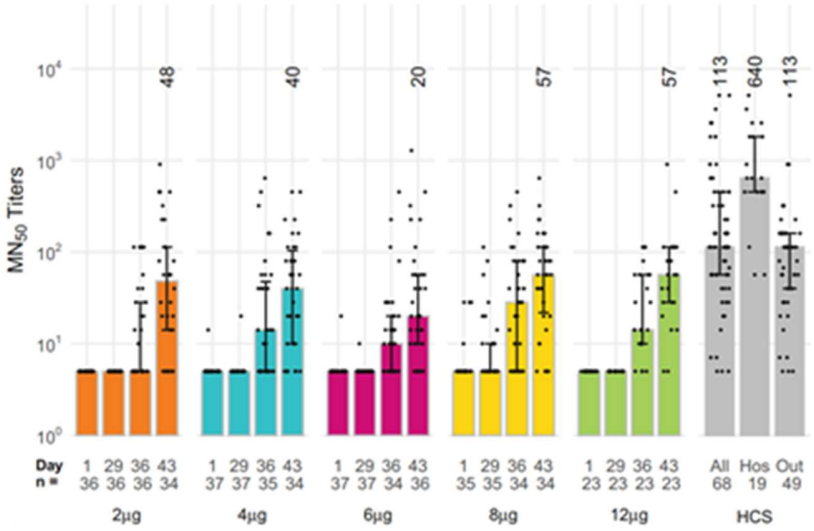


Figure. Anti-SARS-CoV-2 virus-neutralizing titers in the different study groups and convalescent sera measured by micro-neutralization. Bars show median values per group at each study time point, individual GMT values for each sample are shown as diamonds. Numbers show median MN50 values at day 43, two weeks after the second vaccination, for each group and in the convalescent sera panel.

In initially SARS-CoV-2-seropositive participants the lowest doses of CVnCoV, 2µg or 4µg induced increases in antibody titers against the spike protein and RBD binding antibodies and neutralizing antibodies within 1 week after the first vaccination.Median RBD titers increased from 204 (IQR: 87, 366) at day 1 to 2494 (1399, 3204) at day 8 in the eight seropositive participants who received a 2µg dose of CVnCoV; in the 4µg group the respective increase was from 183 (50, 2296) to 3737 (999, 6814). There was no further increase after the second dose and median titers at day 43 were 3017 (IQR: 1576, 5828) and 5107 (2772, 9889) in the 2µg or 4µg groups, falling within the same range as the seronegative participants after two 12µg doses. In seropositive subjects median MN_{50} titers were 108 (IQR: 40, 339) and 273 (113, 386) at day 1 in the 2µg or 4µg groups (n= 8 in each), increasing to 679 (IQR: 453, 905) and 1093 (640, 1920) at day 8, respectively. After small further increases at day 36 following the second dose to 1545 (IQR: 773, 1810) and 1810 (1543, 3840) titers then remained stable at least up to day 43.

First-generation SARS-CoV-2 mRNA vaccine candidate, CVnCoV, boosted preexisting immune response

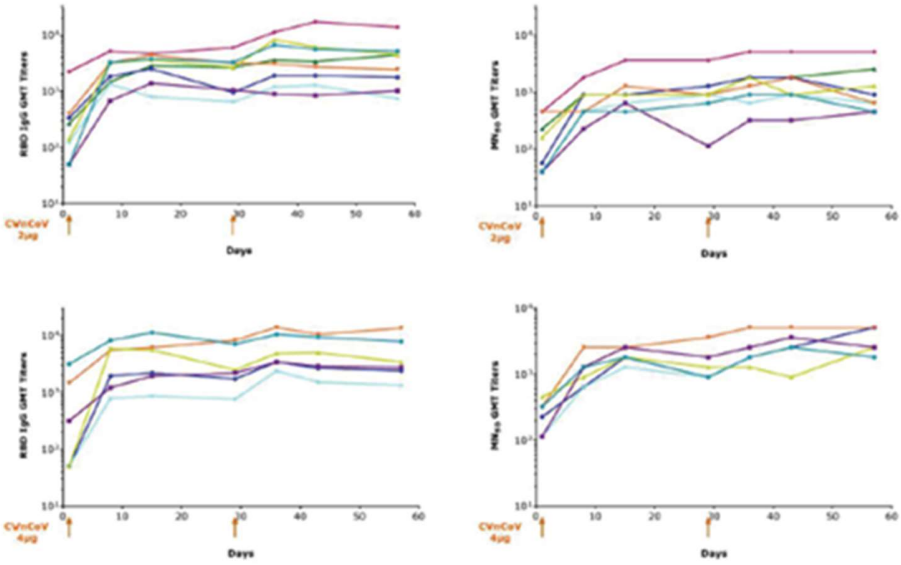


Figure. Boosting of antibody responses in seropositive subjects. Seropositive subjects were vaccinated either with 2µg (upper panel) or 4µg (lower panel) of CVnCoV on day 1 and 29. RBD binding antibodies as well as SARS-CoV-2 neutralizing antibodies were analyzed at multiple time points. Lines show individual subjects in both dose groups.

In summary, all investigated dosages elicited an immune response against SARS-CoV-2. Induction of an adaptive humoral immune response was demonstrated by the increase in neutralizing antibodies; 56–77% of participants achieved MN_{50} seroconversion 2 weeks after 2 doses of 2–8µg and 83% after 2 doses of 12µg. Neutralizing activity was associated with marked spike protein-specific and RBD-specific IgG antibody responses; notably 100% of 12µg recipients seroconverted to either spike protein or RBD by day 43. The spike protein IgG and neutralizing antibody responses were low but detectable after the first vaccination, but all markedly increased within 7 days of the second vaccination indicating efficient priming by the first dose.

CVnCoV was well tolerated in SARS-CoV-2 seropositive participants in whom immune memory appeared to have been induced by the natural infection. Low doses of CVnCoV (either 2 or 4µg) were able to induce greater than 10-fold increases in antibody titers within 1 week, even in participants with low baseline antibody titers, while there was little or no response in seronegative participants 1 week after the first dose. Furthermore, a second vaccination in that population did not lead to a further increase in antibody titer, suggesting that persons with prior SARS-CoV-2 infection might not benefit from additional vaccinations and could be limited to a single dose application.

Furthermore, as part of the Phase 1 study, we administered higher doses of 16 µg and 20 µg to investigate the boundaries of the safety window and for completion of the assessments of the present groups. Subjects of all study groups were being followed up with until one year post-vaccination.

Clinical Rabies Vaccines (first-generation mRNA backbone): CV7202

CV7202 is our rabies vaccine candidate encoding the rabies virus glycoprotein, RABV-G protein formulated with LNPs. RABV-G is one of only five proteins encoded by the rabies virus. As a dominant part of the virus surface and its role in virus entry into the host cell, RABV-G is the only target of virus-neutralizing antibodies conferring protection against challenge.

A Phase 1 clinical trial for CV7202 initiated in the fourth quarter of 2018 has been completed with all follow-up times as per trial protocol. Data of the Phase 1 trial was published in Vaccine on January 22, 2021.

Rabies Disease Background

Rabies is an infectious viral disease that is almost always fatal following the onset of clinical symptoms. In up to 99% of cases, domestic dogs are responsible for rabies virus transmission to humans.

Rabies can affect both domestic and wild animals. It is spread to people through bites or scratches, usually via saliva. According to the World Health Organization, rabies remains an important disease, leading to close to 60,000 human deaths every year worldwide, with 95% of human deaths occurring in Asia and Africa regions, where dog rabies is endemic.

There are commercially available rabies vaccines that are both safe and effective. They can be used to prevent rabies before and for a period of time after exposure to the virus (such as by a dog or bat bite). However, these vaccines require multiple vaccinations both before and after virus exposure. Additional major limitations for the commercially available rabies vaccines are cost and access, particularly in the developing world, as well as supply shortages.

CV7202 Phase 1 Clinical Trial

The Phase 1 clinical trial for CV7202, initiated in the fourth quarter of 2018, was conducted as a non-randomized, open-label, controlled, dose-escalation, multi-center Phase 1 study evaluating safety, reactogenicity and immunogenicity of different dosages of CV7202 administered as intramuscular injections in healthy adults 18 to 40 years of age in one- or two-dose regimens. A control group received Rabipur according to the standard schedule. The primary objective was assessment of safety and reactogenicity up to 28 days after administration by intramuscular injection of either a first or second dose of in a range of increasing dosages starting at 5 µg. Main secondary objectives were the evaluation of safety follow-up to two years after vaccination and comparison of the immune response to CV7202 with the licensed rabies vaccine, Rabipur®, administered in its recommended three dose schedule. Following observation of excess reactogenicity to 5µg CV7202 the protocol was modified to assess lower (1µg and 2µg) rather than higher dosages.

Patient demographics

The study enrolled a total of 53 subjects in three CV7202 groups, 1µg (n=16), 2µg (n=16) and 5µg (n=10), and one Rabipur group (n=11) as control. In both the CV7202 1µg and 2µg groups, all subjects received a single dose of CV7202 on day 1 with half the cohort (n=8) in each dose group receiving a second dose of CV7202 on day 29. In the CV7202 5µg group, the 10 subjects received a single dose of CV7202 on day 1. Of the 11 subjects enrolled in the Rabipur group received, 10 subjects received the licensed three-dose primary vaccination schedule on days 1, 8 and 29, respectively.

Interim safety results

Following observations of high reactogenicity when using the 5µg dose of CV7202 we found 1 and 2µg dosages were better tolerated, with no safety concerns. Preliminary investigation of the 5µg response suggests that high innate immune responses driven by type 1 interferon and cytokines and strong induction of toll-like receptor signaling pathways observed in most participants, might have contributed to unfavorable reactogenicity and immunogenicity profiles. In this small trial, CV7202 appeared to be safe, with no vaccine-related serious adverse events or withdrawals due to adverse events. Although over half the recipients of the highest dose of CV7202 reported severe solicited systemic or unsolicited adverse events, the reactogenicity profiles of the lower doses of CV7202 (1 and 2µg) were more acceptable. The 2µg dose elicited a limited number of severe adverse events in the first 24 h post-vaccination. Local reactions to these dosages consisted almost exclusively of transient mild to moderate injection site pain. Systemic adverse events mainly consisted of transient mild or moderate headache, fatigue and chills, and any cases that were described as initially severe rapidly moderated and resolved, most within 48– 72 h and all within the 7-day reporting period. There were no major changes in reactogenicity after the second dose when compared with the first, although the numbers of participants are small.

Interim immunogenicity results

We showed that all recipients, despite the low amount of mRNA included in the vaccine, had functional antibody responses after two 1 or 2 lg doses of CV7202, with GMTs of both rabies-specific neutralizing and RABV-G-specific IgG antibodies that were not significantly lower than those observed after three doses of licensed rabies vaccine. The neutralizing response profile of CV7202 displayed a strong correlation with production of RABV-G-specific IgG antibodies following two doses. There were also transient increases in IgM antibodies but not IgA after second doses of Rabipur and CV7202 (data not shown), but direct comparison of the kinetics of these responses is complicated by the different vaccination schedules—1 and 8 days for licensed vaccine and 1 and 29 days for CV7202—and no second 5 lg dose. The large IgG responses evident 7 days after the second vaccination, and their direct correlation with the neutralizing response suggest the first dose of lower dosages of CV7202 had primed B cells to respond to the second vaccination with an anamnestic response. Although responses with two doses of 1 or 2 lg CV7202 were not significantly lower than those induced by three doses of Rabipur, it may be interesting to compare CV7202 and Rabipur responses when used in the same schedule of three doses at Days 1, 8 and 29. This interim report presents the immune responses up to four weeks after the second dose, but participants will be monitored for two years to assess long-term safety and persistence of the immune response. Further investigations of antibody responses after a booster vaccination, possibly with lower doses, will be necessary to determine whether long-term immune memory has developed, together with a qualitative comparison of avidity, IgG subclasses and B cell responses for CV7202 and the licensed vaccine.

Virus neutralizing titer (VNT) responses were detected in all four study groups. Following a 5µg dose of CV7202, VNT levels ≥ 0.5 IU/ml were observed from day 29 in two of nine (22%) participants and these responses were maintained up to day 57, the last timepoint assessed.

Neutralizing antibody titers in all four study groups following immunization with CV7202

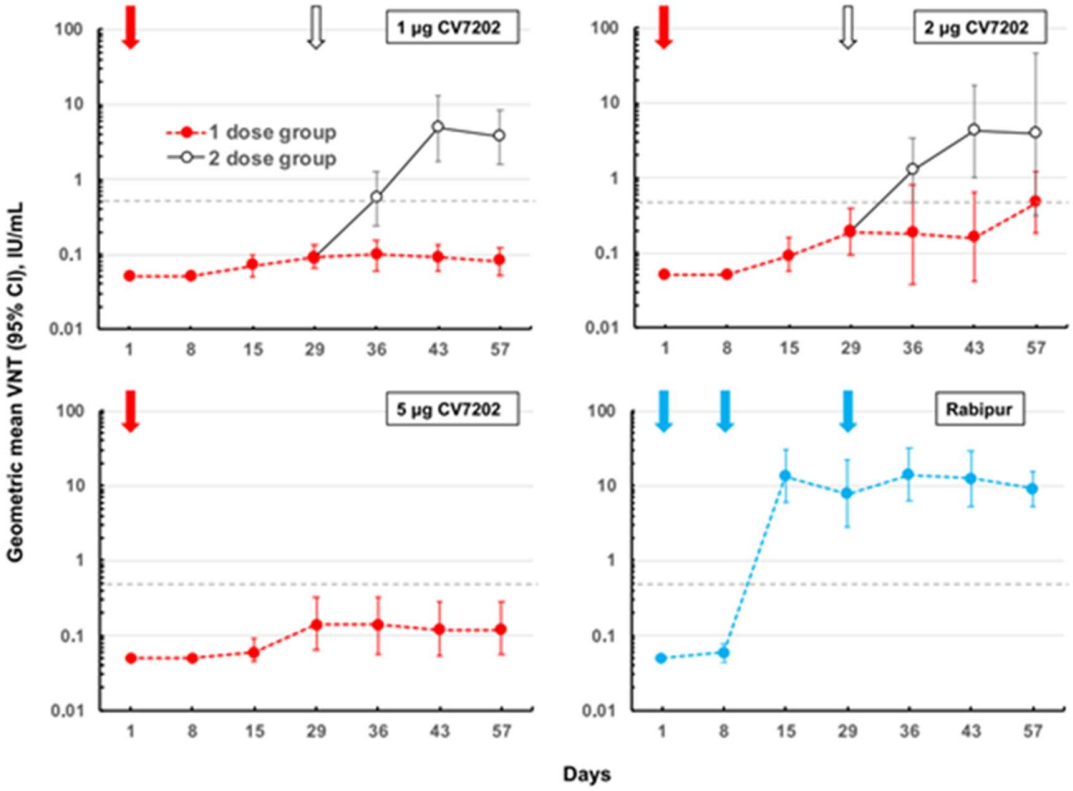


Figure. Geometric mean virus neutralizing titers (with 95% CI) in the four study groups after immunization (indicated by arrows) with CV7202 or Rabipur. Dashed line indicates level considered adequate by the WHO (0.5 IU/mL).

The 1µg and 2µg CV7202 groups also displayed small detectable responses following the first dose. These were more pronounced in the 2µg group in which 5 of 16 (31%) had VNT levels ≥ 0.5 IU/ by day 29, whereas no participants in the 1µg group displayed an adequate response (0.5 IU/mL) by day 29 after one dose. Responses were markedly increased following the second dose on day 29 such that 5 of the 8 (63%) participants who received a second dose of 1µg and 7 of 8 (83%) participants who received a second dose of 2µg had titers ≥ 0.5 IU/mL at day 36. All participants (100%) in both the 1µg and 2 µg groups reached this level at day 43. Geometric mean titers (GMTs) were higher than 0.5 IU/mL at day 36 in both groups and were further increased at days 43 and 57. Peak GMTs were achieved at day 43 with 1µg (4.8 IU/mL 95% CI:1.77–13.0) and 2µg (4.2 IU/mL 1.02–17.2) of CV7202. All participants in the Rabipur group had titers ≥ 0.5 IU/mL by day 15, 7 days after the second vaccination and this 100% rate was maintained up to day 57. Rabipur achieved a peak GMT of 13.5 IU/mL 5.95–30.6) IU/mL at day 15, 7 days after the second dose. The GMT did not further increase following a third dose of Rabipur but was maintained at 9.1 IU/mL through to day 57. Day 43 GMTs after two doses of CV7202 were not statistically significantly lower than those achieved with three doses of Rabipur.

Rate of responders in all four study groups following immunization with CV7202

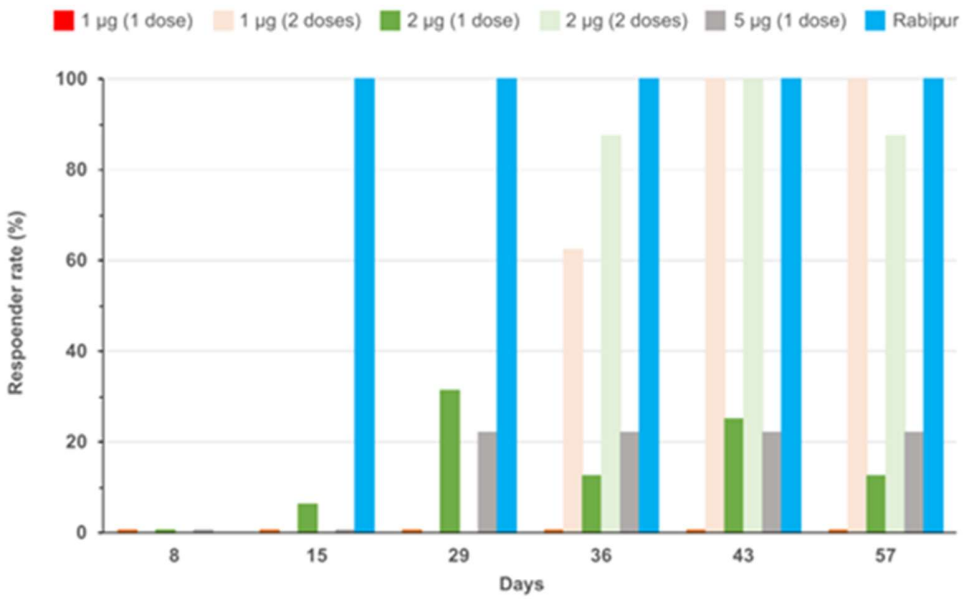


Figure. Responder rates (percentages of each group with a VNT ≥ 0.5 IU/mL) in the four study groups after immunization with CV7202 or Rabipur. Rates represent the numbers of participants achieving the protective VNT of 0.5 IU/mL. The 1 and 2µg CV7202 groups consisted of 16 participants each for days 8, 15 and 29, and 8 participants each for days 36, 43 and 57. The 5µg CV7202 group consisted of 10 participants for days 8 and 15, 9 participants for days 29, 36, 43 and 57. The Rabipur group had 10 participants at each timepoint.

Anti-RABV-G IgG antibodies displayed the same pattern of responses as VNTs. There were detectable increases after one dose with 6 of 16 (38%), 11 of 16 (69%) and 8 of 9 (89%) participants in the 1, 2 and 5µg dosage groups developing low levels of RABV-G-specific IgG, respectively. GMTs were 853 U/mL (95% CI: 455–1599), 1581 U/mL (899–2780) and 2409 U/mL (1113–5215) at day 29 after the first dose in the 1, 2 and 5µg CV7202 groups, respectively, and these levels did not further increase in one dose groups. Much larger increases were observed after second vaccinations, peaking at 34,186 U/mL (13253–88185) and 20,707 U/mL (5592–76678) at day 43 in the 1 and 2µg groups, respectively. There were highly significant positive Spearman correlations between VNT and IgG titers, particularly after two doses of CV7202 ($r2 = 0.8319$, $p < 0.0001$). An IgG response was not detected one week after the first Rabipur vaccination; GMTs were 461 and 464 at days 1 and 8, respectively, but rapidly increased to 12,460 U/mL (95% CI: 6575–23611) at day 15, 7 days after the second dose. A further incremental increase to 33,373 U/mL

(21236–52447) was observed after the third dose and this level was sustained to day 57. As for the VNT, RABV-G IgG GMTs at Day 43 after two doses of CV7202 were not statistically significantly lower than those achieved with three doses of Rabipur.

RABV-G-specific immunoglobulin antibodies in all four study groups following immunization with CV7202

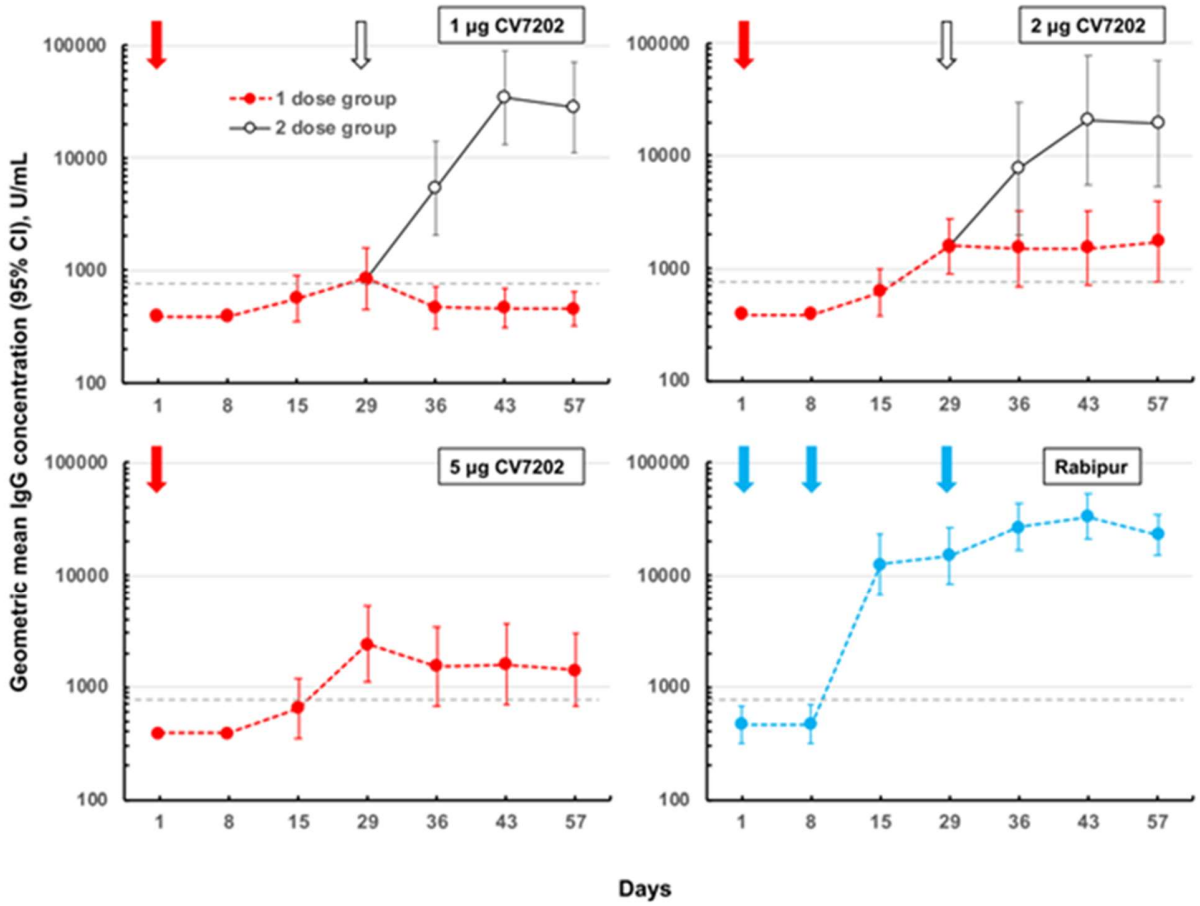


Figure. GMTs (with 95% CI) of RABV-G-specific Ig responses assessed by ELISA. IgG concentrations after immunization with one (red arrow) or two (open arrow) doses of CV7202 or three doses of Rabipur (blue arrows). Dotted lines indicate LLOQ.

Correlation of RABV-G-specific neutralizing and binding antibodies titers after 1 or 2 doses of CV7202

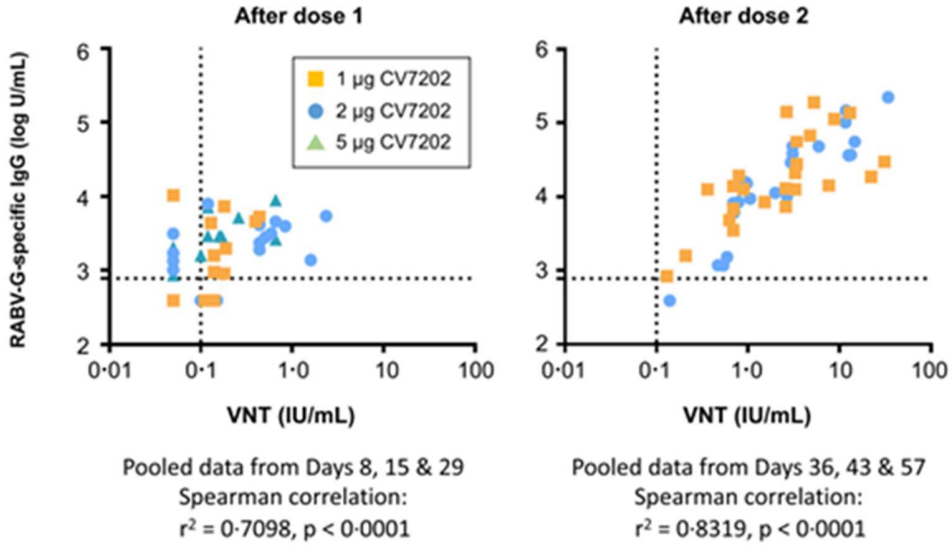


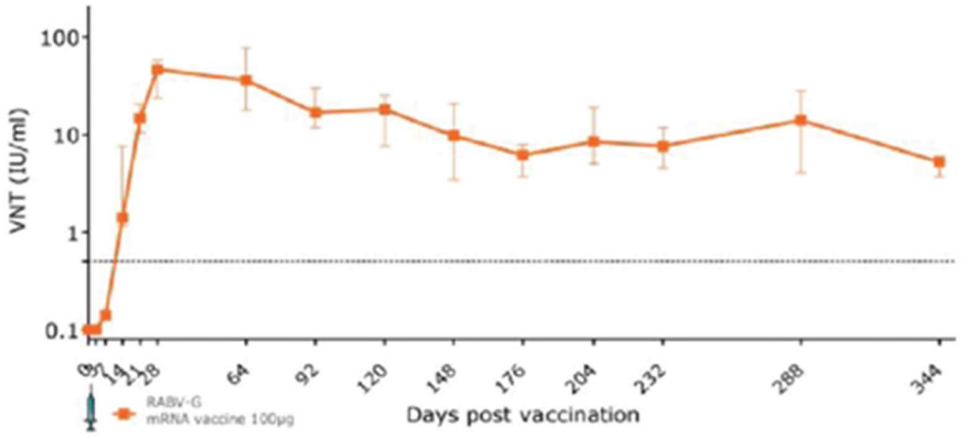
Figure. Correlation of titers of RABV-G-specific neutralizing activity (VNT) and IgG antibodies after one or two doses of CV7202.

In summary, despite the low amount of mRNA included in the vaccine, all recipients had functional antibody responses after two 1 or 2µg doses of CV7202, with GMTs of both rabies-specific neutralizing and RABV-G-specific IgG antibodies that were not significantly lower than those observed after three doses of licensed rabies vaccine. The neutralizing response profile of CV7202 displayed a strong correlation with production of RABV-G-specific IgG antibodies following two doses. The large IgG responses evident 7 days after the second vaccination, and their direct correlation with the neutralizing response suggest the first dose of lower dosages of CV7202 had primed B cells to respond to the second vaccination with an anamnestic response. Although responses with two doses of 1 or 2µg CV7202 were not significantly lower than those induced by three doses of Rabipur, it may be interesting to compare CV7202 and Rabipur responses when used in the same schedule of three doses at days 1, 8 and 29.

Preclinical Rabies Vaccines (first-generation mRNA backbone): CV7202

CV7202 was found to be highly potent in multiple animal studies and protected against the rabies virus infection in non-human primates. CV7202 leads to rapid generation of neutralizing antibodies that exceed the threshold agreed upon by the WHO for rabies protection. These results, obtained after a single administration in non-human primates, were sustained at high levels through at least 344 days post-vaccination.

CV7202 Induces Rabies-Neutralizing Antibodies After Single Administration in Non-Human Primates



Preclinical Influenza Vaccine (first-generation mRNA backbone): *CV-SSIV*

We believe that there is a significant market for a more and broader effective vaccine for influenza that protects over several seasons and that, in case of exceptional changes in the circulating strains, could also be customized to include specific and multiple new strains. We believe that our platform offers the potential for the rapid development of safe and effective vaccines. We believe that the mRNA-based vaccines allows us to address several of the limitations of the currently available seasonal vaccines.

We believe key potential advantages of our approach to traditional seasonal vaccines include:

- Commercial seasonal vaccines usually contain three to four strains of the virus and may offer limited protection as the virus mutates. Adding more strains or further antigens, which can increase or broaden the level of protection conferred by the vaccine, might be an advantage of an mRNA-based vaccine.

- mRNA-based vaccines offer greater production flexibility to adapt to circulating seasonal strains. An mRNA influenza vaccine can be generally produced in under three months from strain identification to a finished GMP product. This rapid vaccine development process would allow treatment of a larger fraction of patients before too many changes are introduced by viral mutations.

- Traditional egg-produced vaccines rely upon high-yielding production strains and often have to contend with egg-adaptation during passage, neither aspect is an issue for mRNA-based vaccination.

We are also developing a Supra Seasonal Influenza Vaccine, or SSIV. We believe that the initial step towards the development of an SSIV is the development of a multivalent, improved seasonal influenza vaccine. Based on performance of our mRNA next-generation influenza vaccine in preclinical studies, including broadening and persistence of immunity, this multivalent formulation could be considered a first-generation multi-year, supra-seasonal influenza vaccine. The characteristics for the mRNA-based seasonal influenza vaccines are a building block in the development of an SSIV where the induction of long-lasting, potent antibody responses, and the possibility to combine several antigens in one vaccine formulation in the absence of antigenic interference are key prerequisites.

CV-SSIV Overview

Our CV-SSIV contains a mixture of antigens derived from hemagglutinin, or HA, and neuraminidase, or NA, constructs, all from seasonal strains recommended by the WHO, targeting both Influenza A and B strains. The inclusion of NA supports a vaccine with extended breadth, given that NA is more conserved compared to HA, and has the potential to confer protection against drifted seasonal but also pandemic strains in upcoming seasons.

Preclinical Data for CV-SSIV

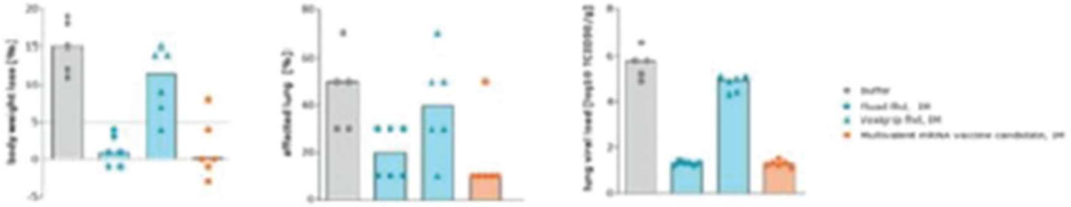
As part of our influenza program, we have evaluated mRNA-based influenza vaccines starting with a monovalent influenza vaccine followed by several seasonal multivalent influenza vaccines. Our preclinical experiments have shown that we can encode for multiple targets in our cocktail mRNA 94abelles without experiencing immuno-dominance.

In these preclinical studies, it was demonstrated that our vaccines induced hemagglutinin-inhibition, or HI, titers above the accepted threshold for protective immunity in ferrets. The immunogenicity of the seasonal influenza vaccine was further evaluated in ferrets testing the breadth of antibody response against historic seasonal viral strains. The HI titer induced by mRNA vaccination against specific isolates were comparable to Fluad produced for the same season. Fluad is the only licensed adjuvanted seasonal influenza vaccine and has been shown to outperform standard of care split vaccine in older adults and very young children. Retrospective studies of the past season could not show a difference between both types of vaccine.

In immunogenicity studies in ferrets, our multivalent influenza vaccine candidate 2, showed no antigenic interference as judged by HI titer due to the addition of more antigens to multivalent influenza vaccine candidate 1. HI titer against influenza A virus strains were over 1:40 and neutralizing antibody against influenza B virus were detected using a microneutralization assay. Additionally, functional anti-NA antibodies were induced against influenza A strains analyzed using an assay and titers were comparable to Fluad. Overall, the immune response to influenza A virus were comparable to Fluad, whereas the responses to influenza B virus were lower for our multivalent vaccine candidate 2 than for Fluad. We anticipate that this response will be significantly enhanced in humans who are influenza pre-immune.

As shown in the figure below, the seasonal multivalent vaccine candidate 2 was tested in a ferret challenge infection model. Ferrets were vaccinated with influenza mRNA vaccine candidate two delivered using LNPs or the licensed vaccine Vaxigrip (left light-blue column) and adjuvanted vaccine Fluad (right light-blue column) via needle-based injection on day 0 and 21 (2-dose regimen). Values from individual animals (dots) and the median (bars) are reported for each group (buffer control grey column). Four weeks after the last vaccination, animals were challenged with influenza A via intratracheal route. Four days after infection, animals were euthanized and virology and pathology were investigated in respiratory tissues. Multivalent vaccine candidate 2 induced better protection in the ferret model than the licensed non-adjuvanted split vaccine (Vaxigrip) and showed comparable activity to the adjuvanted vaccine Fluad.

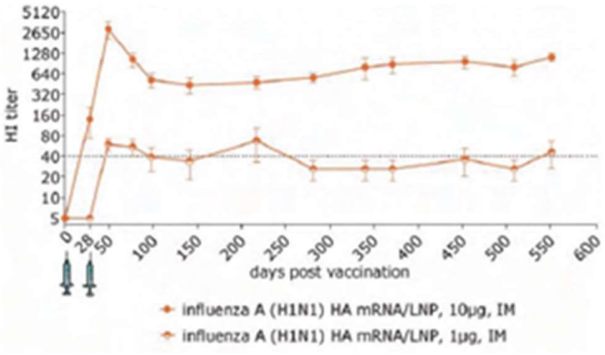
mRNA Vaccination Candidate Protected from Weight Loss and Viral Replication Comparable to the Adjuvanted Influenza Vaccine Fluad in Ferrets



Ferrets (n=6, female) were vaccinated with a multivalent influenza LNP/mRNA vaccine or the licensed vaccine Vaxigrip and adjuvanted vaccine Fluad®2017/2018 via i.m. needle-based injection on days 0 and 28. Four weeks post last vaccination animals were challenged with 106 TCID50 of influenza A/Netherlands/602/2009 H1N1 via intratracheal route. Four days after infection, animals were euthanized and virology and pathology was investigated: in body weight (A), affected lung tissues (B) and viral titers in the lung (C). Values from individual animals (dots) and the median (bars) are reported for each group.

As shown in the figure below, the longevity of antibody response was evaluated in NHP immunized with a monovalent HA vaccine, Cynomolgus monkeys were vaccinated with 1 or 10 µg LNP-formulated mRNA encoding HA of influenza A via intramuscular needle-based injection on days 0 and 28. Functional antibodies were determined in the serum of the immunized animals at the indicated time points using the HI assay. Our vaccine showed HI titers above the protective threshold (>1:40) for at least 1.5 years following a two-dose primary immunization series.

LNP-Formulated Influenza A H1N1 HA mRNA Vaccine Induce High and Long-Lasting Functional Antibody Titers in NHP



Respiratory Syncytial Virus (RSV) Program

Disease Overview

RSV is a leading cause of respiratory disease globally. The virus causes infections at all ages but young infants have the highest incidence of severe disease. The National Institute of Allergy and Infectious Diseases estimates that by the age of two years, almost all children will have been infected with RSV in the United States. Globally, RSV has been estimated to cause approximately 33 million cases of RSV-related acute lower respiratory tract infections, or LRTI, annually in children less than five years of age, with approximately three million cases requiring hospitalization, and approximately 60,000 dying from complications associated with the infection. In addition, RSV infections can be a significant problem for certain immunocompromised adults and high-risk older adults. Adults at highest risk for severe RSV infection include older adults, especially those 65 years and older, adults with chronic heart or lung disease and adults with weakened immune systems. According to the CDC, RSV is responsible for approximately 177,000 hospitalizations and 14,000 deaths annually in people over 65 years of age within the United States.

There are no effective RSV vaccines approved to date and the only approved prophylactic treatment is palivizumab, marketed as Synagis in the United States. Synagis is a monoclonal antibody for the prevention of RSV in premature babies or babies with underlying medical conditions of bronchopulmonary dysplasia or congenital heart disease. Synagis's highly restrictive label, combined with the high cost of prophylactic therapy, has limited wider uptake.

Historical Approaches to RSV Vaccines

In 1968, a formalin-inactivated whole RSV vaccine was tested for newly infected and immunized children but was not effective and resulted in vaccine-induced amplification of disease. Since the most severe cases of RSV occur in the first months of life, past approaches have focused on increasing the maternal immune response by developing maternal anti-RSV antibodies. To date, the efforts to develop maternal anti-RSV antibodies through administration of a vaccine have been unsuccessful.

While the reasons for the failure of RSV vaccines to protect against infection remain unclear, the lack of understanding regarding the identity of the natural protective immune response in subjects has challenged the development of an effective RSV vaccine. In certain previous clinical studies, an increase in the immune response has been detected but has not resulted in any further protection against the progression of the RSV infection. Currently, there are several vaccines for RSV in development, including subunit vaccines, attenuated vaccines and those delivering RSV antigens by recombinant vectors such as vaccinia virus or bovine-based systems.

Our Approach

The surface of RSV contains two glycoproteins: the attachment glycoprotein, or G, and the fusion glycoprotein, or F. Deletion of RSV G leads to a viable but attenuated virus, indicating that RSV G is not essential for viral entry. In contrast, the RSV F protein is essential to the viral replication process, as it facilitates pH-independent fusion of the viral

membrane with the host-cell plasma membrane, leading to infection of the host cell. Expression of RSV F on the surface of cells can also cause fusion with neighboring cells, leading to the formation of multinucleated syncytia. The F protein is expected to induce virus neutralization titer against both subtypes of RSV A and B.

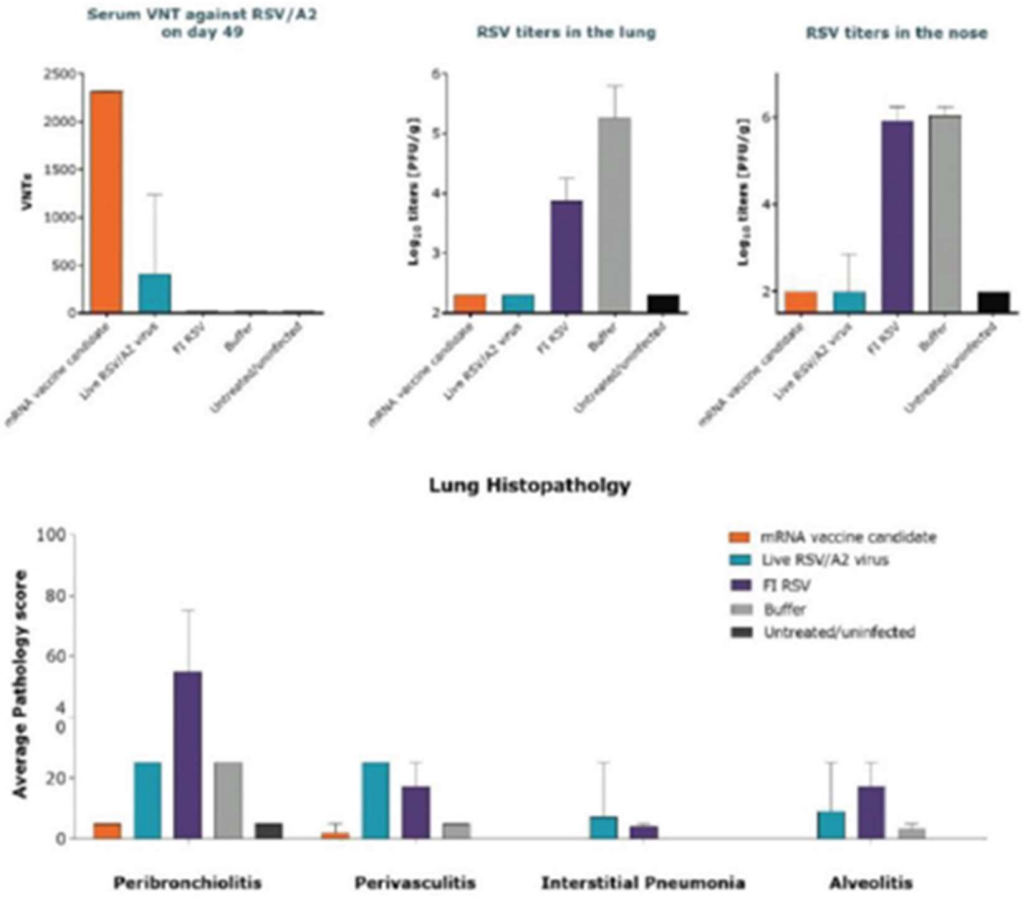
Our approach for the RSV program is based on delivering mRNAs encoding for the RSV F (fusion) protein. This is considered as an advantage over vaccines consisting of the glycoprotein G. Glycoprotein G determines the RSV subtypes and hence, vaccines that aim to protect against all RSV subtypes would need to include a glycoprotein from both RSV A and B each. Therefore, an approach targeting the RSV F as protective antigen has an advantage to target both RSV A and B. Consequently, we have been able to show that our vaccines encoding for RSV F induce high levels of virus neutralizing antibodies, a likely correlate of protection against RSV.

Preclinical Data

In preclinical studies, we showed that the delivery of our mRNA-based vaccines leads to the stimulation of TLR7, thus supporting affinity maturation of antibodies. In addition, we showed that antigen delivery via mRNA mediates correct protein folding and localization. For our RSV vaccine, we also analyzed the potential to minimize worsening immunopathology, a phenomenon also known as vaccine-dependent disease enhancement, or VDE, that may also be relevant for other respiratory viral infections such as for the novel SARS-CoV-2. Our RSV vaccine induces a balanced immune response, thus avoiding the Th2-biased response associated with enhanced respiratory disease or VDE.

In preclinical studies, we have demonstrated that our vaccines encoding for RSV F induce high levels of virus neutralizing antibodies, a likely correlate of protection against RSV. In a cotton rat challenge model, our RSV vaccine was compared to formalin-inactivated virus for evaluating enhanced respiratory disease and live RSV. Cotton rats vaccinated twice at day 0 and day 28 showed high RSV neutralizing antibody titers in the serum 28, 49 or 63 days post-vaccination. Animals were challenged with RSV at day 63 and subjected to histopathologic analysis at day 68. The study showed that our RSV vaccine was able to protect lungs from viral replication and significantly reduced viral titers in the nose, when measured using plaque assay five days post-RSV challenge. Evaluation of signs of VDE were analyzed by

lung histopathology FI virus induced peribronchiolitis in cotton rats, which was not detectable in animals vaccinated with our RSV vaccine.



Cotton rats (n= 5 per group) were vaccinated twice (d0 and d28) as indicated. RSV neutralizing antibody titers in the serum were analyzed 28, 49 or 63 days post-vaccination (top panel). Protection was assessed by measuring viral load in lung and nose at day 5 post-RSV challenge (top right panel). Lung histopathology was analyzed at day 68 after animals were challenged with RSV at day 63 (lower panel). Upper graphs show titers measured on day 63.

In this study RSV F encoding vaccine induced high levels of virus neutralizing antibodies, a likely correlate of protection. Functional antibody responses for mRNA vaccinated groups were higher than live virus vaccinated groups. Protection in lungs and nose are shown in the top right panel (viral titers via plaque assay five days post-RSV challenge). FI virus induces peribronchiolitis in cotton rats, which is not detectable in animals vaccinated with mRNA.

Seasonal Flu Program

The second-generation mRNA backbone using modified mRNA was selected as the preferred technology for further clinical development in the seasonal flu vaccine program. In the Phase 1 study of the monovalent Flu-SV-mRNA, expressing an H1N1 hemagglutinin antigen (subtype of influenza A), five doses ranging from 2 to 54µg with up to 25 subjects per dose cohort were evaluated in younger adults (age 18-45). In this age group, preliminary safety and reactogenicity data showed that the monovalent Flu-SV-mRNA candidate was generally well tolerated with no safety concerns observed to date across all tested dose levels. A single dose of Flu-SV-mRNA (dose level undisclosed) was assessed for safety and reactogenicity in older adults (age 60-80) and was also observed to be safe and well tolerated with no grade 3 adverse events in the 32 subjects who were administered the mRNA construct. Immunogenicity of the monovalent Flu-SV-mRNA was assessed in parallel with a licensed seasonal flu vaccine comparator in both age groups.

In younger adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA increased up to approximately 3.3 times those elicited by the licensed flu vaccine comparator in younger adults. In older adults, adjusted geometric mean hemagglutinin inhibition antibody titers elicited by Flu-SV-mRNA were approximately 2.3 times those elicited by the licensed flu vaccine comparator. In the same age group, the percentage of subjects achieving seroconversion was 89.7% for Flu-SV-mRNA and 56.2% for the licensed flu vaccine comparator.

Interim data support the progression of the modified second-generation mRNA technology for the development of a multivalent mRNA flu vaccine. The vaccine candidate for future clinical development is expected to target all four strains recommended by the WHO fo½nfluenza vaccines. A Phase 1/2 study for multivalent vaccine candidates is expected to start in the second quarter of 2023.

Other Prophylactic Vaccines for Infectious Diseases

In partnership with the Bill & Melinda Gates Foundation, we are developing prophylactic vaccines for prevention of other infectious diseases associated with high mortality in the developing world including malaria and rotavirus. Preclinical studies are ongoing, with encouraging results, which could lead to the decision for further clinical development of the candidate vaccines.

Furthermore, we are collaborating on several vaccine projects with CEPI, a public-private initiative to strengthen the vaccine research. This focuses on the development of the mRNA Printer, a mobile, automated production unit for rapid mRNA supply. This innovative platform is being designed to provide a rapid supply of LNP-formulated mRNA vaccine candidates that can target known pathogens (including Lassa fever, yellow fever and SARS-CoV-2) and prepare for rapid response to new and previously unknown pathogens.

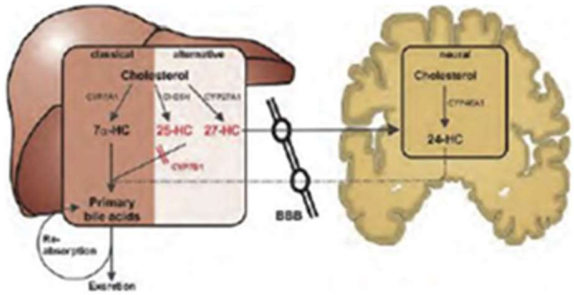
RNA-Based Therapeutics in Molecular Therapies

mRNA-based protein supplementation offers a therapeutic approach to compensate for lack of proteins in monogenetic diseases caused by loss-of-function mutations. It offers a potentially curative treatment option, especially in diseases in which the protein is expressed predominantly in organs that can be reached by intravenous delivery (such as the liver). Despite the success of classical enzyme-replacement therapy in several metabolic disorders, this therapeutic approach is not well suited for treatment of diseases caused by the lack of functional intracellular proteins, especially if the proteins are located in or on intracellular compartments. Additionally, as therapeutic proteins are conventionally manufactured by using human, animal or even plant cells, the pharmacological and biochemical properties of such recombinant proteins may differ from endogenously expressed enzymes. Cellular localization, folding and post-translational modifications can especially be critical for the correct function of a therapeutic protein. Delivery of mRNA can overcome these limitations and is likely to result in expression of a functional protein at a physiological cellular location. An example of our rare disease approach is for the potential treatment of hereditary spastic paraplegia, or HSP.

Hereditary Spastic Paraplegia

HSP is a group of inherited disorders that are characterized by progressive weakness and spasticity of the legs due to axonal degeneration of the corticospinal tract. Hereditary spastic paraplegia type 5, or SPG5, is caused by autosomal recessive loss-of-function mutations in CYP7B1, a gene encoding for the cytochrome P-450 oxysterol 7-α-hydroxylase, essential for the alternative pathway of bile acid synthesis in the liver. Mutations causing SPG5 lead to decreased enzyme activity of CYP7B1 and accumulation of oxysterols in the serum, the liver and then the central nervous system. The accumulation of hydroxyl cholesterol, or HC, in the brain is what is believed to be the pathologic correlate of this particular disease, which leads to spasms and paraplegia as symptoms. To date, no curative treatment for SPG5 is

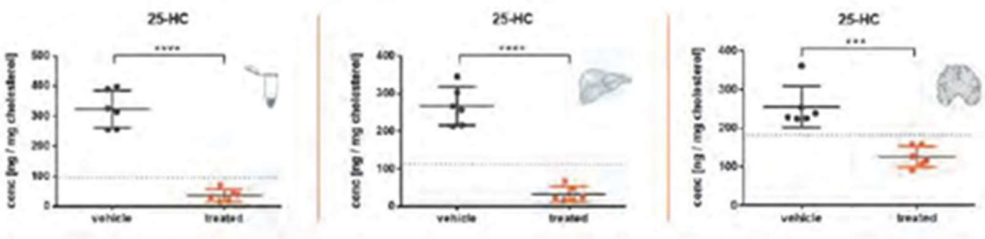
available. Current clinical treatment strategies for SPG5 are based on the reduction of cholesterol by applying cholesterol-lowering drugs (statins), which consequently lead to a reduction of oxysterols.



Our approach is based on replacement of CYP7B1 by administration of mRNA. We have studied the intravenous application of formulated CYP7B1 mRNA in mice lacking the endogenous *Cyp7b1* gene. Comparable to the human situation in SPG5 patients, a drastic increase of these oxysterols was detected in all three compartments (serum, liver and brain) of knockout mice. Using this *in vivo* model, we were able to demonstrate that a therapeutic approach with mRNA can restore human CYP7B1 protein that exhibits physiological function and eliminates abnormal cholesterol metabolites.

As shown below, we investigated the safety and efficiency of repeated dosing with four consecutive doses of 40 µg LNP-encoded mRNA of CYP7B1 administered intravenously every five days. LNP loaded with a non-translating mRNA were applied as control (vehicle). Prior to the administration, serum samples were taken to determine basal oxysterol levels. Two days after the last injection (17 days of treatment), animals were sacrificed, and serum, liver and brain samples were analyzed. Oxysterol analysis of these samples demonstrated a significant decrease of 25 hydroxy cholesterol, or 25 HC, in the serum and liver. mRNA expression of the human CYP7B1 in the liver led to a reduction of 25 HC in the liver by 8-fold and in serum by approximately 88%. These effects are accompanied by a reduction of the accumulation of 25 HC in the brain by more than 50%. Additionally, repetitive treatment resulted in a significant decrease of 27-HC and 3β-HCA in livers of treated compared to vehicle animals.

In addition, repeat intravenous delivery of CYP7B1 mRNA was found to be well tolerated in this study. Neither the CYP7B1 mRNA nor the restored protein nor the LNP induced liver toxicity. None of the treated animals presented signs of toxic or adverse effects. LNP particles encapsulating non-coding mRNA led to a temporary increase in oxysterol levels (25-HC and 27-HC) in liver and serum in the vehicle group, which is expected given cholesterol is an essential component of LNPs.



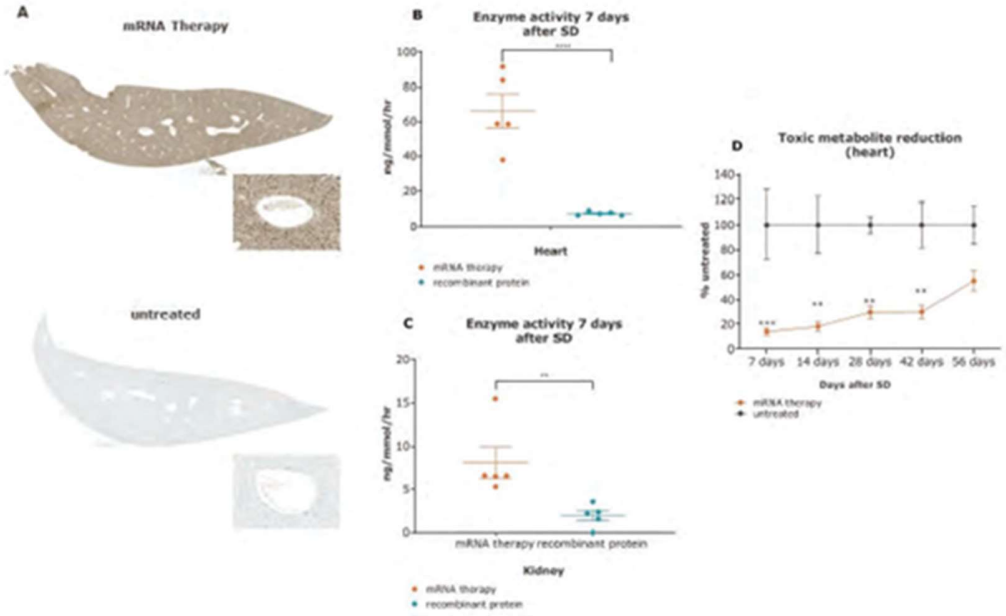
Lysosomal Storage Disorders

Lysosomal storage diseases are well-defined, single-gene disorders that are amenable to correction by systemic mRNA therapy.

We have conducted preclinical studies in an undisclosed lysosomal storage disease, or LSD, to evaluate LNP delivery of mRNA encoding the deficient enzyme to the liver, production of the enzyme by the liver and subsequent secretion and systemic distribution of the enzyme to the primary organs affected by the disease. In this specific LSD, the enzyme deficiency results in a progressive accumulation of lipid in cellular lysosomes, which ultimately affect the functioning of the heart and kidneys. Enzyme replacement therapy, or ERT, which involves intravenous administration of recombinant

enzyme, has been the standard of care for this specific LSD. In contrast to ERTs, our LNP mRNA technology specifically and efficiently targets the liver to naturally produce the missing enzyme, which is subsequently secreted into the bloodstream and distributed to the affected organs. In this specific LSD, the liver is not the target organ, but is used to produce the endogenous native enzyme.

As shown below, LNP delivered mRNA therapy produces a high and homogenous expression of the missing enzyme in the livers of knockout mice (Figure A, brownish stain). The endogenously produced enzyme is then secreted into the bloodstream with a better pharmacokinetic profile than the injected recombinant protein. The enzyme is then taken up by the target organs. In this example, the enzyme is taken up by the heart (Figure B) and kidney (Figure C) and localized into the lysosomes. Our mRNA therapy, through prolonged synthesis and secretion by the liver, led to higher enzyme activity in the organs compared to the infused recombinant enzyme (Figures B and C). This higher enzyme activity leads to a significant and prolonged reduction of accumulated lipids in the organs of mRNA-treated animals (Figure D).



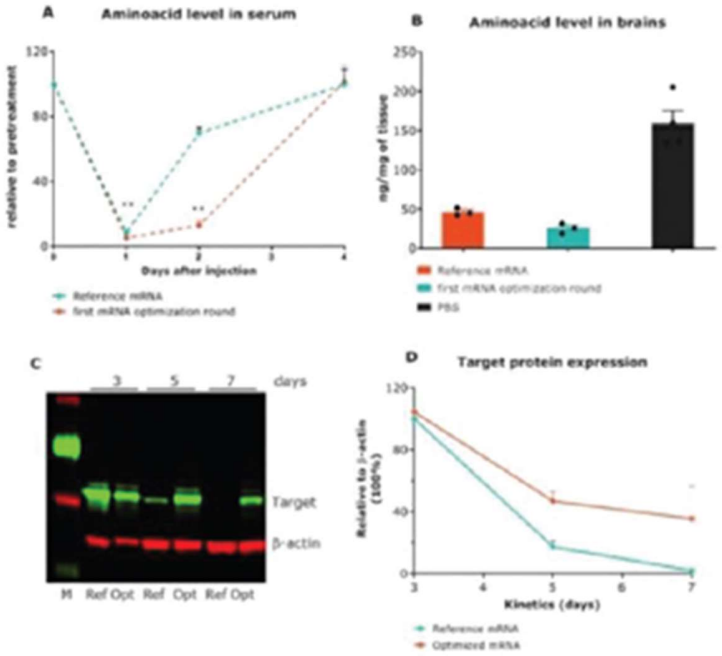
Liver-Specific Metabolic Diseases

We are applying a similar approach to inherited liver-specific metabolic disorders of amino acids, nitrogen and essential nutrients. The goal of these studies is to restore the specific enzyme or protein that is deficient in the liver by LNP-mediated delivery of mRNA to the liver. As such, the target organ for correction is the liver, and secretion and systemic distribution of the enzyme or protein to other organs is not required for a therapeutic effect.

Our ability to optimize mRNA stability and translation, in combination with optimization of the expressed protein, is an important part of our technical expertise. Using a process of mRNA and protein optimization, we believe that we are able to extend the duration of protein expression to meet a defined target product profile.

One example of this technology is the mRNA that we are developing for a metabolic amino acid disorder. In this inherited disorder, a liver-specific intracellular enzyme is deficient resulting in decreased metabolism of the amino acid. As a result, there is a toxic build-up of the amino acid in the blood, which leads to severe consequences for the central nervous system.

A single intravenous injection of a liver-targeted LNP formulation containing the therapeutic mRNA leads to a marked decrease in the level of the amino acid in the sera of knockdown animals (Figure A), but also in the brain (Figure B). Several rounds of mRNA and protein optimization were subsequently performed. Improving the mRNA molecular structure during the first round of optimization prolonged the protein and its therapeutic effect (Figure A) compared to the reference mRNA. Protein optimization (Figures C and D) of the expressed target enzyme increased its expression/stability and/or activity *in vitro*. The combination of both optimization programs resulted in a candidate with improved characteristics.

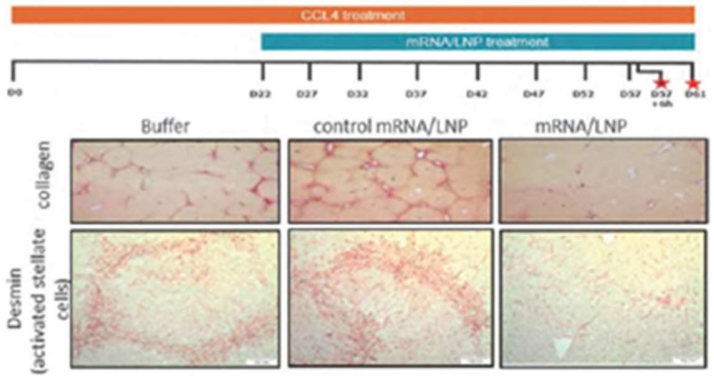


Fibrotic Liver Diseases

According to published literature, chronic liver diseases cause two million deaths a year worldwide. We have shown that the delivery of liver-specific protein factors, which are down regulated in fibrosis, can resolve liver fibrosis, a key pathological feature of NAFLD, NASH, cirrhosis and hepatocellular carcinoma. Protein factor treatment of liver diseases is uniquely suited to mRNA medicines enabling the expression of intracellular proteins. Moreover, we believe that in this particular case, the LNP technology allows us to deliver mRNA almost exclusively to the target cells, hepatocytes.

In a CCL4 chemically induced mouse model of liver fibrosis, we delivered eight doses of LNP-mRNA at an interval of five days at 2 mg/kg. The figure below illustrates the ability of an mRNA-delivered protein factor to reduce collagen, the main fibrotic material deposited in fibrosis, and eliminate activated stellate cells, the source of collagen (stained red). To confirm the potential activity of this mRNA therapy, we obtained similar data in two other unrelated murine models: a diet-induced model and a knockout mouse model of liver fibrosis. These findings offer preclinical proof of concept for this therapeutic concept to treat acute and chronic liver diseases, as well as diseases of other organs.

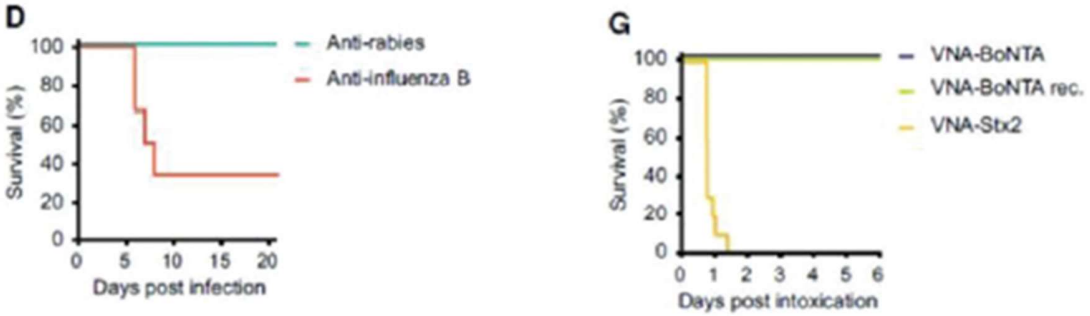
We are currently focused on significantly lowering the dose by employing two parallel strategies – mRNA sequence optimization to improve expression and optimization of the protein sequence for higher and sustained activity.



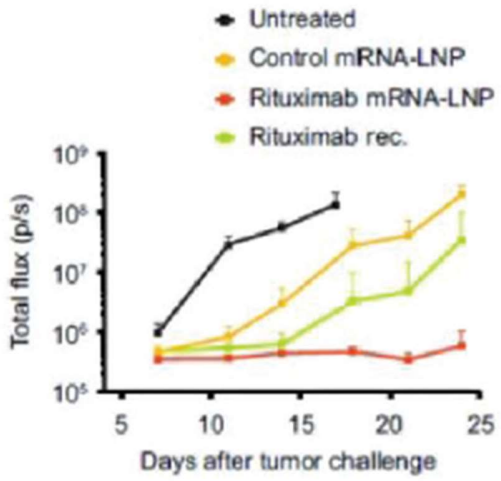
mRNA has the potential to promote expression without inducing an adverse immune response against the encoded protein. We have tested various antibodies using different designs to evaluate our platform's potential for prophylactic and therapeutic antibodies.

We evaluated the use of mRNA for passive immunization in two indications, rabies and botulism, that can be considered prototypes for anti-pathogen and anti-toxin therapies, respectively. Single injections of mRNA-LNPs were sufficient to establish rapid, strong and long-lasting serum antibody titers *in vivo*, thereby enabling both prophylactic and therapeutic protection against lethal rabies infection or botulinum intoxication. In both models, the high levels of *in vivo* serum expression conferred full protection in pre- and post-exposure scenarios.

The left side of the graphic below shows that mice expressing the anti-rabies mAb survived, whereas the majority of control animals which received anti-influenza mAb mRNA succumbed to the rabies infection. The right side of the graphic below shows that mice treated post-intoxication with VNA-BoNTA mRNA or recombinant VNA-BoNTA also survived.



In addition, we have demonstrated that mRNA-mediated antibody expression may be effective in the field of cancer immunotherapy, where mAbs are widely used in medical practice. In a preclinical study conducted in mice, we compared the efficacy of rituximab-encoding mRNAs to recombinant rituximab. We inoculated mice intravenously with luciferase expressing Raji lymphoma cells and started treatment with 50 µg of mRNA-LNP encoding rituximab and 200 µg of recombinant rituximab at various time points. mRNA-LNPs coding for an irrelevant antibody were used as further control. Control animals revealed strong tumor cell proliferation and had to be euthanized 17 days after inoculation due to severe symptoms. As shown in the picture below, repeated administration of mRNA-LNP for rituximab strongly decelerated or even abolished tumor cell growth compared to continued tumor growth for recombinant rituximab.



Therapeutic HNF4A mRNA to Attenuate Liver Fibrosis in Mice

On August 25, 2021, we published first preclinical data on the restoration of hepatocyte functions and attenuation of liver fibrosis and cirrhosis in multiple mouse models via an HNF4A encoding mRNA in the Journal of Hepatology. Owing to the extensive amount of data featured in the scientific publication, the following data excerpts represent only a selection of important findings of the preclinical studies. Full data can be accessed via the corresponding publication.

As a first step within the study, existing clinical data was collected that confirmed reduced endogenous HNF4A mRNA levels in patients with liver fibrosis, graded by the Ishak score. In two cohorts from Hannover Medical School, Germany, and Shanghai Zhongshan Hospital, China, liver tissues showed fibrosis stage-dependent reduction in HNF4A mRNA. Subsequently, it was examined whether in vitro synthesized *HNF4A* mRNA produces functionally active HNF4A protein. The wild-type (non-codon-optimized) or codon-optimized HNF4A mRNA were transfected into the human cervical carcinoma cell line (HeLa) cells as these lack endogenous HNF4A expression. Codon-optimized *HNF4A* mRNA-transfected cells showed higher HNF4A protein levels than those transfected with wild-type *HNF4A* mRNA. ZsGreen mRNA-transfected HeLa cells served as a control.

Human HNF4A mRNA restoration improves function of fibrotic hepatocytes

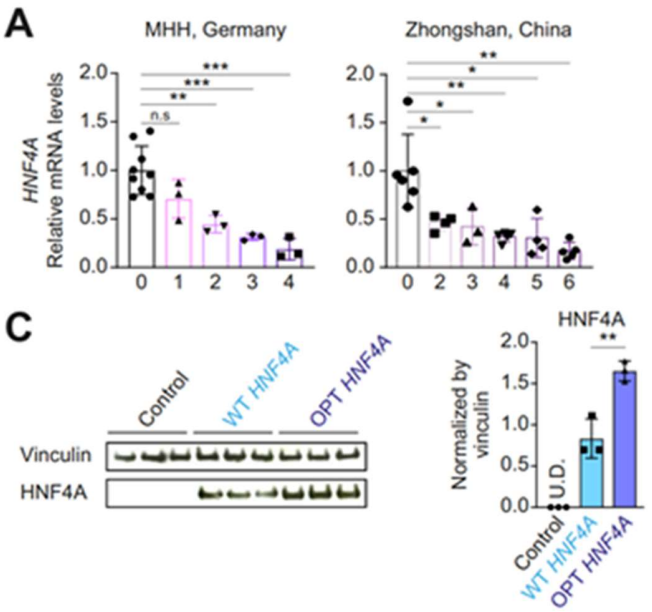


Figure. (A) qPCR analyses of human HNF4A mRNA in patients with fibrosis; 0 (n = 9), 1 (n = 3), 2 (n = 3), 3 (n = 3) and 4 (n = 3) from MHH, Germany and 0 (n = 6), 2 (n = 4) 3 (n = 3), 4 (n = 5), 5 (n = 4), 6 (n = 5) from Zhongshan Hospital, China. (C) Western blot and its quantification for wild-type (non-codon-optimized) and codon-optimized HNF4A mRNA in HeLa cells, 6 hours after HNF4A mRNA delivery.

Efficient Lipid Nanoparticle (LNP)-mediated mRNA delivery into hepatocytes of murine fibrotic livers was established. LNPs interact with apolipoprotein E at the surface of hepatocytes and are subsequently internalized via endocytosis. However, whether LNP-formulated mRNA reaches hepatocytes of fibrotic livers efficiently has remained unknown. LNP carrying mRNA encoding for Photinus pyralis luciferase (Luc/LNP) or ZsGreen (ZsGreen/LNP) were injected into CCl4-induced fibrotic and non-fibrotic control (wild-type) mice i.v. In-vivo imaging revealed robust bioluminescence exclusively in the liver from 8 hours to 120 hours after Luc/LNP injection in both groups (graphic shown below). Co-localization studies showed robust ZsGreen protein expression specifically in hepatocytes of fibrotic and control mice, but not in other hepatic cells. Our results demonstrated that LNP-formulated mRNA technology could specifically and efficiently target hepatocytes in murine fibrotic livers (data not shown below).

Targeted delivery of LNP-encapsulated mRNA into hepatocytes of fibrotic livers

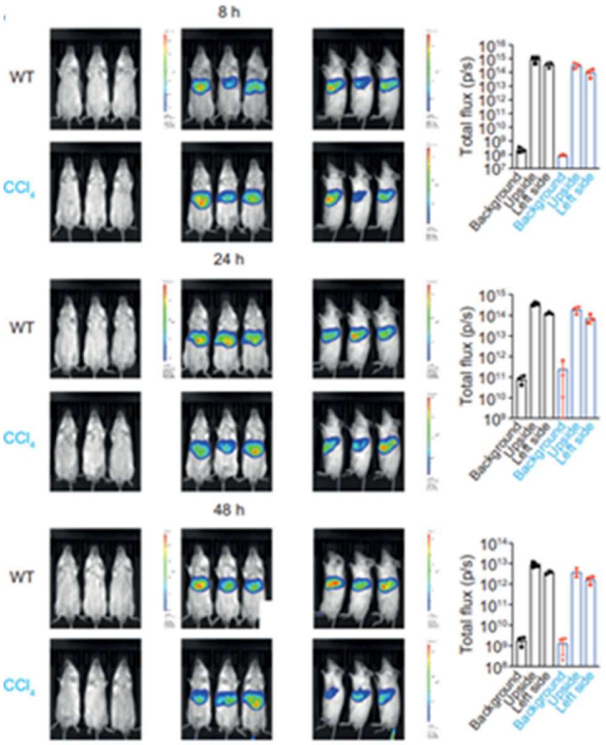


Figure. Successful mRNA delivery into hepatocytes of fibrotic BALB/c mice by LNP. Bioluminescence analyses at 8 h, 24 h and 48 h in wild type control and CCl4-induced fibrotic mice (n = 3 mice per group) injected i.v. with 40µg luciferase mRNA-encapsulated LNP (Luc/LNP).

To address whether systemic administration of *HNF4A* mRNA inhibits liver fibrosis, mice with toxin- (repeated CCl4 injection, data shown below) or cholestasis-induced fibrosis (induced via 3,5-diethoxycarbonyl-1,4-dihydrocollidine DDC-containing diet, data not shown) were used. *HNF4A* mRNA levels significantly decreased in fibrotic livers from both models. *HNF4A*/LNP or ZsGreen/LNP (henceforth referred to as control) were injected i.v. into fibrotic mice at 2 mg/kg per injection. HNF4A protein expression was confirmed in *HNF4A*/LNP-injected mouse livers and was absent in control mice, since the HNF4A antibody was only specific to human but not mouse HNF4A. *HNF4A*/LNP-injected mice showed significantly reduced alanine aminotransferase (ALT) and bilirubin indicating improved liver function, and significantly reduced levels of collagen (hydroxyproline assay), suggesting decreased fibrosis in both CCl4 and DDC models. Histological analyses, desmin (profibrogenic activated stellate cell marker) and Sirius red (collagen marker) staining further confirmed reduced fibrosis in CCl4 (Fig. F, N). Our data together provide evidence that HNF4A mRNA delivery attenuates fibrosis in mouse models of toxin as well as cholestasis-induced fibrosis.

Therapeutic HNF4A/LNP delivery inhibits toxin induced liver fibrosis

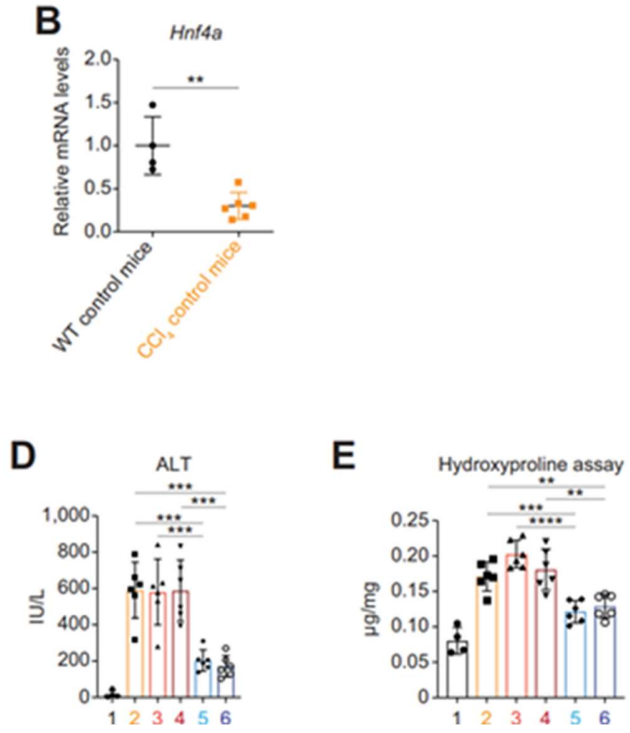
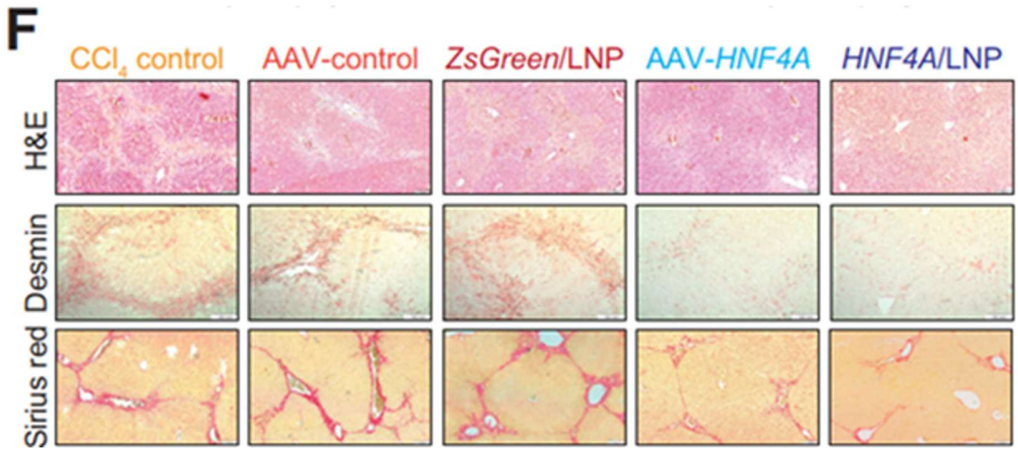


Figure. Therapeutic HNF4A/LNP delivery inhibits toxin induced liver fibrosis. CCl4-induced liver fibrosis (n = 6 mice per CCl4 model). (B) Hnf4a qPCRs after CCl4 injection. (D) Liver function tests for ALT shows reduced injury u€ HNF4A/LNP administration. (E) Hydroxyproline assay shows reduced collagen content.



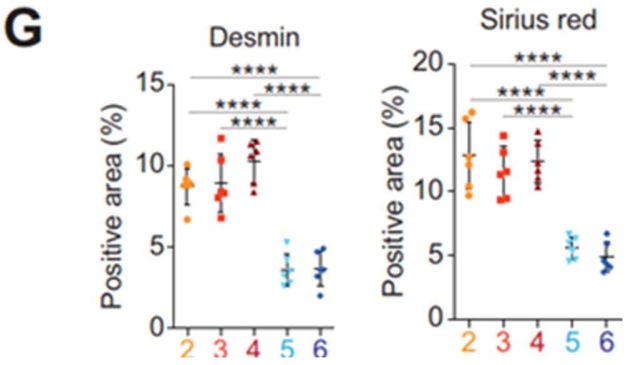


Figure. Therapeutic HNF4A/LNP delivery inhibits toxin induced liver fibrosis. CCl4-induced liver fibrosis (n = 6 mice per CCl4 model). (F) Immunohistochemical images of H&E, desmin and Sirius red stainings. Scale bars, 100 lm. (G) Quantification of Sirius red and desmin stainings.

In summary, the preclinical work shown here provides the first evidence that therapeutic mRNA delivery restores intracellular HNF4A transcription factor levels, induces endogenous Hnf4a expression, and improves metabolic activity of targeted hepatocytes. The data show that hepatocyte-specific delivery of HNF4A mRNA in injured livers attenuates fibrosis and cirrhosis in multiple independent mouse models of liver diseases. The shown data represents only a selection of important findings of the comprehensive preclinical studies. Full data can be accessed via the corresponding publication.

Eye Diseases

We are exploring the treatment of eye diseases with mRNA therapy. We have strategic collaborations with SERI for the development of mRNA-based treatments for currently undisclosed eye indications. We believe that the treatment of eye diseases with mRNA therapy represents an excellent opportunity for the mRNA approach for the following reasons:

- Therapeutic protein can be produced directly and locally within the target tissue;
- Local treatment in the eye requires lower mRNA doses, thereby minimizing systemic exposure;
- Enables production of endogenous proteins to stop or prevent pathological processes locally in the eye, such as neo-vascularization or apoptosis;
- Enables expression of multi-domain intracellular or transmembrane proteins in key cells within the eye overcoming limitations of recombinant proteins;
- No concern with potential side effects typical for viral gene vector;
- No mRNA construct size restrictions as with viral gene vectors; and
- The eye is an immune-privileged organ.

Based on positive preclinical data the agreement and collaboration with SERI moved ahead. We believe that the clinical and research expertise in eye diseases at SERI would allow us to fully leverage our mRNA in the discovery and validation of eye disease targets amenable to mRNA treatment. In collaboration with SERI, a high-priority rare eye condition has been identified for development. Multiple therapeutic targets have been identified for this condition and mRNAs have been generated and are currently being tested in preclinical studies, including models of disease.

Significant Agreements

Collaborations

We have entered into various licensing and commercialization agreements, including the following agreements with respect to product candidates:

Collaboration and License Agreements

2020 GlaxoSmithKline Collaboration and License Agreement

In July 2020, we entered into a Collaboration and License Agreement with GSK, which we refer to as the 2020 GSK Agreement, pursuant to which we are collaborating with GSK to research, develop and commercialize prophylactic and therapeutic non-replicating mRNA-based vaccines and antibodies targeting infectious disease pathogens. Under the terms of the 2020 GSK Agreement, we granted GSK a worldwide exclusive, sublicensable (subject to certain conditions) license under certain of our intellectual property relating to vaccines and antibodies encoded by our proprietary mRNA targeting certain selected pathogens, or GSK Program Products, and a non-exclusive license under certain LNP technology to develop, manufacture and commercialize a certain number of such GSK Program Products for use in connection with the infectious diseases targeted under the 2020 GSK Agreement. We additionally granted GSK an exclusive option for a certain period to add additional products in the field of infectious diseases as GSK Program Products. If such additional product targets a coronavirus other than SARS-CoV-2, at our election such product will be developed and commercialized on a cost and profit split basis under the GSK COVID Agreement. GSK is permitted for a certain period to replace any of the GSK Program Products with an alternative product, up to a certain number of times, and to exchange any antigen or antibody for which we have granted GSK a license under LNP technology for an alternative antigen or antibody, up to a certain number of times. In the event we obtain rights to any intellectual property controlled by a third party that is useful for the development, manufacture or commercialization of the GSK Program Products, but which is not necessary to obtain freedom to operate with respect to the use or exploitation of our technology or know-how, we must, at GSK's election, use commercially reasonable efforts to obtain a sublicense to such rights on behalf of GSK. Under the terms of the 2020 GSK Agreement, GSK granted us a royalty-free, non-exclusive license under certain GSK-controlled technology to perform certain development and manufacturing activities under the 2020 GSK Agreement. The 2020 GSK Agreement was amended and restated in April 2021, September 2021, February 2022 and March 2022. Under the September 2021 Amendment, each party also granted the other party a royalty-free, perpetual, worldwide, non-exclusive, sublicensable license under certain inventions created by such party to freely practice, use and exploit such inventions in any field.

For a certain period after the effective date, GSK has the right to reserve up to a certain number of antigens and we and our affiliates will be prohibited from granting any rights to a third party with respect to any such antigen for use in connection with infectious diseases. Under the terms of the 2020 GSK Agreement, GSK and its affiliates and sublicensees and we and our affiliates are additionally prohibited from developing, manufacturing or commercializing, directly or indirectly, any prophylactic or therapeutic mRNA-based vaccine or mRNA-based antibody targeting a pathogen targeted by a GSK Program Product, other than as contemplated under the 2020 GSK Agreement. Such exclusivity obligation will continue on a pathogen-by-pathogen basis for the duration of the 2020 GSK Agreement, so long as such pathogen is targeted by a GSK Program Product. We are additionally prohibited from granting any third party any license under the licensed LNP technology, or using such LNP technology ourselves, in connection with any GSK Program Product for so long as such GSK Program Product is being developed or commercialized under the 2020 GSK Agreement, except as contemplated under the 2020 GSK Agreement. We are additionally prohibited, for the period during which GSK's option to license additional GSK Program Products remains outstanding, from commercializing or granting any third-party the right to develop or commercialize any prophylactic or therapeutic mRNA-based vaccine or mRNA-based antibody targeting certain pathogens for use in connection with infectious diseases.

We and GSK are required to complete certain development activities with respect to the GSK Program Products set forth in various development plans. Among other development responsibilities, we are required to provide clinical supply and will in principle be responsible for sponsoring Phase 1 clinical trials for the GSK Program Products. We and GSK agree to decide whether the products required for clinical studies will be manufactured by us, GSK or jointly. At GSK's request, we are required to transfer to GSK all know-how necessary for GSK's development activities under the 2020 GSK Agreement and all know-how necessary for the manufacture of the GSK Program Products. GSK is generally responsible for development activities following completion of Phase 1 clinical trials and is required to use diligent efforts to secure marketing authorization following completion of all necessary clinical trials. GSK is responsible for the commercialization of approved GSK Program Products in all countries other than Austria, Germany and Switzerland and is required to use diligent efforts to commercialize approved GSK Program Products in certain major market countries. At our request, we and GSK will negotiate and agree in good faith to a distribution agreement pursuant to which we will have the exclusive right to commercialize GSK Program Products in Austria, Germany and Switzerland, and we will pay GSK royalties at the rate set out below. We and GSK are required to provide development data to the other party thorough a joint steering committee.

GSK paid us an upfront payment of €120 million and is required to pay us a manufacturing capacity reservation fee of €30 million following a certain regulatory milestone event, which is creditable against future milestone payments. We are eligible to receive up to between €28 million to €45 million in development milestone payments, €32 million to €35 million in regulatory milestone payments and €70 to €100 million in commercial milestone payments, depending on the GSK Program Product. Upon each exercise of its option to add additional products as GSK Program Products, GSK is required to compensate us for certain development costs and pay any accrued milestone payments. If GSK exercises its right to replace a GSK Program Product and if the replacement product was already under development by us, GSK must compensate us for certain development costs and pay any accrued milestone payments. We are eligible to receive tiered royalty payments ranging from a single-digit percentage to a low teens percentage on net sales, subject to certain customary reductions. GSK's royalty obligations continue on a product-by-product and country-by-country basis until the later of (i) the expiration of the last to expire valid claim covering such product in such country, (ii) the earlier of expiration of regulatory exclusivity for such product in such country or 12 years following the first commercial sale of such product in such country or (iii) ten years following the first commercial sale of such product in such country provided our proprietary know-how is required for such product. In any event, GSK's royalty obligations with respect to a product will expire in all countries no later than 20 years following the first commercial sale of such product in any country in which GSK is responsible for the commercialization of approved GSK Program Products. GSK is required to compensate us for certain development and regulatory costs we may incur in connection with our performance of our obligations under the 2020 GSK Agreement and we are eligible to receive up to €20,000 in reimbursements for expenses incurred recording or registering the licenses granted under the 2020 GSK Agreement. Under any distribution agreement entered into between us and GSK in connection with our distribution of a GSK Program Product in Austria, Germany and Switzerland, we will be required to purchase supply from GSK and pay GSK a low thirties percentage royalty on net sales. Under the March 2022 amendment, GSK and CureVac agreed on certain changes to the manufacturing strategy for the products developed under the collaboration, as a part of which GSK agreed to reimburse us for certain manufacturing expenses amounting to €42 million.

The term of the 2020 GSK Agreement will continue until the expiration of the last-to-expire royalty term, unless terminated earlier by either party. GSK has the right to terminate the 2020 GSK Agreement in its entirety or on a program-by-program basis for convenience following a certain notice period. We and GSK both have the right to terminate the 2020 GSK Agreement on a program-by-program basis before the first commercial sale of a GSK Program Product under such program in the event of the other party's material breach following a cure period or after the first commercial sale of a GSK Program Product under such program if the other party fails to make any payments due, commits any willful and material breach of the restrictions on any license granted to such party, commits a material breach of its non-compete obligations or commits a persistent and material breach of its confidentiality obligations following a cure period. We additionally have the right to terminate on a program-by-program basis after the first commercial sale of a GSK Program Product under such program if GSK commits a material breach of its commercialization diligence obligations following a cure period.

Upon expiration, the licenses granted to GSK under the 2020 GSK Agreement will become fully paid-up, perpetual and non-exclusive. In the event GSK terminates the 2020 GSK Agreement or a program under the 2020 GSK Agreement for convenience or we terminate a program under the 2020 GSK Agreement for cause, we will have the right to elect to continue with the development and commercialization of such program ourselves. If we decline to continue with the development and commercialization of a terminated program, all licenses granted under the 2020 GSK Agreement will terminate. If we elect to continue with the development and commercialization of a terminated program, all licenses granted by us to GSK will terminate and GSK must grant us an exclusive license under any intellectual property developed under the 2020 GSK Agreement and, at our election, a non-exclusive license under technology, which was used by GSK for the development, manufacture or commercialization of such terminated product. In the case of termination for GSK's convenience and if we elect to obtain such nonexclusive license, we will be required to pay GSK a single-digit percentage royalty on net sales. In the case of our termination for cause, the grant of rights and transition of the assets from GSK will be subject to a payment to GSK to be mutually agreed by the parties. In the event GSK terminates a program under the 2020 GSK Agreement for cause, GSK will have the right to elect to continue the development and commercialization of such program. If GSK declines to continue with the development and commercialization of a terminated program, all licenses granted under the 2020 GSK Agreement will terminate. If GSK elects to continue development and commercialization, all licenses granted to GSK under the 2020 GSK Agreement will survive termination and all payment obligations will remain in effect except that GSK will have the right to suspend payments until the amount of damages suffered by GSK has been agreed and set off against such payments.

GlaxoSmithKline COVID Collaboration and License Agreement

In April 2021, we entered into a collaboration agreement with GSK, which we refer to as the GSK COVID Agreement, pursuant to which we are collaborating with GSK to research, develop and manufacture next-generation mRNA vaccines targeting the original SARS-CoV-2 strain as well as emerging variants, including multivalent and monovalent approaches, such as our second-generation COVID-19 vaccine candidate, CV2CoV. These vaccine candidates may either be used to protect unvaccinated individuals or to serve as boosters in the event that SARS-CoV-2 immunity gained from an initial vaccination reduces over time.

Under the terms of the GSK COVID Agreement, we granted GSK a worldwide, exclusive, sublicensable (subject to certain conditions) license under certain of our intellectual property relating to mRNA-based vaccines targeting SARS-CoV-2 and a non-exclusive license under certain LNP technology to develop, manufacture and commercialize certain SARS-CoV-2 pathogen vaccine products, or the GSK COVID Products, for use in connection with the prevention or treatment of diseases caused by the SARS-CoV-2 pathogen. The GSK COVID Products consist of (i) next-generation SARS-CoV-2 pathogen vaccine products (other than CVnCoV), (ii) vaccine products targeting coronaviruses other than SARS-CoV-2 for which GSK exercises its exclusive option pursuant to the 2020 GSK Agreement and where we elect to develop and commercialize such product on a cost and profit split basis under the GSK COVID Agreement and (iii) next-generation SARS-CoV-2 pathogen vaccine products (other than CVnCoV) that also target one or more pathogens that the parties are targeting under the 2020 GSK Agreement, which we refer to as Combination Products. In the event we obtain rights to any intellectual property controlled by a third-party that is useful for the development, manufacture or commercialization of the GSK COVID Products, but which is not necessary to obtain freedom to operate with respect to the use or exploitation of our technology or know-how, we must, at GSK's election, use commercially reasonable efforts to obtain a sublicense to such rights on behalf of GSK. Under the terms of the GSK COVID Agreement, GSK granted us a royalty-free, non-exclusive license under certain GSK-controlled technology to perform certain development and manufacturing activities under the GSK COVID Agreement. Under the September 2021 Amendment, each party also granted the other party a royalty-free, perpetual, worldwide, non-exclusive, sublicensable license under certain inventions created by such party to freely practice, use and exploit such inventions in any field.

GSK and its affiliates and sublicensees and we and our affiliates are prohibited from, subject to certain exceptions, developing, manufacturing or commercializing, directly or indirectly, any mRNA-based vaccine or mRNA-based antibody products targeting the SARS-CoV-2 pathogen, other than a GSK COVID Product as contemplated under the GSK COVID Agreement or CVnCoV. The exclusivity obligations remain in effect until the expiration or termination of the GSK COVID Agreement.

We and GSK are required to complete certain development activities with respect to the GSK COVID Products set forth in various development plans. The GSK COVID Agreement was amended and restated in September 2021, February 2022 and March 2022, as described below, and further amended in August 2022 to reflect conforming updates to the development plans. Pursuant to the amendment in September 2021, we and GSK are required to complete certain development activities with respect to the GSK COVID Products set forth in updated development plans. We and GSK agree to decide whether the GSK COVID Products required for clinical studies will be manufactured by us, GSK or jointly. Once a manufacturing and supply strategy for a given GSK COVID Product has been agreed upon between the parties, we must negotiate and agree in good faith on a commercial supply agreement pursuant to which we may be required to reserve certain manufacturing capacity for GSK. At GSK's request, we are required to transfer to GSK all know-how necessary for GSK's development activities under the GSK COVID Agreement and all know-how necessary for the manufacture of the GSK COVID Products. GSK is responsible for the commercialization of GSK COVID Products in all countries other than Austria, Germany and Switzerland and is required to use diligent efforts to commercialize approved GSK COVID Products in certain major market countries. At our request, we and GSK will negotiate and agree in good faith to a distribution agreement pursuant to which we will have the exclusive right to commercialize GSK COVID Products in Austria, Germany and Switzerland. We and GSK are required to provide development data to the other party thorough a joint steering committee.

Under the GSK COVID Agreement, GSK paid us an upfront payment of €75 million. Upon GSK's exercise of its option to add CVnCoV and boosters for such vaccine as GSK COVID Products, GSK is required to compensate us for certain development costs. We and GSK agreed to equally share all development costs for GSK COVID Products, subject to certain exceptions. We and GSK will share all net profits generated from sales of GSK COVID Products, other than Combination Products, under profit sharing arrangements that in certain cases vary depending upon the GSK COVID Product in question, the time of sale, the number of doses sold and the party to whom the sale is made. We are eligible to receive tiered royalty payments ranging from a sub-teen percentage to a mid-teens percentage on net sales of Combination Products, subject to certain customary reductions. We will pay GSK a high-teen percentage royalty on net sales of all Combination Products in Austria, Germany and Switzerland. All royalty obligations continue on a product-by-product and country-by-country basis until the later of (i) the expiration of the last to expire valid claim covering such product in such country (ii) the earlier of expiration of regulatory exclusivity for such product in such country or 12 years following the first commercial sale of such product in such country, or (iii) 10 years following the first commercial sale of such product in such country provided our proprietary know-how is required for such product. In any event, GSK's royalty obligations with respect to a product will expire in all countries no later than 20 years following the first commercial sale of such product in the respective party's territory.

The term of the GSK COVID Agreement will continue until the expiration of all applicable payment obligations, unless terminated earlier by either party. GSK has the right to terminate the GSK COVID Agreement in its entirety for convenience following a certain notice period, and we have the right to opt out of the funding of the development, manufacture and commercialization of a GSK COVID Products on a product-by-product basis. In the event we opt out of funding the development of a GSK COVID Product, GSK can elect to cease the development and commercialization of the relevant product, or to continue it on the terms of the 2020 GSK Agreement. If GSK declines to continue with the development and commercialization, the agreement terminates in connection with that GSK COVID Product and all licenses granted under the GSK COVID Agreement will terminate. We and GSK both have the right to terminate the GSK COVID Agreement before the first commercial sale of a GSK COVID Product in the event of the other party's material breach following a cure period or after the first commercial sale of a GSK COVID Product if the other party fails to make any payments due, commits any willful and material breach of the restrictions on any license granted to such party, commits a material breach of its non-compete obligations or commits a persistent and material breach of its confidentiality obligations following a cure period. We additionally have the right to terminate after the first commercial sale of a GSK COVID Product if GSK commits a material breach of its commercialization diligence obligations following a cure period.

Upon expiration, the licenses granted to GSK under the GSK COVID Agreement will become fully paid-up, perpetual and non-exclusive. In the event GSK terminates the GSK COVID Agreement for convenience or we terminate the GSK COVID Agreement for cause, all licenses granted to GSK under the GSK COVID Agreement will terminate and we will have the right to elect to continue with the development and commercialization of the GSK COVID Products ourselves. If we elect to continue with the development and commercialization of the COVID Products, GSK must grant us an exclusive license under any intellectual property developed under the GSK COVID Agreement and, at our election, a non-exclusive license under technology which was used by GSK for the development, manufacture or commercialization of the GSK COVID Products. In the case of termination for GSK's convenience and if we elect to obtain such non-exclusive license, we will be required to pay GSK a royalty ranging from a sub-single-digit percentage to a low single-digit percentage on net sales. In the case of our termination for cause, the grant of rights and transition of the assets from GSK will be subject to a payment to GSK to be mutually agreed by the parties. In the event GSK terminates the GSK COVID Agreement for cause, GSK will have the right to elect to continue the development and commercialization of the GSK COVID Products. If GSK declines to continue with the development and commercialization of the GSK COVID Products, all licenses granted under the GSK COVID Agreement will terminate. If GSK elects to continue development and commercialization, all licenses granted to GSK under the GSK COVID Agreement will survive termination, provided that for GSK COVID Products other than Combination Products a one-time payment from GSK to Curevac (in replacement of a continuous profit sharing mechanism) will be mutually agreed upon by the parties. All payment obligations for Combination Products will remain in effect. In each case, GSK will have the right to suspend payments until the amount of damages suffered by GSK has been agreed and set off against such payments.

CureVac-GSK Consortium Agreement

The Federal Republic of Germany, represented by the Vaccine Production Taskforce on behalf of the Federal Ministry of Health, called for tenders relating to pandemic preparedness, which we refer to as the Tender Procedure. The Tender Procedure resulted in framework agreements for the provision to the Federal Republic of Germany of production capacities and, upon demand, the production and supply of mRNA vaccines (referred to as lot 1) and vector- or protein-based vaccines (referred to as lot 2). Because neither we nor GSK were alone in a position to provide the full range of services requested by the Federal Republic of Germany under the Tender Procedure, we established a consortium with GSK (referred to as the CureVac-GSK Consortium) for the purpose of participating in the Tender Procedure, entering into a framework agreement for the provision of production capacities and, upon demand, the production and supply of mRNA vaccines (lot 1), which we refer to as a Pandemic Preparedness Agreement.

The CureVac-GSK Consortium submitted an application and offer under the Tender Procedure for the award of a Pandemic Preparedness Agreement. On April 8, 2022, the Federal Republic of Germany sent a letter confirming that the CureVac-GSK Consortium had been awarded a Pandemic Preparedness Agreement. Following a qualification phase of a maximum of two years from the award date, the Pandemic Preparedness Agreement grants the government access to a manufacturing capacity of 80 million doses of mRNA-based vaccine per year until 2029, subject to extension. Under the contract, after successful achievement of pandemic preparedness by the end of the qualification phase, the contract will enter into a stand-by phase during which the government will pay the CureVac-GSK Consortium an annual stand-by fee. During the stand-by phase, the CureVac-GSK Consortium is required to maintain a manufacturing capacity of 80 million doses of mRNA-based vaccine per year at constant readiness. The Pandemic Preparedness Agreement is subject to termination by the Federal Republic of Germany or the CureVac-GSK Consortium if, a112abellithings, by the end of the qualification phase the CureVac-GSK Consortium does not have an mRNA-based vaccine for which a marketing authorization (which may be temporary) for the German market has been granted.

Genmab Collaboration and License Agreement

In December 2019, we entered into a Collaboration and License Agreement with Genmab, which we refer to as the Genmab Agreement, to research and develop up to four potential differentiated mRNA-based antibody products, to be selected by Genmab, based on the combination of our proprietary RNAntibody technology with Genmab's proprietary antibody technology for the treatment of human diseases. The Genmab Agreement was amended in July 2020, December 2020 and June 2021. Pursuant to the Genmab Agreement we granted Genmab an exclusive, worldwide, sublicensable (subject to certain conditions) license under our mRNA technology for the development, manufacture and commercialization of an mRNA antibody product designed to express a certain Genmab proprietary antibody, which we refer to as the Genmab First Program. The parties will collaborate on research to identify an initial product candidate under the Genmab First Program. We additionally granted Genmab an exclusive, worldwide, sublicensable license under our mRNA technology for the research and preclinical development of up to four additional mRNA antibody product

concepts and an option to obtain an exclusive, worldwide, sublicensable (subject to certain conditions) license to develop, manufacture and commercialize product candidates for up to three of such product concepts. We have the option to share in the costs and profits in connection with the development, manufacture and commercialization of one of the additional mRNA antibody product concepts under predefined terms and conditions.

We may not, directly or indirectly, offer any rights to a third party under the technology we license to Genmab for the product concepts and targets being developed under the Genmab Agreement or conduct or participate in the development, manufacture or commercialization of any antibody product that is directed at a target being developed under the Genmab Agreement. For the Genmab First Program, these obligations will last for the duration of the Genmab Agreement. For the additional product concepts, certain time limitations apply to the above obligations. Genmab may not develop or commercialize any mRNA-based single antibody product or monoclonal recombinant antibody that is based on the Genmab First Program outside of the scope of the Genmab Agreement.

In partial consideration for entering into the Genmab Agreement, Genmab paid us an upfront fee of $10 million and made a €20 million equity investment. Genmab additionally will be obligated to pay us a $0.5 million reservation fee upon the selection of each additional product concept for development and $5 million upon selection of a product from the Genmab First Program for further development and commercialization. Genmab is additionally required to pay us up to $30 million in option exercise fees. If Genmab exercises any of its options to obtain commercial licenses for the additional mRNA antibody concepts, Genmab would fund all research and would develop and commercialize any resulting product candidates. We are additionally eligible to receive up to between $25 million and $43 million in development milestone payments, $100 million and $125 million in regulatory milestone payments and $150 million and $200 million in commercial milestone payments for each product, depending on the specific product concept. In addition, we are eligible to receive a mid-single-digit to low teens percentage tiered royalty on aggregate net sales of licensed products, on a per product basis and subject to certain customary reductions. Genmab's royalty obligation continues on a country-by-country and product-by-product basis until the later of the expiration of the last-to-expire valid claim in the licensed patents in such country covering such licensed product, expiration of regulatory exclusivity for such product in such country or 10 years from the date of the first commercial sale of such product. If Genmab grants a sublicense to the Genmab First Program product before a certain milestone event, Genmab must pay us a one-time $10 million payment. We are responsible for a portion of the overall costs for development with respect to the Genmab First Program product until submission of an IND within an agreed budget, and Genmab will otherwise reimburse us for costs incurred in performing certain development activities in connection with the Genmab Agreement. We are responsible for any payments to third parties related to the LNP technology we license to Genmab for use in relation to the Genmab First Program and a portion of such payments with respect to LNP technology used in the additional product concepts. In the event we exercise our right to share in the development, manufacture and commercialization of a product, we must pay Genmab a one-time payment of $3 million and refund any option fee paid by Genmab with respect to such product. As of December 31, 2022, we have received $1 million in development cost reimbursements, and we have not received any reservation, product selection, option exercise or sublicense fees or milestone or royalty payments.

We are required to use commercially reasonable efforts to perform our obligations under the research and development plans established in connection with the Genmab Agreement. Genmab is required to use commercially reasonable efforts to identify and develop the Genmab First Program product and each additional product Genmab adds to the development program under the Genmab Agreement, and to further develop the Genmab First Program product and each optioned product to marketing authorization and to commercialize each product for which it obtains regulatory approval. We and Genmab are required to make available to the other party all preclinical development data for each program under development under the Genmab Agreement until filing of an IND for such program. Following IND filing for a product, we and Genmab will establish a collaboration committee where Genmab will share the status, progress and results of the development of the respective product.

The term of the Genmab Agreement will continue until the expiration of the royalty term, unless terminated earlier by either party. The Genmab Agreement may be terminated upon written notice by either party upon the other party's material breach or default of any of its obligations following a cure period. Genmab may terminate the Genmab Agreement for convenience after a certain notice period. Upon expiration of the Genmab Agreement, the license rights we granted to Genmab under the Genmab Agreement will become fully paid-up, perpetual and non-exclusive. In the event of termination for our material breach, we will grant Genmab an exclusive (even to us), worldwide and sublicensable license to exploit any product identified prior to termination, subject to Genmab's continued milestone and royalty obligations. In the event of termination by us for Genmab's material breach, or Genmab's termination for

convenience, the licenses granted to Genmab will automatically terminate. Additionally, at our request, Genmab will grant us a non-exclusive, royalty-free, sublicensable, perpetual and worldwide license under certain Genmab intellectual property that is created under the Genmab Agreement and that is required to develop, manufacture and commercialize our own mRNA antibody products targeting the collaboration targets under the Genmab Agreement prior to termination. Such license would not include any license to Genmab background intellectual property or the specific products or antibodies developed by Genmab.

Arcturus Development and Option Agreement

In January 2018, we entered into a Development and Option Agreement with Arcturus, which we refer to as the Arcturus Agreement, pursuant to which Arcturus granted us the right to reserve a certain number of targets and an irrevocable offer to obtain a license to a certain number of such reserved targets to develop, manufacture and commercialize products containing Arcturus's LNP technology (LMD technology) and mRNA constructs intended to express such targets. The Arcturus Agreement was amended in May 2018, September 2018 and July 2019. As of December 31, 2022, we have not accepted the offer with respect to any targets.

Under the Arcturus Agreement, Arcturus is responsible for the LNP chemistry and formulation and characterization work, and we are responsible for mRNA construct development.

Both parties will undertake certain allocated preclinical studies. Each party is required to use diligent efforts to perform its obligations under the work plans established in connection with the Arcturus Agreement, and Arcturus is required to use diligent efforts to manufacture and supply us with certain formulated products. The Arcturus Agreement provides for the establishment of a joint development committee for the discussion of development efforts under the Arcturus Agreement.

We paid Arcturus an upfront fee of $5 million in connection with the Arcturus Agreement and must pay an extension fee of $1 million if we exercise our option to extend the initial term of the Arcturus Agreement beyond July 2023. We are further required to reimburse Arcturus for certain costs incurred in connection with development activities and provide certain FTE funding. We are additionally required to pay up to an aggregate of $5 million in connection with our acceptance of the irrevocable offer to obtain licenses for further development and commercialization of selected targets. Under each license agreement to be entered into in connection with our selection of targets, we will additionally be required to make certain royalty payments, which are not in excess of 10%, subject to certain customary reductions, on a country-by-country and a product-by-product basis until the later of the expiration of the last-to-expire valid patent in such country covering such licensed product, expiration of regulatory exclusivity for such product in such country or ten years from the date of the first commercial sale of such product in such country. We additionally must pay Arcturus up to $6 million in development milestone payments, $9 million in regulatory milestone payments and $8 million in commercial milestone payments in connection with each license agreement we enter into under the Arcturus Agreement. As of December 31, 2022, we have made payments totaling $5.5 million to Arcturus reimbursing Arcturus for development costs and in connection with our FTE funding obligations. Additionally, we have not accepted the irrevocable offer with respect to any target and therefore have not paid any acceptance fees or made any milestone or royalty payments to Arcturus.

Under the Arcturus Agreement, Arcturus granted us a worldwide, nonexclusive license under its LNP technology for research and preclinical development. We granted Arcturus a worldwide, nonexclusive license under our mRNA technology solely to enable Arcturus to perform development activities in connection with the Arcturus Agreement.

The Arcturus Agreement will expire in July 2023 unless earlier terminated or extended for an additional 18-month term. We have the right to terminate the Arcturus Agreement in full or on a target-by-target basis in the event of a material breach by Arcturus following a cure period. We additionally have the right to terminate the Arcturus Agreement for convenience following a certain notice period and for change of control of Arcturus. In the event we terminate for Arcturus's breach, for convenience or for Arcturus's change of control, Arcturus will transfer all deliverables created under the Arcturus Agreement to us and all licenses granted under the Arcturus Agreement will terminate. In the event we terminate for Arcturus's breach, Arcturus will transfer any technology and provide licenses as reasonably necessary for us to complete work contemplated under any work plan relating to the terminated target and the acceptance fee relating to such target and payments due under any associated license agreement will be reduced by a certain percentage. Arcturus has the right to terminate the Arcturus Agreement in the event of a material breach by us

following a cure period, in which event all licenses granted under the Arcturus Agreement will terminate. Termination of the Arcturus Agreement shall not affect any then-existing license agreements between us and Arcturus.

Acuitas Development and Option Agreement

In April 2016, we entered into a Development and Option Agreement with Acuitas, which as amended we refer to as the Acuitas Agreement, pursuant to which Acuitas granted us the right to reserve a certain number of vaccine and other targets and an option to obtain a license to a certain number of such reserved targets to develop, manufacture and commercialize products containing Acuitas's LNP technology and mRNA constructs intended to express such targets. With respect to a certain number of nonexclusive licenses to vaccine targets that we obtain under the Acuitas Agreement, Acuitas additionally granted us an option to exchange each vaccine target licensed under such nonexclusive license for an alternate vaccine target for a certain period. As of December 31, 2022, we have exercised our option to obtain a nonexclusive license to 17 targets, and have not exercised our option to exchange a vaccine target licensed under any nonexclusive license.

Under the Acuitas Agreement, Acuitas is responsible for the LNP chemistry and formulation and characterization work, and we are responsible for mRNA construct development. Both parties will undertake certain allocated preclinical studies. Each party is required to use diligent efforts to perform its obligations under the work plans established in connection with the Acuitas Agreement. Acuitas is further required to use diligent efforts to manufacture and supply us with certain formulated products. The Acuitas Agreement provides for the establishment of a joint development committee for the discussion of development efforts under the Acuitas Agreement. We are required to reimburse Acuitas for certain costs incurred in connection with development activities and certain FTE costs.

We are further required to pay Acuitas annual target reservation and maintenance fees of up to $1.4 million if we reserve the maximum number of targets permitted under the Acuitas Agreement. We are additionally required to pay an option exercise fee ranging from $50,000 to $2 million upon each exercise of our option under the Acuitas Agreement, subject to certain additional fees ranging from $10,000 to $200,000 for the exercise of our option for certain other vaccine targets. We paid Acuitas a $5 million upfront fee in connection with an amendment to the Acuitas Agreement dated July 2020 and, upon each exercise of our option to exchange a vaccine target licensed under any non-exclusive license, we paid an exchange fee of $3 million. We paid Acuitas a $3 million upfront fee in connection with an amendment to the Acuitas Agreement dated December 2020 and are required to pay an additional $250,000 in April 2023 for certain options not yet exercised. Under each license agreement we enter into in connection with our exercise of our option, we will additionally be required to make low single-digit percentage tiered royalty payments, subject to certain customary reductions, on a country-by-country and a product-by-product basis until the later of the expiration of the last-to-expire licensed patent in such country covering such licensed product, expiration of regulatory exclusivity for such product in such country or 10 years from the date of the first commercial sale of such product in such country. Under each such license we additionally must pay up to between $1.1 million and $9 million in development milestone payments, $1.3 million and $7 million in regulatory milestone payments and $1.3 million and $7 million in commercial milestone payments, depending on whether the license is exclusive or non-exclusive and the number of options exercised to date. As of December 31, 2022, we have exercised our option to obtain a non-exclusive license to 17 targets. As of December 31, 2022, we have paid Acuitas $3.7 million in reservation and option exercise fees, $1.25 million for certain options not yet exercised and have made payments totaling $8.7 million reimbursing Acuitas for development costs and LNP batches and in connection with our FTE funding obligations. Payments made under the license agreements entered into in connection with our exercise of our option under the Acuitas Agreement are described below.

Under the Acuitas Agreement, Acuitas granted us a worldwide, non-exclusive license under its LNP technology for us to perform development activities, and we granted Acuitas a worldwide, non-exclusive license under our mRNA technology solely to enable Acuitas to perform development activities in connection with the Acuitas Agreement.

The Acuitas Agreement will expire in April 2025 unless earlier terminated or extended. Both parties have the right to terminate the Acuitas Agreement in whole or on a program-by-program basis in the event of a material breach by the other party following a cure period. We additionally have the right to terminate the Acuitas Agreement for convenience following a certain notice period or for Acuitas's change of control. In the event of termination for any reason, Acuitas will transfer all deliverables created under the Acuitas Agreement to us and in the event we terminate for reasons other than for Acuitas's material breach, we must make any payments owed to Acuitas up to the time of

termination. In the event we terminate for Acuitas's material breach or for Acuitas's change of control, Acuitas will transfer any technology and provide licenses as reasonably necessary for us to complete work contemplated under the Acuitas Agreement and, in the case of termination for Acuitas's material breach, Acuitas must refund to us any target reservation and maintenance fees for the remainder of the contract year in which such termination is effective.

Acuitas Non-exclusive License Agreements

For each option we have exercised under the Acuitas Agreement, we have entered into a non-exclusive license agreement with Acuitas with respect to such optioned product, all based on the same form agreement, which we collectively refer to as the Acuitas License Agreements. Under the Acuitas License Agreements, Acuitas grants us a non-exclusive, non-transferable, sublicensable (subject to certain conditions) worldwide license under Acuitas's LNP technology to develop, manufacture and commercialize licensed products directed to the optioned targets. We may convert the non-exclusive licenses to exclusive licenses subject to certain additional financial obligations. As of December 31, 2022, we have not converted any non-exclusive license to an exclusive license.

We must pay Acuitas up to between $1.1 million and $1.6 million in development milestone payments, $1.3 million and $1.8 million in regulatory milestone payments and $1.3 million and $1.8 million in commercial milestone payments under each Acuitas License Agreement upon the occurrence of certain milestone events. We additionally are obligated to pay Acuitas annual fees ranging from $5,000 to $10,000 for any additional protein targeted by a vaccine product licensed under an Acuitas License Agreement after a certain milestone event. We are further required to pay Acuitas a low single-digit tiered percentage royalty on net sales of licensed products, subject to certain potential customary reductions. Our royalty obligations continue under each Acuitas License Agreement on a country-by-country and product-by-product basis until the later of the expiration of the last-to-expire licensed patent claim covering such licensed product in such country, expiration of any regulatory exclusivity period for such product in such country and 10 years following the first commercial sale of such product in such country. As of December 31, 2022, we have made $100,000 in development milestone payments to Acuitas with respect to the license agreement relating to Rabies RAV-G, $1.4 million in development milestone payments (Phase I, Phase II and Phase III milestone payments) to Acuitas with respect to the license agreement relating to the SARS-CoV-2 Spike protein S, $100,000 in development milestone payments to Acuitas with respect to the license agreement relating to the Influenza hemagglutinin (HA) antigen, and have not made any royalty payments.

Each Acuitas License Agreement will continue on a product-by-product and a country-by-country basis until there are no more payments owed to Acuitas for such product in such country. Either party may terminate an Acuitas License Agreement in the event of a material breach by the other party following a cure period. We additionally have the right to terminate the Acuitas License Agreements for convenience following a certain notice period. Upon expiration of an Acuitas License Agreement, the licenses granted to us under such Acuitas License Agreement will become fully paid-up and will remain in effect. In the event of our termination of an Acuitas License Agreement for Acuitas's material breach, the rights and licenses granted to us under such agreement will become perpetual and irrevocable. Alternatively, instead of exercising our right to terminate in the event of Acuitas's material breach, we may elect to instead continue the license but reduce our milestone and royalty payment obligations to Acuitas by a certain percentage. In the event of termination of an Acuitas License Agreement by us for convenience or by Acuitas for our material breach, the licenses granted under such agreement will terminate, except that we will have the right to sell off any remaining inventories of licensed products for a certain period of time.

CRISPR Therapeutics Development and License Agreement

In November 2017, we entered into a Development and License Agreement with CRISPR Therapeutics, which as amended by an amendment entered into in June 2020, we refer to as the CRISPR Therapeutics Agreement, pursuant to which we will develop novel Cas9 mRNA constructs for use in gene editing therapeutics. Under the terms of the CRISPR Therapeutics Agreement, we granted CRISPR Therapeutics a worldwide, exclusive (even to us), sublicensable (subject to certain conditions) license under certain intellectual property rights that are reasonably necessary or useful to develop, manufacture or commercialize products comprising Cas9 mRNA constructs, and under any patents controlled by us that arise from inventions discovered under the CRISPR Therapeutics Agreement to develop, manufacture and commercialize three of CRISPR Therapeutics' *in vivo* gene-editing programs for certain diseases. CRISPR Therapeutics granted us an exclusive (even as to CRISPR Therapeutics), worldwide, cost-free sublicense to manufacture products comprising Cas9 mRNA constructs for CRISPR Therapeutics.

CRISPR Therapeutics has paid us an upfront one-time technology access fee of $3 million and we are eligible to receive up to $13 million in development milestone payments, $33 million in regulatory milestone payments and $133 million in commercial milestone payments, as well as mid single-digit percentage royalties from CRISPR Therapeutics on the net sales of licensed products on a product-by-product and country-by-country basis, subject to certain potential customary reductions. CRISPR Therapeutics' royalty obligations continue on a product-by-product and country-by-country basis until the later of the date when there are no valid patent claims under our licensed patents covering such licensed product in such country, the date when regulatory exclusivity for such licensed product in such country expires and 10 years following the date of first commercial sale of such licensed product in such country. CRISPR Therapeutics is additionally required to reimburse us for our FTE costs and reasonable out-of-pocket expenses incurred performing development activities under the CRISPR Therapeutics Agreement. In the event CRISPR Therapeutics exercises its right to sublicense under the agreement, CRISPR Therapeutics must pay us a low teens to mid-twenties percentage of any non-royalty sublicense income, depending on the timing of the sublicense and whether the117abellingse is granted through an affiliate of CRISPR Therapeutics. As of December 31, 2022, we have received €3.6 million in payments, and we have invoiced €0.6 million for the supply of materials and FTE cost, development reimbursements and upfront one-time technology access fee and have made no milestone, royalty or sublicense fee payments.

We are required to use commercially reasonable efforts to perform our development obligations under the CRISPR Therapeutics Agreement and to supply certain materials to CRISPR Therapeutics. CRISPR Therapeutics is required to use commercially reasonable efforts to perform its obligations under the development plan and to develop and commercialize licensed products. We and CRISPR are required to keep the other party informed regarding the progress and results of performance of all development activities under the CRISPR Therapeutics Agreement.

The term of the CRISPR Therapeutics Agreement will continue on a product-by-product and country-by-country basis, until the last-to-expire royalty term expires in such country for such product, unless terminated earlier by either party. The CRISPR Therapeutics Agreement may be terminated (i) by CRISPR Therapeutics for convenience following a certain notice period, (ii) by us if CRISPR Therapeutics or any of its affiliates, either directly or indirectly, challenges or assists a third party to challenge the licensed patent rights or in the event CRISPR Therapeutics undergoes a change of control, or (iii) by either party in the event of the other party's material breach following a cure period (including on a program-by-program basis) or in the event of the other party's insolvency. Upon expiration, the license granted to CRISPR Therapeutics converts into a fully paid-up, royalty-free, perpetual and irrevocable license. Upon termination, the licenses granted to CRISPR Therapeutics will terminate and, in the case of termination for CRISPR Therapeutics' material breach or insolvency or for convenience by CRISPR Therapeutics, CRISPR Therapeutics must transfer all Cas9 mRNA constructs and related data to us.

Boehringer Ingelheim Exclusive Collaboration and License Agreement

In August 2014, we entered into an Exclusive Collaboration and License Agreement with Boehringer Ingelheim, which we refer to as the Boehringer Agreement, whereby we granted Boehringer Ingelheim exclusive global rights for development and commercialization of our investigational therapeutic mRNA vaccine BI 1361849 (formerly CV9202) formulated with our protamine technology, and products containing such vaccine for all uses for cancer in humans. We received an upfront payment of €30 million, as well as an option fee payment of €5 million and an additional €7 million in development milestone payments. As of December 31, 2021, we received €7.6 million for the supply of materials and reimbursing us for development costs. In June 2021, Boehringer Ingelheim provided notice of its intention to terminate the Boehringer Agreement, with such termination becoming effective on November 17, 2021.

Bill & Melinda Gates Foundation Partnership

In May 2014, we entered into a grant agreement with the Bill & Melinda Gates Foundation for the development of a vaccine for rotaviruses. Under the terms of the grant, as amended by an amendment entered into November 2020, the Bill & Melinda Gates Foundation will provide up to $2.8 million in funding, and we are required to perform certain activities specified in a project collaboration plan. As of December 31, 2022, we have received $3.0 million in funding under the agreement. We own all intellectual property created using grant funding; however, we must make any Bill & Melinda Gates Foundation-funded products available at an affordable price in a list of clearly defined low and lower middle-income countries. The term of the rotavirus agreement expired in June 2022, and both parties are currently assessing options to continue the project. Our global access commitments survive termination or expiration of the agreement. We and the Bill & Melinda Gates Foundation are currently assessing options to continue the rotavirus project.

In March 2015, the Bill & Melinda Gates Foundation made an equity investment of $40 million to support continued development of our RNA technology platform and the construction of an industrial-scale cGMP production facility, and we entered into the Global Access Commitments Agreement with the Bill & Melinda Gates Foundation in February 2015 pursuant to which we are required to take certain actions to support the Bill & Melinda Gates Foundation's mission. In particular, we are required to conduct development activities for up to three concurrent projects to be proposed by the Bill & Melinda Gates Foundation, subject to our right to reject proposed projects where we believe there is a reasonable likelihood of a material adverse effect on us. The costs of such projects will be allocated on a project-by-project basis in proportion to the allocation of the expected benefits. All intellectual property developed in connection with such projects will be owned by us.

Under the terms of the Global Access Commitments Agreement, any Bill & Melinda Gates Foundation-funded products will be made available by us at an affordable price in a list of clearly defined low and lower middle-income countries, while we will be able to market such products in developed countries on our own or through licensees. In addition, the new manufacturing facility will have dedicated capacity to focus on products resulting from Bill & Melinda Gates Foundation-related projects for distribution in such low and lower middle-income countries.

Our global access commitments are perpetual, however, our obligation to commence new development programs expires in February 2025. In the event that we commit a material breach of the Global Access Agreement, following a cure period, we must grant the Bill & Melinda Gates Foundation a non-exclusive, perpetual, irrevocable, fully paid-up, royalty-free license under any intellectual property controlled by us covering any Bill & Melinda Gates Foundation-funded products to develop, manufacture and commercialize such products in low and lower middle-income countries, and the Bill & Melinda Gates Foundation will have certain withdrawal rights with respect to its equity investment in us. For more information on the Bill & Melinda Gates Foundation's withdrawal rights, see section 7 related party transactions.

In November 2016 in connection with and subject to the terms of the Global Access Agreement, we were awarded a grant for up to $0.9 million in funding from the Bill & Melinda Gates Foundation for the development of a vaccine for picornaviruses. As of December 31, 2022, we have received $0.7 million in funding under the grant agreement. We granted the Bill & Melinda Gates Foundation a non-exclusive, perpetual, irrevocable, worldwide, royalty-free, fully paid-up, sublicensable license to make, use, sell, offer to sell, import, distribute, copy, modify, create derivative works, publicly perform and display any products developed using grant funding; however, in the event we demonstrate to the satisfaction of the Bill & Melinda Gates Foundation that we are able to meet its global access requirements, such license will be modified or terminated. The term of the picornavirus grant expired in June 2022; however, our global access commitments survive.

In November 2017, also in connection with and subject to the terms of the Global Access Agreement, we were awarded two additional grants for up to $1.9 million and $1.5 million from the Bill & Melinda Gates Foundation for the development of a universal influenza vaccine and a malaria vaccine, respectively. By an amendment entered into November 2020, our grant for the development of a malaria vaccine was increased by an additional $0.8 million. As of December 31, 2022, we have received $1.9 million and $2.2 million, respectively, in funding under each grant agreement. The programs will leverage our advanced RNActive® prophylactic vaccine technology to develop mRNA-based universal influenza and malaria vaccines. The malaria grant agreement expired in December 2022 and the universal influenza grant agreement expired in March 2022. We and the Bill & Melinda Gates Foundation are currently assessing options to continue the influenza grant agreement.

The Bill & Melinda Gates Foundation can terminate any of the three grant agreements entered into in connection with the Global Access Agreement early if it is not reasonably satisfied with our progress on a specific project, there are significant changes to our leadership, another issue arises which threatens a specific project's success, there is a change in our control or tax status, or we fail to comply with the grant agreement. Our global access commitments survive termination or expiration. Any grant funds that have not been used for, or committed to, the underlying project upon expiration or termination of a grant agreement must be returned to the Bill & Melinda Gates Foundation.

In July 2020, we amended the Global Access Agreement and entered into a Letter Agreement with GSK and the Bill & Melinda Gates Foundation. Pursuant to this letter agreement, the Bill & Melinda Gates Foundation released us of our global access commitments with respect to certain prophylactic and therapeutic vaccines based on our mRNA technology platform to be developed under the 2020 GSK Agreement. This release will remain in effect for a vaccine or medicine only for so long as it is in development or being commercialized under the 2020 GSK Agreement. The letter agreement does not release us from any of our obligations to initiate or continue projects under the Global Access Agreement or related grant agreements and GSK granted to us and the Bill & Melinda Gates Foundation a non-exclusive, royalty-free, perpetual license under intellectual property arising from certain activities under the 2020 GSK Agreement to make vaccines arising from those projects available in low and lower middle-income countries as set forth in the Global Access Agreement.

Coalition for Epidemic Preparedness Innovations Framework Partnering Agreement

In February 2019, we entered into a framework partnership agreement with CEPI, which as amended we refer to as the CEPI Agreement, to develop our RNA Printer using certain intellectual property controlled by us covering the development and manufacture of mRNA products as well as certain additional intellectual property licensed to us. In connection with the CEPI Agreement we have entered into work orders for the preclinical development of a Lassa virus vaccine, a yellow fever vaccine and our rabies virus vaccine. In addition, we entered into a work package for the preclinical development and a Phase 1 clinical trial for our first-generation SARS-CoV-2 vaccine, CVnCoV.

We are required to use reasonable efforts to achieve certain development milestones and are responsible for conducting certain clinical trials. We are required to share clinical trial data with CEPI, subject to the terms of specific work packages entered into in connection with the CEPI Agreement. In the event of an infectious disease outbreak, where such outbreak can be addressed by a Lassa virus, SARS-CoV-2 or future vaccine developed under the CEPI Agreement, we must manufacture such vaccine for use in the area affected by the outbreak on economic terms that satisfy CEPI's equitable access guidelines or otherwise allow CEPI or a third-party to supply such vaccine in the affected area. For the initial term of the CEPI Agreement and for a certain period thereafter, in the event of an outbreak that cannot be addressed by a vaccine already developed under the CEPI Agreement, CEPI may request, and we may agree, that we will develop a product targeted against such outbreak, or we will assist CEPI to develop a candidate product against such outbreak. In the event we decline to enter into such a development agreement, we will grant CEPI the right to develop and stockpile such vaccines under certain of our background intellectual property and intellectual property developed under the CEPI Agreement. We are additionally required to use reasonable efforts, at CEPI's request, to submit certain optimized antigen nucleotide sequences for up to three specified pathogens in order for CEPI to start its own product development program. We have a right of first refusal to manufacture any pharmaceutical products developed by CEPI using the antigen nucleotide sequences we provide. In certain scenarios, including if we fail to provide Lassa virus, SARS-CoV-2 or future vaccines developed under the CEPI Agreement at prices that comply with CEPI's equitable access guidelines, we must grant CEPI a license under certain of our background intellectual property and intellectual property developed under the CEPI Agreement to, among other things, develop our automation solution for use in treating such infectious diseases and to develop, manufacture and market such pharmaceutical products for use in geographic areas where there is a disease outbreak.

In connection with a December 2020 amendment to the CEPI agreement, we agreed to provide CVnCoV to organizations operating under the COVAX Facility, a global collaboration to accelerate the development, production and equitable access to SARS-CoV-2 tests, treatments and vaccines. Under this amendment, we agreed to supply a certain percentage of our total capacity for distribution of CVnCoV to organizations participating in the COVAX Facility.

We are required to grant certain approved manufacturers all necessary rights to use certain of our preexisting intellectual property and intellectual property developed under the CEPI Agreement to further develop our automation solution and manufacture products for the treatment of certain diseases in geographic areas where there is an outbreak on economic terms that satisfy CEPI's equitable access guidelines. We must provide all necessary commercially reasonable support to such approved manufacturers to facilitate such efforts.

CEPI agreed to contribute up to $34 million in funding for projects undertaken under the CEPI Agreement and an additional $15.3 million in connection with development of CVnCoV. In the event of our commercial use of the pharmaceutical products developed under the CEPI Agreement, other than CVnCoV, we must notify CEPI and agree in

good faith how such commercial benefits are to be equitably managed between the parties. As of December 31, 2022, we have received €27.1 million in funding for projects undertaken under the CEPI Agreement.

We solely own all intellectual property developed under the CEPI Agreement but are required to obtain CEPI's consent prior to exploiting any intellectual property developed under the CEPI Agreement if such exploitation is in conflict with or goes against CEPI's mission or policies.

The CEPI Agreement terminated in February 2022, except with respect to certain ongoing projects, which are contemplated to be completed in December 2023. Following the completion of the CEPI Agreement, CEPI requested a partial reimbursement of $1.0 million for unspent funds. See note 3.7 to our financial statements contained elsewhere in this Annual Report for further information on the terms of the funding provided by CEPI.

Tesla Automation Development and Intellectual Property Agreement

In November 2015, we entered into a development and intellectual property agreement with Tesla Automation, formerly trading under the name of Tesla Grohmann Automation, which we refer to as the Tesla Automation Agreement, pursuant to which Tesla Automation agreed to design, develop and manufacture certain automated manufacturing machines on our behalf. We are obligated to pay Tesla Automation a fee for each machine delivered by Tesla Automation and up to $50 million to $60 million in commercial milestone payments as well as certain development costs under each associated work order. As of December 31, 2022, we have paid Tesla Automation €20 million to €21 million in development costs under various work orders, and we have not paid any fees for machines provided under the Tesla Automation Agreement or made any milestone payments.

The parties jointly own any intellectual property developed under the Tesla Automation Agreement, and Tesla Automation granted us a non-exclusive, royalty-free, perpetual, irrevocable as to existing machines, worldwide license to use, sublicense and distribute Tesla Automation background intellectual property that is incorporated into any machine developed under the Tesla Automation Agreement and an exclusive (only with respect to the machines, and until a certain period after the first commercial use of a machine, after which the license shall be non-exclusive), royalty-free, perpetual, irrevocable as to existing machines, worldwide license under Tesla Automation's interest in any jointly owned intellectual property. We granted Tesla Automation a non-exclusive, nontransferable, no-charge license during the term of the Tesla Automation Agreement under our background intellectual property for Tesla Automation's performance of its obligations under the Tesla Automation Agreement and a non-exclusive, royalty-free, perpetual, irrevocable as to existing machines, worldwide license under our interest in any jointly owned intellectual property to perform its obligations under the Tesla Automation Agreement and for applications and uses unrelated to the machines developed under the Tesla Automation Agreement.

The Tesla Automation Agreement continues on a machine-by-machine basis until 10 years after the first commercial use of such machine. Either party may terminate any work order entered into in connection with the Tesla Automation Agreement for convenience upon written notice to the other party, and either party may terminate a work order for the other party's material breach following a cure period, or for the other party's insolvency. In the event Tesla Automation terminates a work order for convenience or we terminate for Tesla Automation's material breach or insolvency, Tesla Automation must grant us a non-exclusive, fully paid-up, worldwide, irrevocable, perpetual, transferable and sublicensable license under Tesla Automation background intellectual property and Tesla Automation's interest in intellectual property developed under the Tesla Automation Agreement for us to complete, either on our own or with another supplier, the work under such terminated work order. In the event we terminate for convenience, we must pay Tesla Automation a termination fee. In the event Tesla Automation terminates for our material breach or insolvency, we must pay Tesla Automation a termination fee and grant Tesla Automation a non-exclusive, fully paid-up, sublicensable, worldwide irrevocable and perpetual license under our background intellectual property and our interest in the intellectual property developed under the Tesla Automation Agreement to manufacture machines relevant to the applicable work order.

Research and Option Agreement with myNEO

On May 12, 2022, we entered into a Research and Option Agreement ("R&O") with myNEO NV ("myNEO"), pursuant to which we will collaborate to identify specific antigens found on the surface of tumors for the development of novel mRNA immunotherapies. To achieve this goal, myNEO will leverage its biological datasets, its integrated machine learning and bioinformatics platform to identify and validate specific antigen targets predicted to elicit a strong immune response. Under the R&O, we aim to develop and commercialize at least two new medicinal products for the treatment of non-small cell lung cancer and melanoma (the "Main Indications") and potentially other indications. We are required to use commercially reasonable efforts to develop at least one product for each of the Main Indications, to file marketing approval applications for such products and commercialize such products in at least one of certain countries. Under the R&O, myNEO will own all intellectual property rights generated solely by myNEO or jointly with us during the first three phases of the R&D plan (the "R&D Project IP"). We received a non-exclusive, royalty-free, non-assignable, sublicensable, worldwide license under certain patents and know-how owned by myNEO and R&D Project IP to the extent required to perform our research and development obligations under the agreement until the completion of a certain phase of the R&D plan. We were also granted with an exclusive option to acquire all of myNEO's rights under certain R&D Project IP, which can be exercised until a certain period after we receive a validation report, provided that we will grant myNEO a non-exclusive, royalty-free, perpetual license back to such IP to make, use or sell certain targets in the field of patient-specific vaccines. Under the R&O, myNEO agrees to work exclusively with us to develop and validate shared antigens for the Main Indications until the earlier of the date of the first phase I clinical trial for either Main Indication or 24 months after we exercise our option.

Under the R&O, we paid myNEO an upfront one-time technology access fee of €138,000 and myNEO is eligible to receive up to €17.5 million in research and development milestone payments with respect to the Main Indications, up to €175,000 in research and development milestones payments with respect to indications other than the Main Indications, up to €30 million in commercial milestone payments with respect to the Main Indications and up to €7.5 million in commercial milestone payments with respect to indications other than the Main Indications, as well as low single-digit percentage royalties on the net sales of licensed products in the Main Indications and sub single-digit percentage royalties on the net sales of licensed products for indications other than the Main Indications. Our royalty obligations continue on a product-by-product and country-by-country basis until the earlier of the date when there are no valid patent claims covering such licensed product in such country and 10 years following the date of first commercial sale of such licensed product in such country.

The term of the R&O will continue until (i) the expiration of the option period if we do not exercise any of our exclusive options or (ii) the expiry of all applicable royalty payment obligations to myNEO, unless terminated earlier by either party. We have the right to terminate the R&O if certain milestones or if provisions of certain reports are delayed by a certain period, for convenience or in the case of a change of control of myNEO. We and myNEO both have the right to terminate the R&O in the event of the other party's material breach following a cure period.

Sponsored Collaboration Agreements

Schepens Institute Research Agreement

In March 2019, we entered into a sponsored research agreement, as amended in April 2020, July 2021, September 2021, August 2022 and January 2023 (as amended, the "Schepens Agreement"), with The Schepens Eye Research Institute, Inc. ("SERI") and Massachusetts Eye and Ear Infirmary ("MEEI"), pursuant to which SERI and MEEI agreed to perform certain research activities for mRNA-based eye therapy candidates. Under the Schepens Agreement, SERI and MEEI granted us an exclusive option to initiate negotiations for an exclusive or non-exclusive license to SERI's interest in any inventions developed under the Schepens Agreement. SERI and MEEI additionally granted us an exclusive option to negotiate an exclusive license to certain background intellectual property. Upon the exercise of such option and upon execution of the contemplated license, we would be required to pay SERI a $30,000 upfront payment, up to $0.8 million in development milestone payments and $1.8 million in regulatory milestone payments, and a low single-digit percentage royalty on net sales subject to certain minimum annual payments. We are required to provide $1.7 million in funding to SERI and MEEI in multiple payments during the term of the Schepens Agreement. As of December 31, 2022, we have provided $1.6 million in funding to SERI and MEEI under the Schepens Agreement.

Each party will solely own inventions it solely develops and will jointly own jointly developed inventions. We are responsible for all patent prosecution costs regarding intellectual property developed under the Schepens Agreement, and if we elect not to cover the prosecution costs for such intellectual property, SERI and MEEI will have the right to license such intellectual property to third parties, and we will have no rights in such intellectual property.

The Schepens Agreement continues until June 2023, unless extended by mutual agreement or earlier terminated. Both parties have the right to terminate the Schepens Agreement for the other party's material breach following a cure period, and SERI has the right to terminate in the event of our insolvency. We additionally have the right to terminate the Schepens Agreement for convenience following a notice period. In the event SERI terminates for our material breach or insolvency or we terminate for convenience, we must reimburse SERI for all costs incurred to date and provide certain additional funding for a three-month period. In the event we terminate for SERI's material breach, we must reimburse SERI for all noncancellable commitments.

Advance Purchase Agreements

European Commission — COVID-19 Vaccine Candidate

Advance Purchase Agreement for our COVID-19 Vaccine Candidate

On November 30, 2020, we entered into an APA with the EC, acting on behalf and in the name of all Member States of the European Union, which provided for the advance purchase by the Member States of 225 million doses of the vaccine to be allocated among the Member States, and the option to purchase up to an additional 180 million doses. Pursuant to the APA, we received an upfront payment of €450 million. Such upfront payment had to be used solely for the development and commercial supply of CVnCoV. We were required to return any unspent amounts of the upfront payment if, among others, we failed to successfully develop CVnCoV, or if we successfully develop CVnCoV without receiving EU marketing authorization, or if we failed to supply any doses of CVnCoV to any of the Member States by late 2021 (unless we and the EC mutually agree to a later date). In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which notification automatically terminated the APA. According to the APA, in such case of termination, we would only be required to return any unspent amount of the upfront payment. In the context of the APA, "spent" means either costs incurred or commitments made in connection with the purposes set forth in the APA. On March 8, 2022, we received a letter signed by the EC acknowledging and outlining that we will not be required to return any portion of the upfront payment. Due to the termination of the APA, we will not receive any further payments related to the APA.

In other respects, upon the EC's request, we will transfer any raw materials and/or primary components paid for with the upfront payment that were not used as of the termination date. Additionally, should the EC request, or should we successfully sell, any raw materials and/or primary components, then an applicable portion of such raw materials, primary components or proceeds, as the case may be, will be remitted to the EC. This repayment agreement expired at the end of 2022 and an amount of €4.1 million is accrued as of December 31, 2022 for the related amount due to be remitted to the EC.

Pandemic Preparedness Agreement

Federal Republic of Germany

Pandemic Preparedness Agreement with the Federal Republic of Germany

On February 20, 2022, the CureVac-GSK Consortium submitted its best and final offer in the Tender Procedure for the conclusion of framework agreements for the provision of production capacities and, on demand, for the production and supply of mRNA vaccines (lot 1). On April 8, 2022, the CureVac-GSK Consortium received a letter from the Federal Republic of Germany's counsel confirming that the CureVac-GSK Consortium had been awarded a Pandemic Preparedness Agreement. Pursuant to the Pandemic Preparedness Agreement, the CureVac-GSK Consortium will have to achieve, within a two years' time frame beginning from the award of the Pandemic Preparedness Agreement, a state in which it is considered qualified to provide manufacturing capacities in Germany for 160 million doses of mRNA vaccine per year, including procurement of the required nonproduct specific manufacturing licenses and insurances and to have achieved "pandemic preparedness," which means, inter alia, that we maintain the GMP IV facility in a stand-by mode that can be activated for manufacture of a so-called selected vaccine at any time and that the CureVac-GSK Consortium is complying with the material requirements set out in the Pandemic Preparedness Plan (in particular with the requirements regarding the assurance of a supplier network and the availability of the critical supplier products).

If qualification and pandemic preparedness is achieved by the end of the two years' time frame beginning from the award of the Pandemic Preparedness Agreement (and if the Pandemic Preparedness Agreement is not terminated because the CureVac-GSK Consortium does not have an mRNA-based vaccine for which a marketing authorization for the (at least temporary) placing on the German market has been granted at this time), the CureVac-GSK Consortium will receive a stand-by fee which will be shared between us and GSK in accordance with the agreement governing the CureVac-GSK Consortium. The phase following the qualification phase (stand-by phase) during which pandemic preparedness is to be maintained is for five years, it being understood that this term may be extended by mutual agreement up to three times for a subsequent one-year renewal term.

At any time during the stand-by phase, in case there is a public health emergency, the Federal Republic of Germany may exercise its preferred purchase right and/or its preferred manufacturing right. If the preferred purchase right is exercised the CureVac-GSK Consortium will have to deliver up to 80 million doses of the mRNA vaccine of the CureVac-GSK Consortium, and if the preferred manufacturing right is exercised the CureVac-GSK Consortium will have to act as a contract manufacturer and manufacture a third party's mRNA vaccine in our GMP IV facility. However, there are strict and narrow requirements to be fulfilled before the Federal Republic of Germany may exercise the preferred manufacturing right.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates, and our core technologies and other know-how, defend and enforce our patents, preserve the confidentiality of our trade secrets, operate our business without infringing, misappropriating or otherwise violating the intellectual property or proprietary rights of third parties and prevent third parties from infringing, misappropriating or otherwise violating our proprietary or intellectual property rights. We seek to protect our proprietary and intellectual property position by, among other methods, seeking and maintaining patents in the United States and other major markets. We also rely on trade secrets and know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, which we generally seek to protect through contractual obligations with third parties.

Patents

As of April 3, 2023, we own approximately 102 issued U.S. patents, 122 pending U.S. patent applications, 233 issued foreign patents (including 50 European patents, which have been validated in various European countries resulting in a total of approximately 518 national patents in European countries), 347 pending foreign patent applications (including 85 pending European patent applications) and 17 pending Patent Cooperation Treaty, or PCT, patent applications, including several patent families that are jointly owned with third parties. These patents include claims relating to our RNAoptimizer technology platform, CV8102, CV7202, CVSQIV, our COVID-19 vaccine candidates, and our proprietary LNP technology, as described further below.

RNAoptimizer

As of April 3, 2023, we own 26 issued U.S. patents, 18 pending U.S. patent applications, 106 issued foreign patents, including in Europe, Canada, China, India, Japan, the Republic of Korea, Singapore, Russia, Mexico and Australia, and 103 pending foreign patent applications and five PCT patent applications relating to our RNAoptimizer technology, including patents and patent applications relating to ORF optimization, UTR optimization, protein optimization and formulation. Our RNAoptimizer technology is used in our CV7202, CVSQIV and SARS-CoV-2 product candidates. The issued patents are expected to expire between 2025 and 2037, excluding any additional term for patent term adjustments or patent term extensions. If granted, the pending patent applications would be expected to expire between 2023 and 2044, excluding any additional term for patent term adjustments or patent term extensions.

CV8102

As of April 3, 2023, we own four issued U.S. patents, five pending U.S. patent applications, 26 issued foreign patents, including in Europe, Brazil, Canada, China, India, Japan, the Republic of Korea, Singapore, Taiwan, Russia, Mexico and Australia, and 19 pending foreign patent applications relating to our CV8102 product candidate. The issued patents are expected to expire between 2028 and 2037, excluding any additional term for patent term adjustments or patent term

extensions. If granted, the pending applications would be expected to expire between 2029 and 2037, excluding any additional term for patent term adjustments or patent term extensions.

CV7202

As of April 3, 2023, we own eight issued U.S. patents, five pending U.S. patent applications, 25 issued foreign patents, including in Europe, Canada, China, India, Japan, the Republic of Korea, Singapore, Russia, Mexico and Australia, and 23 pending foreign patent applications relating to our CV7202 product candidate. The issued patents are expected to expire between 2025 and 2037, excluding any additional term for patent term adjustments or patent term extensions. If granted, the pending patent applications would be expected to expire between 2023 and 2037, excluding any additional term for patent term adjustments or patent term extensions.

CV-SQIV

As of April 3, 2023, we own 10 issued U.S. patents, 13 pending U.S. patent applications, 44 issued foreign patents, including in Europe, Canada, China, India, Japan, the Republic of Korea, Singapore, Russia, Mexico and Australia and 56 pending foreign patent applications relating to our CVSQIV product candidate. The issued patents are expected to expire between 2025 and 2037, excluding any additional term for patent term adjustments or patent term extensions. If granted, the pending patent applications would be expected to expire between 2023 and 2043, excluding any additional term for patent term adjustments or patent term extensions.

COVID-19 Vaccine Candidates

As of April 3, 2023, we own 13 issued U.S. patents, 15 pending U.S. patent applications, 43 issued foreign patents, including in Europe, Canada, China, India, Japan, the Republic of Korea, Singapore, Russia, Mexico and Australia, 71 pending foreign patent applications and one PCT patent application relating to our COVID-19 product candidates, CVnCoV and CV2CoV. The issued patents are expected to expire between 2025 and 2041, excluding any additional term for patent term adjustments or patent term extensions. If granted, the pending patent applications would be expected to expire between 2023 and 2043, excluding any additional term for patent term adjustments or patent term extensions.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries in which we have filed patent applications, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the USPTO in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted for a portion of the term effectively lost as a result of the FDA regulatory review period, subject to certain limitations and provided statutory and regulatory requirements are met. For more information on patent term extension, see sec"ion 2.2 Business Over"iew u"der "Government Regulation" and "Pate"t Term Restoration and Extension".

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, our owned and licensed pending patent applications, and any patent applications that we may in the future file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future may be challenged, invalidated, narrowed, held unenforceable, infringed or circumvented. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby limiting the protection such patent would afford the respective product and any competitive advantage such patent may provide. See section 4.3 Risk Factors — Risks Related to Our Intellectual Property Rights.

Trademarks

As of April 3, 2023, we own trademark registrations or registration applications for CureVac, and the CureVac logo in the United States and in certain foreign jurisdictions including Europe.

Trade Secrets and Proprietary Information

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and know-how can be difficult to protect. We seek to protect our proprietary information, in part, by executing confidentiality agreements with our collaborators and scientific advisors, and non-competition, non-solicitation, confidentiality, and invention assignment agreements with our employees, consultants, and independent contractors. We have also executed agreements requiring assignment of inventions with selected scientific advisors and collaborators. The confidentiality agreements we enter into are designed to protect our proprietary information and the agreements or clauses requiring assignment of inventions to us are designed to grant us ownership of technologies that are developed through our relationship with the respective counterparty. We cannot guarantee, however, that we have executed such agreements with all applicable counterparties, such agreements will not be breached, or that these agreements will afford us adequate protection of our intellectual property and proprietary rights. See section 4.3 Risk Factors — Risks Related to Our Intellectual Property Rights.

Government Regulation

Government authorities in the United States, at the federal, state and local level, in other countries and jurisdictions and in the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, pa125abelling storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products, including biological products. In addition, some jurisdictions regulate the pricing of pharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other requirements of regulatory authorities, require the expenditure of substantial time and financial resources.

Patent Term Restoration and Extension

Depending upon the timing, duration and specifics of FDA approval of product candidates, some of a sponsor's U.S. patents may be eligible for limited patent term extension under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period generally is one-half the time between the effective date of an IND and the submission date of a BLA less any time the sponsor did not act with due diligence during the period, plus the time between the submission date of a BLA and the approval of that application less any time the sponsor did not act with due diligence during the period. Only one patent applicable to an approved biologic product is eligible for the extension, only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended, and the application for the extension must be submitted prior to the expiration of the patent. Moreover, a given patent may only be extended once based on a single product. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our products receive FDA approval, we expect to apply for patent term extensions on patents covering those products, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see section 4.3 Risk Factors — Risks Related to Our Intellectual Property Rights.

Regulation and Procedures Governing Approval of Biological Products in the United States

In the United States, we expect our product candidates will be regulated as biological products, or biologics, under the Public Health Service Act, or PHSA, and the Federal Food, Drug, and Cosmetic Act, or FDCA, and their implementing regulations, and other federal, state, local and foreign statutes and regulations. The failure to comply with the applicable U.S. requirements at any time during the product development process, including during nonclinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of a study or regulatory review and approval, and/or to administrative or judicial sanctions and adverse publicity. Sanctions may

include, but are not limited to, the U.S. Food and Drug Administration, or FDA's, refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, debarment, disgorgement of profits and civil or criminal investigations and penalties brought by the FDA or the Department of Justice or other governmental entities.

An applicant seeking approval to market and distribute a new biologic in the United States generally must satisfactorily complete each of the following steps:

- nonclinical laboratory tests, animal studies and formulation studies all performed in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an Institutional Review Board, or IRB, or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with applicable regulations, including with GCP regulations;
- after completion of all pivotal clinical trials, preparation and submission to the FDA of a BLA requesting authorization to market the product candidate for one or more proposed indications;
- satisfactory completion of an FDA advisory committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities, including those of third parties, at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, safety, strength, quality and purity;
- satisfactory completion of any FDA audits of the clinical study sites to assure compliance with GCPs, and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA; and
- compliance with any post-approval requirements, including the potential requirement to implement a REMS and to conduct any post approval studies required by the FDA.

Nonclinical Studies and Investigational New Drug Application

Before testing any biologic product candidate in humans, the product candidate must undergo nonclinical testing. Nonclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as animal studies to evaluate the potential for activity and toxicity. The conduct of the nonclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, are submitted to the FDA as part of an IND or similar application in other jurisdictions. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and *in vitro* studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless within the 30-day time period, the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research

subjects will be exposed to unreasonable health risks, and places the trial on a clinical hold. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trial can begin.

As a result, submission of the IND may result in the FDA not allowing the trial to commence or not be conducted on the terms originally specified by the sponsor in the IND. In addition, the FDA may raise concerns or questions at any time after the IND has become effective, and may impose a clinical hold even after clinical studies have initiated. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. A clinical hold issued by the FDA may therefore delay either a proposed clinical study or cause suspension of an ongoing study, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigation may proceed. This could cause significant difficulties in completing planned clinical trials in a timely manner.

Human Clinical Trials in Support of a BLA

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with GCP requirements. Clinical trials are conducted under study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety, dosing procedures and the effectiveness criteria to be evaluated. A separate protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND.

A sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of the BLA so long as the clinical trial is well-designed and well-conducted in accordance with GCP, including review and approval by an independent ethics committee, and the FDA is able to validate the study data through an onsite inspection, if necessary.

Further, each clinical trial must be reviewed and approved by an IRB either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors and the safety of human subjects. An IRB must operate in compliance with FDA regulations. The FDA, IRB, or the clinical trial sponsor may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements, the trial is unlikely to meet its stated objectives or that the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules, including the requirements for informed consent. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group may recommend continuation of the study as planned, changes in study conduct, or cessation of the study at designated check points based on access to certain data from the study.

Clinical trials typically are conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may be required after approval.

- Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or, on occasion, in patients, such as in the case of some products for severe or life-threatening diseases as cancer, especially when the product may be too inherently toxic to ethically administer to healthy volunteers.

- Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, preliminarily evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger Phase 3 clinical trials.

- Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a certain dose or dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are

undertaken within an expanded patient population, often at geographically dispersed clinical trial sites, to gather additional information about safety and effectiveness necessary to evaluate the overall benefit-risk relationship of the investigational product and to provide128abellinguate basis for physician labeling and product approval.

In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials, or Phase 4. These studies may be used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of biologics approved under accelerated approval regulations. Failure to exhibit due diligence with regard to conducting required Phase 4 clinical trials could result in withdrawal of approval for products. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other trials, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological candidate has been associated with unexpected serious harm to patients.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of clinical trials of FDA-regulated products, including biologics, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved.

Review and Approval of a BLA

The results of product candidate development, nonclinical testing and clinical trials, including negative or ambiguous results as well as positive findings, are submitted to the FDA as part of a BLA requesting a license to market the product for one or more indications. The BLA must contain extensive chemistry manufacturing and controls information and detailed information on the composi128abellingthe product and proposed labeling. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee to the FDA, and the sponsor of an approved BLA is also subject to annual program fees. The FDA adjusts the Prescription Drug User Fee Act, or PDUFA, user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the biological product candidate for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The Food and Drug Administration Safety and Innovation Act, or FDASIA, requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan,

or PSP, within sixty days after an end-of-Phase 2 meeting or as may be agreed between the sponsor and FDA. Unless otherwise required by regulation, PREA does not apply to any biological product for an indication for which orphan designation has been granted.

The FDA has 60 days after submission of the application to conduct an initial review to determine whether the BLA is sufficient to accept for filing based on the agency's threshold determination that it is substantially complete so as to permit substantive review. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies agreed to by the FDA under PDUFA, the FDA aims to complete its initial review of a standard application and respond to the applicant within 10 months of the 60-day filing date, and for a priority review application within six months. The FDA does not always meet its PDUFA goal dates for standard and priority BLAs, and its review goals are subject to change from time to time. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may also be extended by three months if the FDA requests or if the applicant otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

The FDA reviews a BLA to determine, among other things, whether the proposed product is safe and potent, or effective, for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP requirements to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

On the basis of the FDA's evaluation of the application and accompanying information, including the results of the inspection of the manufacturing facilities and any FDA audits of clinical trial sites to assure compliance with GCPs, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the application is not approved, the FDA may issue a complete response letter indicating that the review cycle is complete and the application is not ready for approval. A complete response letter will describe the deficiencies that must be addressed in order to secure final approval of the application, and when possible, will outline recommended actions the sponsor might take to obtain approval of the application. If a complete response letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. The FDA may also request additional information or clarification.

Sponsors that receive a complete response letter who elect to address the deficiencies may submit to the FDA information that represents a complete response to the issues identified by the FDA in the response letter. Such resubmissions are classified under PDUFA as either Class 1 or Class 2, based on the information submitted by an applicant in response to an action letter. Under the goals and policies agreed to by the FDA under PDUFA, the FDA aims to review and act on a Class 1 resubmission with two months of receipt and, with respect to a Class 2 resubmission, within six months of receipt. The FDA will not approve an application until issues identified in the complete response letter have been addressed. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If the FDA approves a new product, it may limit the approved indications for use of the product, or limit the approval to specific dosages. It may also require development of adequate controls or specifications and that certain contraindications, warnings or precau129abelling included in the product labeling. In addition, the FDA may call for post-approval studies, including Phase 4 clinical trials, to further assess the product's safety after approval and may limit further marketing of the product based on the results of these post-marketing studies. The agency may also require

testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS; the FDA will not approve the BLA without a REMS, if required. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manu130abellingg changes and additional labeling claims, are subject to further testing requirements and FDA review and approval. Once approved, the FDA may withdraw the product approval if compliance with pre-and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Development and Review Programs

The FDA has a number of programs intended to expedite the development and/or review of new products intended for serious or life-threatening diseases or conditions. These programs include fast track designation, breakthrough therapy designation, priority review and accelerated approval.

The FDA may issue a fast track designation to a product candidate if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new biologic may request that the FDA designate the biologic as a fast track product at any time during the clinical development of the product. For fast track products, sponsors may have greater interactions with the FDA during product development. A fast track product may also be eligible for rolling review, where the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. However, the FDA's PDUFA goal for reviewing a BLA fast track application does not begin until the last section of the application is submitted. Fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to facilitate the design of clinical trials in an efficient manner. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Any marketing application for a biologic submitted to the FDA for approval, including a product with a fast track designation and/or breakthrough therapy designation, may be eligible for other types of FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. The FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes and evidence of safety and effectiveness in a new subpopulation. A priority review is intended to

direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on an original BLA from 10 months to six months from the 60-day filing date.

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has stated that although it has limited experience with accelerated approvals based on intermediate clinical endpoints, such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a 131abcal or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, may lead the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Fast track designation, priority review, accelerated approval, and breakthrough therapy designation may expedite the development or approval process, but do not change the standards for approval. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Regulation

If regulatory approval for marketing of a product or for a new indication for an existing product is obtained, the sponsor will be required to comply with rigorous and extensive post-approval regulatory requirements as well as any post-approval requirements that the FDA has imposed on the particular product as part of the approval process. The sponsor will be required, among other things, to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements con131abellingadvertising, promotional labeling, product sampling and distribution. Manufacturers and certain of their subcontractors are required to register their establishment131abell the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers. Accordingly, the BLA-holder and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-

party manufacturers that we or our partners may decide to use. In addition, changes to the manufacturing process or facility are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented, and other types of changes to the approved product, such as addin132abellingdications and additional labeling claims, are also subject to further FDA review and approval.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may res132abellingevisions to the approved labeling to add new safety information; imposition of post-market study requirements or clinical trial requirements to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, untitled letters or warning letters or holds on post-approval clinical trials;
- adverse publicity;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions, fines, debarment, disgorgement of profits or the imposition of civil or criminal penalties.

The 132abellingely regulates marketing, labeling, advertising and promotion of products that are placed on the market. Pharmaceutical products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that ar132abellingscribed in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict marketing authorization holders' communications on the subject of off-label use of their products.

Orphan Drug Designation

Orphan drug designation in the United States is designed to encourage sponsors to develop products intended for rare diseases or conditions. In the United States, a rare disease or condition is statutorily defined as a disease or condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States but for which there is no reasonable expectation that the cost of developing and making available the product for the disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation qualifies a company for certain financial incentives, including tax advantages, waiver of the BLA application user fee and, if the product receives the first FDA approval for the indication for which it has orphan designation, market exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years from the approval of the BLA, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. An application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product.

In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first product. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a second application for a clinically superior version of the product for the same use. The FDA cannot, however, approve the same product made by another manufacturer for the same indication during the market exclusivity period unless it has the consent of the sponsor, the manufacturer makes a showing of clinical superiority over the product with orphan exclusivity, or the sponsor is unable to provide sufficient quantities.

An orphan-designated product may not receive orphan exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, orphan exclusivity in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition.

Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

Biosimilars and Exclusivity

The BPCIA (under the Affordable Care Act) created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. The FDA has issued several guidance documents outlining an approach to review and approve of biosimilars.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies, and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product, and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

A biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation, and impact of the BPCIA is subject to significant uncertainty.

Regulation and Procedures Governing Approval of Medicinal Products in the European Union

In order to market any product outside the United States, a company also must comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can initiate clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of pharmaceutical development, nonclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the medicinal product for each proposed indication.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trial Regulation (EU) No 536/2014 became effective, replacing Clinical Trials Directive 2001/20/EC (which can still be applied for new clinical studies during a transition period until January 2023). This new legislation, which is directly applicable in all Member States, aims at simplifying and streamlining the approval of clinical trials in the European Union by allowing for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications. The Clinical Trial Regulation harmonizes the assessment and supervision processes for clinical trials throughout the European Union, via a Clinical Trials Information System, or CTIS, which contains the centralized European Union portal and database for clinical trials foreseen by the Regulation. The EMA sets up and maintains CTIS, in collaboration with the competent national authority of each European Union Member Sate and the EC.

Marketing Authorization

To obtain a marketing authorization for a product under the European Union regulatory system, an applicant must obtain Marketing Authorization, or MA. There are two types of MAs:

- The Community MA, which is issued by the EC through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, advanced therapy medicinal products (such as gene therapies, somatic cell therapies and tissue engineered products), and medicinal products that contain a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum time frame for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210-day review period is reduced to 150 days.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in other Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

An MA may be granted only to an applicant established in the European Union. Regulation 1901/2006 on Medicinal Products for Pediatric Use provides that prior to obtaining a marketing authorization in the European Union in the centralized procedure, an applicant must demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, class waiver, or a deferral for one or more of the measures included in the Pediatric Investigation Plan.

The European Union also provides opportunities for market exclusivity. For example, in the European Union, upon receiving marketing authorization, new chemical entities generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic or biosimilar application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar product can be marketed until the expiration of the market exclusivity. However, there is no guarantee that a product will be considered by the European Union's regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity.

Periods of Authorization and Renewals

A marketing authorization is valid for five years, in principle, and it may be renewed after five years on the basis of a reevaluation of the risk-benefit balance by the EMA or by the competent authority of the authorizing Member State. To that end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least nine months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization is valid for an unlimited period, unless the EC or the competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal period. Any authorization that is not followed by the placement of the product on the European Union market (in the case of the centralized procedure) or on the market of the authorizing Member State within three years after authorization ceases to be valid.

Regulatory Requirements After Marketing Authorization

Following approval, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of the medicinal product. These include compliance with the European Union's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed. In addition, the manufacturing of authorized products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EMA's cGMP requirements and comparable requirements of other regulatory bodies in the European Union, which mandate the methods, facilities and controls used in manufacturing, processing and packing of products to assure their safety and identity. Finally, the marketing and promotion of authorized products, including industry-sponsored continuing medical education and advertising directed toward the prescribers of products and/or the general public, are strictly regulated in the European Union under Directive 2001/83.

Orphan Drug Designation and Exclusivity

Regulation 141/2000 and Regulation 847/2000 provide that a product can be designated as an orphan drug by the EC if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Union when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the European Union and that without incentives it is unlikely that the marketing of the product in the European Union would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention, or treatment of the condition in question that has been authorized in the European Union or, if such method exists, the product has to be of significant benefit compared to products available for the condition.

An orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance and the possibility to apply for a centralized European Union marketing authorization. Orphan drugs also benefit from a 10-year period of market exclusivity. During this market exclusivity period, neither the EMA nor the EC or the Member States can accept an application or grant a marketing authorization for a "similar medicinal product." A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. The market exclusivity period for the authorized therapeutic indication may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation because, for example, the

product is sufficiently profitable not to justify market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior, the applicant consents to a second orphan medicinal product application, or applicant cannot supply enough orphan medicinal product.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may obtain regulatory approval. Even if our product candidates are approved for marketing, sales of such product candidates will depend, in part, on the extent to which third-party payors, including government health programs in the United States (such as Medicare and Medicaid), commercial health insurers, and managed care organizations, provide coverage and establish adequate reimbursement levels for such product candidates. In the United States, the Member States of the European Union and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Reimbursement rules and levels are not harmonized in the European Union and therefore differ from Member State to Member State. Patients are unlikely to use any product candidates we may develop unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of such product candidates. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the price and examining the medical necessity and cost effectiveness of medical products and services and imposing controls to manage costs.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, and the cost of these studies would be in addition to the costs required to obtain FDA or other comparable marketing approvals. Even after pharmacogenomic studies are conducted, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover any product candidates we may develop could reduce physician utilization of such product candidates once approved and have a material adverse effect on our sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. For example, the payor may require co-payments that patients find unacceptably high. Further, one payor's determination to provide coverage for a product does not assure that such coverage will continue or that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor. Third-party reimbursement and coverage may not be adequate to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. The insurance coverage and reimbursement status of newly approved products for orphan diseases is particularly uncertain, and failure to obtain or maintain adequate coverage and reimbursement for any such product candidates could limit a company's ability to generate revenue.

The containment of healthcare costs also has become a priority of federal, state and foreign governments as well as other third-party payors such as statutory health insurance funds and the prices of pharmaceuticals have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented or coverage may be ended in the future.

Outside the United States, we will face challenges in ensuring obtaining adequate coverage and payment for any product candidates we may develop. Pricing of prescription pharmaceuticals is subject to governmental control in many countries. Pricing negotiations with governmental authorities or other third-party payors such as statutory health insurance funds can extend well beyond the receipt of regulatory marketing approval for a product and may require us to conduct a clinical trial that compares the cost effectiveness of any product candidates we may develop to other

available therapies. The conduct of such a clinical trial could be expensive and result in delays in our commercialization efforts.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost effectiveness of a particular product candidate to currently available therapies (so-called health technology assessments) in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union Member States may approve a specific price for a product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union Member States and parallel trade (arbitrage between low-priced and high-priced Member States) can further reduce prices. Special pricing and reimbursement rules may apply to orphan drugs. Inclusion of orphan drugs in reimbursement systems tend to focus on the medical usefulness, need, quality and economic benefits to patients and the healthcare system as for any product. Acceptance of any medicinal product for reimbursement may come with cost, use and often volume restrictions, which again can vary by country. In addition, results based rules of reimbursement may apply. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products, if approved in those countries.

Healthcare Laws and Regulations

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of pharmaceutical products that are granted marketing approval. Our current and future arrangements with providers, researchers, consultants, third-party payors and customers are subject to broadly applicable federal and state fraud and abuse, anti-kickback, false claims, physician payment transparency and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations include, without limitation, the following:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, in cash or in-kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or a specific intent to violate it in order to have committed a violation;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent or knowingly making, using, or causing to be made or used a false record or statement to avoid, decrease, or conceal an obligation to pay money to the federal government. Moreover, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or a specific intent to violate it in order to have committed a violation;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the CMS, within the HHS, information related to payments and other transfers of value made by that entity to physicians (as defined by statute), certain other healthcare providers beginning in 2022, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers;

- federal government price reporting laws, which require us to calculate and report complex pricing metrics to government programs and which may be used in the calculation of reimbursement and/or discounts on marketed products;

- the Foreign Corrupt Practices Act, a U.S. law which regulates certain financial relationships with foreign government officials (which could include, for example, certain medical professionals); and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers; and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring pharmaceutical manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information.

Violations of these laws can subject us to criminal, civil and administrative sanctions including monetary penalties, damages, fines, disgorgement, individual imprisonment and exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws, reputational harm, and we may be required to curtail or restructure our operations. Moreover, we expect that there will continue to be federal and state laws and regulations, proposed and implemented, that could impact our future operations and business.

Data Privacy and Security Laws

We may be subject to, or our marketing activities may be limited by, HIPAA and its implementing regulations, which established uniform standards for certain covered entities (healthcare providers, health plans and healthcare clearinghouses) governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of protected health information, including, among other requirements, mandatory contractual terms and technical safeguards to protect the privacy, security and transmission of protected health information and notification to affected individuals and regulatory authorities in the event of certain breaches of security of protected health information. The American Recovery and Reinvestment Act of 2009, commonly referred to as the economic stimulus package, included sweeping expansion of HIPAA's privacy and security standards called the Health Information Technology for Economic and Clinical Health Act, or HITECH, which became effective on February 17, 2010. Among other things, the HITECH makes HIPAA's privacy and security standards directly applicable to business associates, or independent contractors or agents of covered entities, that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

Even when HIPAA does not apply, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce and be construed as a violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The FTC expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards and the FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule.

State laws may be more stringent, broader in scope or offer greater individual rights with respect to protected health information, or PHI, than HIPAA, and state laws may differ from each other, which may complicate compliance efforts. By way of example, the California Consumer Privacy Act as amended by the California Privacy Rights Act, or CCPA, gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase our compliance costs and potential liability. The CCPA also creates a new state agency that will be vested with authority to implement and enforce the CCPA. In addition, other states may choose to adopt more stringent privacy legislation, which could increase our potential liability and compliance costs and adversely affect our business.

In the European Union, we may be subject to strict data protection regulations, in particular with regard to health data of individuals pursuant to Art. 4 Nr. 15 of the GDPR, effective since May 25, 2018. The GDPR, together with national legislation, regulations and guidelines of the European Union Member States and the United Kingdom governing the processing of personal data, impose strict obligations with respect to, and restrictions on, the collection, use, retention, protection, disclosure, transfer and processing of personal data. In particular, the GDPR includes obligations and restrictions concerning the consent and rights of data subjects, the transfer of personal data to countries outside the European Union, security breach notifications, and other requirements concerning the security and confidentiality of personal data. For example, in 2016, the European Union and United States agreed to a transfer framework for data transferred from the European Union to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union. The standard contractual clauses issued by the European Commission for the transfer of personal data may be similarly invalidated by the Court of Justice of the European Union. On June 4, 2021, the European Commission adopted new standard contractual clauses, which impose on companies additional obligations relating to data transfers, including the obligation to conduct a transfer impact assessment and, depending on a party's role in the transfer, to implement additional security measures and to update internal privacy practices. It remains to be seen whether these standard contractual clauses will remain available and whether additional means for lawful data transfers will become available. The GDPR imposes special requirements concerning the protection of special categories of personal data which include health and genetic information of data subjects. These special categories of data may only be processed under certain circumstances, including if the data subject consented to such processing or if (i) processing is necessary in order to protect vital interests of the data subject or of another natural person, insofar as the data subject is unable to provide consent for physical or legal reasons; (ii) the data concerned have manifestly been made public by the data subject; (iii) processing is necessary in order to assert, exercise or defend legal claims; or (iv) processing is necessary for the purposes of scientific research and to ensure that any additional requirements under applicable data protection laws, including national legislation, regulations and guidelines, are met.

Therefore, we may be subject to and our marketing activities may be limited by the regulations regarding the data protection of individuals according to the GDPR, the German Federal Data Protection Act and other applicable data protection laws. These regulations could also restrict the transfer of data from European Union member states to the United States. The general transfer of personal data outside of the European Union is prohibited unless the conditions laid out in Art. 44 et. seq. of the GDPR are fulfilled and an adequate level of data protection can be ensured. Currently the United States is not considered to be a country with an adequate level of data protection, and further contractual arrangements must be adopted to permit the international transfer of personal data to the United States. European data protection authorities may interpret the GDPR and national laws differently and impose additional requirements, which contributes to the complexity of processing personal data in or from the European Union. Guidance on implementation and compliance practices is regularly updated or otherwise revised. The GDPR has increased our responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the relevant data protection regimes. Separately, Brexit could also lead to further legislative and regulatory changes and increase our compliance costs. As of January 1, 2021, and the expiry of transitional arrangements agreed to between the United Kingdom and the European Union, data processing in the United Kingdom is governed by a United Kingdom version of the GDPR (combining the GDPR and the Data Protection Act 2018), exposing us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. On June 28, 2021, the European Commission adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from European Union member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless

the European Commission re-assesses and renews or extends that decision. For more information regarding the risks related to data security and privacy, see section 4.3 Risk Factors — Risks Related to Our Business and Industry.

Competition

We participate in an industry that is characterized by a rapidly growing understanding of disease biology, quickly changing technologies, strong emphasis on proprietary products, and a multitude of companies involved in the creation, development and commercialization of novel therapeutics. These companies are highly sophisticated and often collaborate strategically with each other.

We are developing a broad portfolio of product candidates that, coupled with our capabilities across mRNA technology, development and manufacturing, we believe position us at the forefront of targeted immune active and immune silent mRNA-based medicines. However, we compete with a wide range of pharmaceutical companies, biotechnology companies, academic institutions and other research organizations for novel therapeutic targets, new technologies, talent, financial resources, intellectual property rights and collaboration opportunities. As such, many of our competitors and potential competitors have substantially greater scientific, research and product development capabilities as well as greater financial, manufacturing, marketing and human resources than we do. In addition, there is intense competition to establish clinical trial sites and register patients for clinical trials. Many specialized biotechnology firms have formed collaborations with large, established companies to support the research, development and commercialization of products that may be competitive with ours. Accordingly, our competitors may be more successful than we may be in developing, commercializing and achieving widespread market acceptance. In addition, our competitors' products may be more effective or more effectively marketed and sold than any treatment we or our development partners may commercialize and may render our product candidates obsolete or noncompetitive before we can recover the expenses related to developing and commercializing any of our product candidates.

There are additional companies that are working on potential mRNA medicines. Companies with clinical programs with mRNA include BioNTech/Pfizer, Moderna, eTheRNA Immunotherapies, Translate Bio, GlaxoSmithKline Sanofi, AstraZeneca, Merck & Co. and Arcturus Therapeutics and those programs include, Ethris and Genevant Sciences. Specifically, our vaccine candidate, CV2CoV, against COVID-19 is currently the main focus of other pharmaceutical companies, some with more considerable capital resources than ours. For example, a limited number of products that utilize mRNA as a prophylactic vaccine against COVID-19 have been approved by the FDA, EMA and other regulatory agencies, such as BioNTech SE and Pfizer Inc.'s mRNA immunotherapy, BNT162b2, which was granted emergency approval by the FDA on December 11, 2020, and granted conditional marketing authorization by the EMA on December 21, 2020, and Moderna's mRNA immunotherapy, mRNA-1273, which was granted emergency approval by the FDA on December 18, 2020, and granted conditional marketing authorization by the EMA on January 6, 2021. Thus, we expect intense competition for our vaccine candidate from other pharmaceutical companies not limited to the field of mRNA medicines. In addition, the oncology therapeutics landscape in general is highly competitive and includes large and specialty pharmaceutical and biotechnology companies, academic research institutions and governmental agencies and public and private research institutions. It includes both competition from marketed therapies as well as potential new therapeutics in development. We may compete with products with different mechanisms of action as well as against established standards of care. We expect our intratumoral immunotherapy candidates for the treatment of solid tumors to face direct competition from companies such as Moderna and BioNTech in collaboration with Sanofi in addition to several non-mRNA-based approaches.

2.3 Organizational Structure

We are a holding company, and our sole asset is the capital stock of our wholly owned subsidiaries. Our major subsidiaries are listed below:

- CureVac SE (Germany);
- CureVac Inc. (United States of America);
- CureVac Belgium SA (Belgium);
- CureVac Swiss AG (Switzerland);

- CureVac Corporate Services GmbH (Germany);
- CureVac Netherlands B.V. (The Netherlands);
- CureVac RNA Printer GmbH (Germany); and
- CureVac Manufacturing GmbH (Germany).

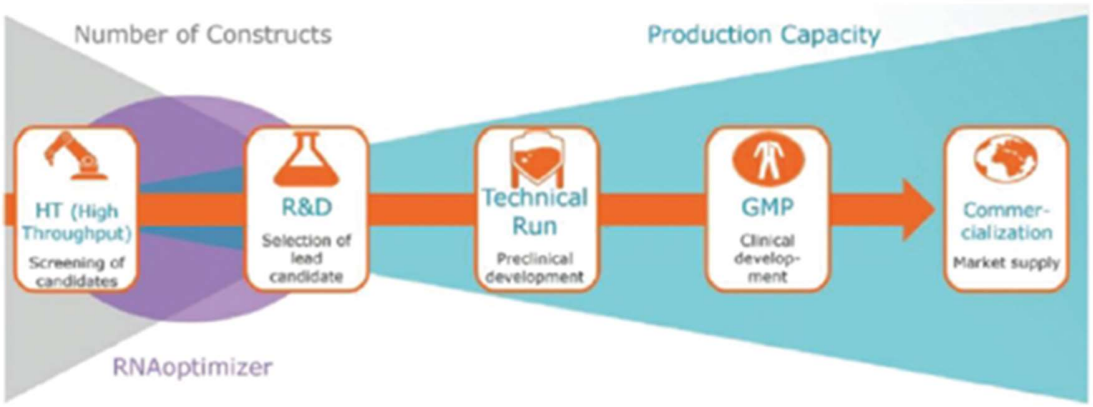
2.4 Property, Plant and Equipment

Our Manufacturing Platform

We are an integrated biopharmaceutical company with in-house manufacturing capabilities and expertise. We consider our manufacturing process an important part of our strategy that allows us to continuously improve our technology platform and maintain flexibility in clinical development and allow us to manufacture potential future commercial products. The close interaction of our technical development and research teams enables us to rapidly implement innovations and robustness to the manufacturing process. We control the critical steps of manufacturing in-house and also collaborate with manufacturing organization partners. Both of which allow us to drive innovation and to maintain flexibility, and in turn allows us to pivot quickly in pandemic settings.

All of our mRNA-based active ingredients for various fields of application originate from a common technology platform and are based on identical source materials. This enables us to produce all mRNA therapies using a platform process concept. Given the differences in the encoded protein only require alterations of the sequence of the mRNA molecule, leaving its physicochemical characteristics largely unaffected, we can use the same mRNA production strategy applying the same unit operations for diverse products. This allows us to save time and reduce costs compared to other manufacturing processes. Our approach supports a seamless production concept based on our experience and know-how in mRNA manufacturing.

Our GMP Manufacturing Facilities



We have continued to invest significantly in building and expanding our manufacturing capabilities since 2006. We currently have the capacity to produce early and late-stage clinical trial RNA material and potential future commercial lots. Since 2006, we have manufactured thousands of mRNA constructs, from high throughput and small amounts for discovery and preclinical development to GMP compliant products.

We are currently operating three GMP-certified suites. Our GMP I and II facilities were designed to run up to 14 different products in parallel, using a lab-scale process. The facilities cover all steps from starting material pDNA, through mRNA manufacturing to formulated bulk. Our GMP I and II facilities are dedicated to providing supplies for early clinical development (Phase 1 and 2), with capacity to produce multiple batches per year. In 2019, we expanded our production capacity to meet the increasing demands for clinical studies and potential future initial commercial supply by adding a GMP III facility. Our GMP III facility allows us to achieve additional scale and reduce manufacturing process time. This facility focuses on the production of mRNA, and formulated bulk. We currently use CMOs for starting material plasmid DNA (pDNA). The GMP III facility is intended to provide supply for our late-stage clinical studies and initial potential market supply and is based on a new scalable process design compared to our GMP I and II facilities. We are currently in the process of qualification and validation of a commercial facility, GMP IV (shown in the picture below), which is being designed to cover all manufacturing steps from starting material (pDNA) to formulation, to support our potential future commercial launches.

GMP IV facility

The RNA Printer

In addition to our GMP manufacturing facilities, we are currently developing a new automated and mobile production concept, The RNA Printer®. The RNA Printer® is a GMP production system that is being designed to downscale the manufacturing process and automate major manufacturing steps. This fully synthetic production process would allow us to have rapid manufacturing of products and offer reproducibility and high standardization. It will also include automated cleaning and sanitization in place procedures and continuous process validation. The current setup covers DNA and RNA production for automated downstream and upstream production up to drug substance. It is currently undergoing regulatory approval processes.

The RNA Printer®

The key characteristics of The RNA Printer® are rapid throughput, easy operator access to equipment, sophisticated precision control software and data capture, and the small footprint that allows for easy decentralization. With its modular design, it could be used for a rapid first response in outbreak scenarios or even be placed as a stand-alone device for epidemic areas. We view The RNA Printer® as complementary to our manufacturing strategy. With its modular design and decentralized concept, we believe The RNA Printer® could be used to facilitate broad access to mRNA technology and enable mRNA product developments, e.g. for rapid supply of new mRNA-based vaccines in pandemic situations as well as patient access to advanced and personalized mRNA-based therapies in oncology.

Our vision is to have a flexible, mobile and automated end-to-end solution for the different fields of application. Our objective is to cover the entire production stream, and we believe efficient accompanying analytics will help to rapidly produce high-quality material. All data generated during production would be collected to further improve production processes and product development.

Facilities

Our headquarters are in Tübingen, Germany, Friedrich-Miescher-Strasse 15, where we occupy approximately 123,000 square feet of office and laboratory space under a sublease agreement entered into with CureVac Real Estate GmbH that started on June 6, 2018. The fixed-term 15-year lease payment period began on March 1, 2020. We also occupy approximately 53,000 square feet of additional office and laboratory space in Tübingen, Germany, Paul-Ehrlich-Strasse 15, under sublease agreements also entered into with CureVac Real Estate GmbH, that started on February 1, 2018.

Since 2006, we have operated a manufacturing facility in Tübingen, Germany, the first worldwide GMP-compliant mRNA production plant with two multi-product suites (GMP I and II). These facilities contain approximately 16,145 square feet of laboratory space, including 2,800 square feet of GMP facilities, and are dedicated to providing supplies for early clinical development (Phases 1 and 2 of clinical trials). In addition, we have established a third in-house production suit (GMP III) with an upscaled manufacturing process, which was certified in December 2019. We currently occupy 2,800 square feet of GMP III facility for the production of mRNA. Our GMP III facility is intended to provide supplies for our late-stage clinical studies and anticipated early market supply. These manufacturing facilities are located in Tübingen, Germany, Paul-Ehrlich-Strasse 15 and are leased via the abovementioned sublease agreements entered into with CureVac Real Estate GmbH.

We are also constructing a new CureVac owned manufacturing facility, for a GMP production process at large industrial scale, from starting material to formulation, for potential future market supply (GMP IV). This facility is expected to be approximately 86,000 square feet. The expected cost of completion is €162.3 million, and as of December 31, 2022, we have spent €130.6 million on completing the GMP IV facility.

In addition, we lease land and small- to mid-scale buildings for our offices and laboratories in Tübingen approximately 66,000 sq. feet. We lease an aggregate of approximately 285,000 square feet, in Germany, Europe and the United States. The following table summarizes information with respect to the principal facilities leased by us:

Location	**Area (Approximate Sq. Feet)**
Germany:	
Tübingen	242,000
Frankfurt am Main	8,600
Wiesbaden	7,400
Total:	258,000
Belgium:	
Louvain La Neuve	5,200
Total	5,200
Netherlands:	
Amsterdam	9,100
Total:	9,100
United States:	
Boston	12,900
Total:	12,900
Total	285,200

Our leases expire on various dates from 2021 to 2035. The lease in Boston, United States, is held by our U.S. subsidiary, CureVac Inc. The Lease in Louvain La Neuve, Belgium, is held by our Belgian subsidiary, CureVac Belgium SA. The lease in Amsterdam, Netherlands, is held by our Dutch subsidiary, CureVac Netherlands B.V.

Environmental Issues

To the best of our knowledge, currently there are no foreign, federal, state or local environmental laws, rules or regulations that will materially affect our results of operations or our position with respect to our competitors. However, we can provide no assurance of the effect that any possible future environmental laws will have on our operating results.

2.5 Material subsequent events

See note 22 in the Notes to the consolidated financial statements included in sect"on 9 of this Annual Report ("he "**Company Financial Statements**") for an overview of events which do not ne'd to be discussed in the Company's statutory annual accounts and 'hich might influence the Company's outlook.

3. Financial Overview

3.1 Operating results

Operating Results

The following discussion of our financial condition and results of operations should be read in conjunction with CureVac's audited consolidated financial statements as of December 31, 2021 and 2022, and for the years ended December 31, 2020, 2021 and 2022, and the notes thereto, included elsewhere in this Annual Report. Financial information presented in the consolidated financial statements for periods prior to the completion of our corporate reorganization is that of CureVac AG (currently CureVac SE), our wholly owned subsidiary. The consolidated financial statements of CureVac N.V. are a continuation of the historical consolidated financial statements of CureVac AG (currently CureVac SE). CureVac AG (currently CureVac SE) was acquired by CureVac B.V., which subsequently converted into CureVac N.V. on August 14, 2020, as part of our corporate reorganization. CureVac B.V. had no assets, liabilities or contingent liabilities until the completion of our corporate reorganization. Following the corporate reorganization, CureVac N.V. became the holding company of CureVac AG (currently CureVac SE) and the historical consolidated financial statements of CureVac AG (currently CureVac SE) included in this Annual Report became the historical consolidated financial statements of CureVac N.V. The following discussion is based on our financial information prepared in accordance with IFRS as issued by the IASB (and endorsed in the EU), which may differ in material respects from generally accepted accounting principles in the United States and other jurisdictions. The following discussion includes forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including but not limited to those described under section 4.3 Risk Factors and elsewhere in this Annual Report.

Key Factors Affecting Our Results of Operations

We believe that the most significant factors affecting our results of operations include:

Research and Development Expenses

Our ability to successfully pioneer a robust mRNA technology platform and develop innovative product candidates will be the primary factor affecting our future growth and development. Our approach to the discovery and development of product candidates based on mRNA technology is still being demonstrated. As such, we do not know whether we will be able to successfully develop any products. Developing novel product candidates requires a significant investment of resources over a prolonged period of time, and a core part of our strategy is to continue making sustained investments in this area. We have chosen to leverage our platform to initially focus on advancing our product candidates in the areas of prophylactic vaccines, oncology and molecular therapy.

For more information on our proprietary technology and clinical development pipeline, see section 2.2 Business Overview — Our Product Portfolio.

All of the product candidates are still in development, and we have incurred and will continue to incur significant research and development costs for preclinical studies and clinical trials. We expect that our research and development expenses will constitute the most substantial part of our expenses in future periods in line with the advance and expansion of the development of our product candidates. Due to our accelerated efforts to develop our first-generation backbone COVID-19 vaccine candidate, CVnCoV, we incurred research and development expenses that significantly exceeded our historical levels of research and developments expenses. Additionally, our October 2021 notification to the European Commission of the withdrawal of our regulatory approval application for CVnCoV resulted in our recognition of several expenses, which have contributed to our increased expense levels, but which we do not expect to recur in future periods. In April 2021, we entered into a collaboration agreement with GSK for the development of a broad COVID-19 vaccine program based on our second-generation backbone. CV2CoV, a non-chemically modified mRNA, encoding the prefusion stabilized full-length spike protein of the SARS-CoV-2 virus, and formulated within LNPs, is the first representative of our COVID-19 vaccine program based on the second-generation backbone and presently in the Phase 1 clinical trial, as announced on March 30, 2022. Within this COVID-19 vaccine program, we plan to extend our technology platform also to chemically modified mRNA constructs to allow for data-driven selection of the best candidate. We expect to incur significant expenses related to such second-generation backbone vaccine candidates. But, as we and GSK agreed to equally share the development costs for GSK COVID Products, our current level of research and development expenses will not continue to increase in the level as it did from 2020 to 2021. Once we conclude our research and development efforts related to a selected second-generation backbone vaccine candidate, we expect that our research and development expenses shall be consistent with our past trends before the COVID-19 pandemic, but we may find it necessary to continue such current trend with respect to our research and developments expenses or we may continue to increase further our research and development expenses. For example, we may continue to increase our research and development expenses for future research and development related to the next generation backbone for our COVID-19 vaccine candidates, such as for our second-generation backbone COVID-19 vaccine candidates or may pursue new indications with our technology platform.

We have historically funded the research and development expenses primarily through public offerings of our common stock, private placements of equity securities, convertible loans, grants from government agencies and similar bodies and payments for collaborative research and development services with strategic partners. In addition, we signed an advance purchase agreement, or APA, with the EC that provided substantial support for our efforts to advance our first-generation backbone vaccine candidate, CVnCoV. In October 2021, we notified the European Commission of the withdrawal of our regulatory approval application for CVnCoV, which automatically terminated the APA.

Our and Our Collaborators' Ability to Commercialize Our Product Candidates

Our ability to generate revenue from our product candidates depends on our and our collaborators' ability to successfully advance clinical trials for our product candidates and receive regulatory approval, particularly in the United States, Europe, and other major markets.

We believe that our broad portfolio of product candidates with both novel and validated targets enhances the likelihood that our research and development efforts will yield successful product candidates. Nonetheless, we cannot be certain if any of our product candidates will receive regulatory approvals. Even if such approvals are granted, we will thereafter need to maintain manufacturing and supply arrangements and engage in extensive marketing prior to generating any revenue from such products, and the ultimate commercial success of our products will depend on their acceptance by patients, the medical community and third-party payors and their ability to compete effectively with other therapies on the market. See section 4.3 Risk Factors — Risks Related to the Development, Clinical Testing and Commercialization of Our Product Candidates.

The competitive environment is also an important factor with the commercial success of our product candidates, and our ability to successfully commercialize a product candidate will depend on whether there are competing product candidates being developed or already marketed by other companies.

We currently do not have any product candidates that have received regulatory approval. As such, we have not incurred any material commercialization expenses in connection with an approved product candidate. In February 2021, we initiated a rolling submission for our first generation COVID-19 vaccine candidate, CVnCoV, with the EMA, which was designed to allow the EMA to assess CVnCoV's compliance with standards for vaccine efficacy, safety and pharmaceutical quality as a prerequisite for a formal market authorization application. Later in 2021, EMA informed us that the EMA would not start reviewing our submission for CVnCoV before the beginning of 2022. As a result, we estimated that the earliest possible approval of CVnCoV would come in the second quarter of 2022. Data on the efficacy of CVnCoV was generated and published in June 2021. This efficacy data did not live up to our pre-trial expectations and fell behind the efficacy of competing COVID-19 vaccine products. The application for the marketing authorization for CVnCoV was withdrawn in early October 2021, as a necessary reaction to the efficacy data as well as the concerns and uncertainties resulting from such data on the granting of a marketing authorization and the expected concerns of prescribers and patients about using a COVID-19 vaccine with a lower efficacy compared to the vaccines already available on the market. After the withdrawal of the application for a marketing authorization for CVnCoV, we have focused our efforts on second-generation mRNA vaccines. The decision is aligned with the evolving dynamics of the pandemic response toward greater need for differentiated vaccines with the gradual transition from an acute pandemic to an endemic SARS-CoV-2 environment. In connection with the regulatory approval process, and in preparation for the commercialization of a second-generation COVID-19 vaccine, we expect our expenses related to commercialization to significantly decrease in the short-term due to our past commercialization efforts for CVnCoV. However, we expect that our expenses related to commercialization will significantly increase in the long term if a second-generation COVID-19 vaccine candidate reaches late clinical stages, but we expect that this increase in expenses will be mitigated by the GSK COVID Agreement, as described below. As part of the commercialization process of CVnCoV, we also entered into strategic partnerships with Bayer for the development, production and distribution of CVnCoV. In addition, pursuant to a preliminary agreement regarding the secondary manufacturing of CVnCoV we entered into with GSK, GSK would have supported the secondary manufacturing of up to 100 million doses of CVnCoV in 2021. Additionally, we also partnered with Fareva, Rentschler Biopharma SE, and Novartis AG, among others, to develop an integrated European manufacturing network. Due to our decision to withdraw CVnCoV from the regulatory approval process and focus our efforts on second-generation mRNA vaccine, separate agreements with Celonic and Wacker were terminated.

Our Collaborations, Related License Agreements and Advance Purchase Agreements

On April 8, 2022, we received a letter from the Federal Republic of Germany's counsel confirming that the CureVac-GSK Consortium was awarded with the Pandemic Preparedness Agreement. For further details on our Pandemic Preparedness Agreement, see section 2.2 Business Overview — Pandemic Preparedness Agreement.

Our results of operations have been, and we expect them to continue to be, affected by our contractual collaborations with third parties for the development and commercialization of certain of our product candidates. In addition, our future results of operation may be affected by future advance purchase agreements for our COVID-19 vaccine candidates. To date, our revenues have been recognized pursuant to license and collaboration agreements, which include upfront payments for licenses or options to obtain licenses, milestone payments, payments for product sales and payments for research and development services. Grants from government agencies or similar bodies are recognized as other operating income or as a reduction to depreciation and amortization expense recognized from assets purchased under the associated arrangements.

We have entered into strategic collaborations and license agreements with third parties. In addition, on November 30, 2020, we entered into an advance purchase agreement, or APA, with the European Commission, or EC, which provided for the advance purchase by the commission of our first-generation vaccine candidate, CVnCoV. In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which automatically terminated the APA. As part of our business development strategy, we aim to increase the number of our strategic collaborations in order to derive further value from our platform and more fully exploit the potential of our collaboration and license agreements.

Certain key terms of our current material collaboration and license agreements, as well as our advance purchase agreement with the EC are summarized below. For further details on our collaboration agreements, see section 2.2 Business Overview — Collaborations and section 2.2 Business Overview — Advance Purchase Agreements, respectively.

GlaxoSmithKline

In July 2020, we entered into a Collaboration and License Agreement with GSK, which we refer to as the 2020 GSK Agreement, pursuant to which we are collaborating with GSK to research, develop and commercialize prophylactic and therapeutic non-replicating mRNA-based vaccines and antibodies targeting infectious disease pathogens. The 2020 GSK Agreement was amended and restated in April 2021, September 2021, February 2022 and March 2022.

GSK paid us an upfront payment of €120 million and is required to pay us a manufacturing capacity reservation fee of €30 million following a certain regulatory milestone event, which is creditable against future milestone payments. We are eligible to receive up to between €28 million to €45 million in development milestone payments, €32 million to €35 million in regulatory milestone payments and €70 million to €100 million in commercial milestone payments, depending on the product. Under the 2020 GSK Agreement, we granted GSK an exclusive option to add additional products in the field of infectious diseases to the license granted under the 2020 GSK Agreement and, upon each exercise of such option, GSK is required to compensate us for certain development costs and pay any accrued milestone payments. Additionally, GSK has the right to replace products licensed under the 2020 GSK Agreement and, if the replacement product was already under development by us, GSK must compensate us for certain development costs and pay any accrued milestone payments. We are additionally eligible to receive tiered royalty payments ranging from a single-digit percentage to a low teens percentage on net sales, subject to certain customary reductions. GSK is required to compensate us for certain development and regulatory costs we may incur in connection with performing our obligations under the 2020 GSK Agreement, and we are eligible to receive up to €20,000 in reimbursements for expenses incurred by recording or registering the licenses granted under the 2020 GSK Agreement. We retain the right to commercialize products developed under the 2020 GSK Agreement in Germany, Austria and Switzerland, as GSK's exclusive distributor in these markets. Under any such distribution agreement to be entered into between us and GSK, we will be required to purchase supply from GSK and pay GSK a low thirties percentage royalty on net sales. Pursuant to the amendment in September 2021, we and GSK are required to complete certain development activities set forth in updated development plans. We and GSK agree to decide whether the products required for clinical studies will be manufactured by us, GSK or jointly.

Additionally, in April 2021, we entered into a new collaboration agreement with GSK, which we refer to as the GSK COVID Agreement, pursuant to which we are collaborating with GSK to research, develop and manufacture next-generation mRNA vaccines targeting the original SARS-CoV 2 strain as well as emerging variants, including multivalent and monovalent approaches, such as our second-generation COVID 19 vaccine candidate, CV2CoV. These vaccine candidates may either be used to protect unvaccinated individuals or to serve as boosters in the event that SARS-CoV 2 immunity gained from an initial vaccination reduces over time. The GSK COVID Agreement was amended and restated in September 2021, February 2022 and March 2022, and further amended to update the research and development plan in August 2022. Pursuant to the amendment in September 2021, we and GSK are required to complete certain development activities with respect to the GSK COVID Products set forth in updated development plans. We and GSK agree to decide whether the GSK COVID Products required for clinical studies will be manufactured by us, GSK or jointly.

Under the GSK COVID Agreement, GSK has paid us an upfront payment of €75 million. We and GSK agreed to equally share all development costs for GSK COVID Products, subject to certain exceptions. We and GSK will share all net profits generated from sales of GSK COVID Products, other than Combination Products (as defined therein), under profit sharing arrangements that in certain cases vary depending upon the GSK COVID Product in question, the time of sale, the number of doses sold and the party to whom the sale is made. We are eligible to receive tiered royalty payments ranging from a sub-teen percentage to a mid-teen percentage on net sales of Combination Products, subject to certain customary reductions. Under the GSK COVID Agreement we have the right to commercialize GSK COVID Products in Austria, Germany and Switzerland and if we exercise such right, our sales of GSK COVID Products, other than Combination Products will be subject to the profit share and we will be required to pay GSK a high-teen percentage royalty on net sales of all Combination Products in such countries.

Genmab

In December 2019, we entered into a Collaboration and License Agreement, which we refer to as the Genmab Agreement, with Genmab to research and develop up to four potential differentiated mRNA-based antibody products, to be selected by Genmab, based on the combination of our proprietary RNAntibody technology with Genmab's proprietary antibody technology for the treatment of human diseases. We will collaborate on research to identify an initial product candidate designed to express a certain Genmab proprietary antibody, and we will contribute a portion of the overall costs for the development of such product candidate, until submission of an IND. Genmab will thereafter be responsible for the development and commercialization of the product candidate. Under the Genmab Agreement we further grant Genmab a license for the preclinical development of up to four additional mRNA antibody product concepts and options to obtain commercial licenses under our mRNA technology to develop, manufacture and commercialize product candidates for up to three of such product concepts.

Under the terms of the Genmab Agreement, Genmab paid us a $10 million upfront fee and made a €20 million equity investment in March 2020. Genmab will be obligated to pay us a $0.5 million reservation fee upon the selection of each additional product concept for development under the Genmab Agreement and $5 million upon selection of a product targeting Genmab's proprietary antibody for further development and commercialization. Genmab is additionally required to pay us up to $30 million in option exercise fees. If Genmab exercises any of its options to obtain commercial licenses for the additional mRNA antibody concepts, Genmab would fund all research and would develop and commercialize any resulting product candidates. We are additionally eligible to receive up to between $25 million and $43 million in development milestone payments, $100 million and $125 million in regulatory milestone payments and $150 million and $200 million in commercial milestone payments for each product, depending on the specific product concept. In addition, we are eligible to receive a mid single-digit to low teens percentage tiered royalty on aggregate net sales of licensed products, on a per-product basis and subject to certain customary reductions. If Genmab grants a sublicense to the initial product candidate developed under the Genmab Agreement before a certain milestone event, Genmab must pay us a one-time $10 million payment. We are responsible for any payments to third parties related to the LNP technology we license to Genmab for use in relation to the initial product candidate developed under the Genmab Agreement and a portion of such payments with respect to LNP technology used in the additional product concepts. We retain an option to participate in development and commercialization of one of the potential additional mRNA antibody product concepts under predefined terms and conditions. In the event we exercise such right, we must pay Genmab a one-time payment of $3 million and refund any option fee paid by Genmab with respect to such product. As of December 31, 2022, we have received $1 million in development cost reimbursements and we have not received any reservation, product selection, option exercise or sublicense fees or milestone or royalty payments.

Arcturus

In January 2018, we entered into a Development and Option Agreement, which we refer to as the Arcturus Agreement, with Arcturus, which provides us with access to Arcturus LNP formulation technology which we use in combination with our mRNA technology. We paid Arcturus an upfront fee of $5 million and must pay an extension fee of $1 million if we exercise our option to extend the initial term of the Arcturus Agreement beyond July 2023. We are required to reimburse Arcturus for certain costs incurred in connection with development activities and provide certain FTE funding. We are additionally required to pay up to an aggregate of $5 million in connection with our acceptance of the irrevocable offer to obtain licenses for further development and commercialization of selected targets. As of December 31, 2022, we have not exercised our option to extend and accept any such irrevocable offer. Under each license agreement to be entered into in connection with our acceptance of the irrevocable offer, we will additionally be required to make certain royalty payments, which are not in excess of 10% on net sales of licensed products, and pay Arcturus up to $6 million in development milestone payments, $9 million in regulatory milestone payments and $8 million in commercial milestone payments. As of December 31, 2022, we have made payments totaling $5.5 million to Arcturus reimbursing Arcturus for development costs and in connection with our FTE funding obligations, and we have not accepted the irrevocable offer with respect to any target and therefore have not paid any acceptance fees or made any milestone or royalty payments to Arcturus.

Acuitas

In April 2016, we entered into a Development and Option Agreement, which as amended we refer to as the Acuitas Agreement, with Acuitas, which provides us with access to Acuitas LNP formulation technology that we use in combination with our mRNA technology. We are required to pay Acuitas annual target reservation and maintenance fees of up to $1.4 million if we reserve the maximum number of targets permitted under the Acuitas Agreement and to reimburse Acuitas for certain costs incurred in connection with development activities and certain FTE costs. We are additionally required to pay an option exercise fee ranging from $50,000 to $2 million upon each exercise of our option to obtain a license for further development and commercialization with respect to a selected target, subject to certain additional fees ranging from $10,000 to $200,000 for the exercise of our option for certain other vaccine targets. We paid Acuitas a $5 million upfront fee in connection with an amendment to the Acuitas Agreement dated July 2020 and, upon each exercise of our option to exchange a vaccine target licensed under any non-exclusive license, we are required to pay an exchange fee of $3 million. We additionally paid Acuitas a $3 million upfront fee in connection with an amendment to the Acuitas Agreement dated December 2020 and are required to pay an additional $250,000 in April 2023 for certain options not yet exercised. Under each license agreement in connection with our exercise of our option, we will additionally be required to make low single-digit percentage tiered royalty payments and must pay up to between $1.1 million and $9 million in development milestone payments, $1.3 million and $7 million in regulatory milestone payments and $1.3 million and $7 million in commercial milestone payments, depending on whether the license is exclusive or non-exclusive and the number of options exercised to date. As of December 31, 2022, we have exercised our option to obtain a non-exclusive license to 17 targets, subject to customary closing conditions. As of December 31, 2022, we have paid Acuitas $3.7 million in reservation and option exercise fees and $1.25 million for certain options not yet exercised and have made payments totaling $8.7 million reimbursing Acuitas for development costs and LNP batches and in connection with our FTE funding obligations.

For each option that we have exercised under the Acuitas Agreement, we have entered into a non-exclusive license agreement with Acuitas with respect to such optioned target, all based on the same form agreement, which we refer to as the Acuitas License Agreements. We are required to pay Acuitas up to between $1.1 million and $1.6 million in development milestone payments, $1.3 million and $1.8 million in regulatory milestone payments and between $1.3 million and $1.8 million in commercial milestone payments under each Acuitas License Agreement. We must pay Acuitas annual fees ranging from $5,000 to $10,000 for any additional protein targeted by a vaccine product licensed under each Acuitas License Agreement after a certain milestone event. Additionally, we are obligated to pay Acuitas a low single-digit percentage royalty on net sales of licensed products. As of December 31, 2022, we have made $100,000 in development milestone payments to Acuitas with respect to the license agreement relating to Rabies RAV-G, $1.4 million in development milestone payments (Phase I, Phase II and Phase III milestone payments) to Acuitas with respect to the license agreement relating to the SARS-CoV-2 Spike protein S, $100,000 in development milestone payments to Acuitas with respect to the license agreement relating to the Influenza hemagglutinin (HA) antigen, and have not made any royalty payments.

CRISPR Therapeutics

In November 2017, we entered into a Development and License Agreement with CRISPR Therapeutics which, as amended by an amendment entered into in June 2020, we refer to as the CRISPR Therapeutics Agreement, pursuant to which we will develop novel Cas9 mRNA constructs for use in gene editing therapeutics. Under the CRISPR Therapeutics Agreement, we granted CRISPR Therapeutics an exclusive worldwide license to use our improved Cas9 constructs for the development and commercialization of three of its in vivo gene-editing programs for certain diseases.

CRISPR Therapeutics has paid us an upfront one-time technology access fee of $3 million, and we are eligible to receive up to $13 million in development milestone payments, $33 million in regulatory milestone payments and $133 million in commercial milestone payments, as well as mid-single-digit percentage royalties from CRISPR Therapeutics on the net sales of licensed products on a product-by-product and country-by-country basis, subject to certain potential customary reductions. Additionally, CRISPR Therapeutics will make payments to us for services provided by us in conjunction with research programs under the CRISPR Therapeutics Agreement. In the event CRISPR Therapeutics exercises its right to sublicense under the CRISPR Therapeutics Agreement, CRISPR Therapeutics must pay us a low teens to mid-twenties percentage of any non-royalty sublicense income, depending on the timing of the sublicense and whether the sublicense is granted through an affiliate of CRISPR Therapeutics. As of December 31, 2022, we have received €3.6 million in payments and we have invoiced €0.6 million for the supply of materials and FTE cost, development reimbursements and upfront one-time technology access fee and no milestone, royalty or sublicense fee payments.

Bill & Melinda Gates Foundation

In May 2014, we were awarded a grant from the Bill & Melinda Gates Foundation for the development of a vaccine for rotaviruses, as amended in November 2020, for up to $2.8 million in funding. As of December 31, 2022, we have received $3.0 million in funding under the agreement. In March 2015, the Bill & Melinda Gates Foundation made an equity investment of $40 million to support continued development of our RNA technology platform and the construction of an industrial-scale cGMP production facility. We entered into a Global Access Commitments Agreement with the Bill & Melinda Gates Foundation in February 2015 pursuant to which we are required to take certain actions to support the Bill & Melinda Gates Foundation mission. In connection with the investment by the Bill & Melinda Gates Foundation, we are required to conduct development activities for up to three concurrent projects to be proposed by the Bill & Melinda Gates Foundation. The costs of such projects will be allocated on a project-by-project basis in proportion to the allocation of the expected benefits.

In November 2016, in connection with the Global Access Commitments Agreement, we were awarded a grant for up to $0.9 million in funding from the Bill & Melinda Gates Foundation for the development of a vaccine for picornaviruses. As of December 31, 2022, we have received $0.7 million in funding under the picornaviruses grant agreement. The term of the picornavirus grant expired in June 2022; however, our global access commitments survive. In November 2017, we were awarded two additional grants each for up to $1.9 million and $1.5 million in funding from the Bill & Melinda Gates Foundation for the development of a universal influenza and a malaria vaccine, respectively. By an amendment entered into November 2020, our grant for the development of a malaria vaccine was increased by an additional $0.8 million. As of December 31, 2022, we have received $1.9 million and $2.2 million, respectively, in funding under each grant agreement. The malaria grant agreement expired in December 2022 and the universal influenza grant agreement expired in March 2022. We and the Bill & Melinda Gates Foundation are currently assessing options to continue the influenza grant agreement.

Coalition for Epidemic Preparedness Innovations

In February 2019, we entered into a framework partnership agreement, which as amended we refer to as the CEPI Agreement, with the Coalition for Epidemic Preparedness, or CEPI, to develop our RNA Printer using certain intellectual property controlled by us covering the development and manufacture of mRNA products, as well as certain additional intellectual property licensed to us. In connection with the CEPI Agreement we have entered into work orders for the preclinical development of a Lassa virus vaccine, a yellow fever vaccine and our rabies virus vaccine. In addition, we entered into a work package for the preclinical development and a Phase 1 clinical trial for our first-generation COVID-19 vaccine candidate, CVnCoV. The CEPI Agreement terminated in February 2022, except with respect to certain ongoing projects, which are contemplated to be completed in December 2023. CEPI agreed to contribute up to $34 million in funding for projects undertaken under the CEPI Agreement and an additional $15.3 million in connection with development of CVnCoV. As of December 31, 2022, we have received €27.1 million in funding for projects undertaken under the CEPI Agreement. Following the completion of the CEPI Agreement, CEPI requested a partial reimbursement of $1.0 million for unspent funds.

Tesla Automation

In November 2015, we entered into a development and intellectual property agreement with Tesla Automation, formerly trading under the name of Tesla Grohmann Automation, which we refer to as the Tesla Automation Agreement, pursuant to which Tesla Automation agreed to design, develop and manufacture certain automated manufacturing machines on our behalf. We are obligated to pay Tesla Automation a fee for each machine delivered by Tesla Automation and up to $50 million to $60 million in commercial milestone payments as well as certain development costs under each associated work order. As of December 31, 2022, we have paid Tesla Automation €20 million to €21 million in development costs under various work orders, and we have not paid any fees for machines provided under the Tesla Automation Agreement or made any milestone payments.

Research and Option Agreement with myNEO

On May 12, 2022, we entered into a Research and Option Agreement ("R&O") with myNEO NV ("myNEO"), pursuant to which we will both collaborate to identify specific antigens found on the surface of tumors for the development of novel mRNA immunotherapies. To achieve this goal, myNEO will leverage its biological datasets, its integrated machine learning and bioinformatics platform to identify and validate specific antigen targets predicted to elicit a strong immune response. Under the R&O, we aim to develop and commercialize at least two new medicinal products for the treatment of non-small cell lung cancer and melanoma (the "Main Indications") and potentially other indications. We are required to use commercially reasonable efforts to develop at least one product for each of the Main Indications, to file marketing approval applications for such products and commercialize such products in at least one of certain countries. Under the R&O, myNEO will own all intellectual property rights generated solely by myNEO or jointly with us during the first three phases of the R&D plan (the "R&D Project IP"). We receive a non-exclusive, royalty-free, non-assignable, sublicensable, worldwide license under certain patents and know-how owned by myNEO and R&D Project IP to the extent required to perform our research and development obligations under the agreement until the completion of a certain phase of the R&D plan. We were also granted an exclusive option to acquire all of myNEO's rights under certain R&D Project IP relating to certain target lists, which we exercised on April 12, 2023. myNEO receives a non-exclusive, royalty-free, perpetual license back to such IP to make, use or sell certain targets in the field of patient-specific vaccines. Under the R&O, myNEO agrees to work exclusively with us to develop and validate shared antigens for the Main Indications until the earlier of the date of the first phase I clinical trial for either Main Indication or 24 months after we exercised our option.

Under the R&O, we paid myNEO an upfront one-time technology access fee of €138,000 and myNEO is eligible to receive up to €17.5 million in research and development milestone payments with respect to the Main Indications, up to €175,000 in research and development milestone payments with respect to indications other than the Main Indications, up to €30 million in commercial milestone payments with respect to the Main Indications and up to €7.5 million in commercial milestone payments with respect to indications other than the Main Indications, as well as low single-digit percentage royalties on the net sales of licensed products in the Main Indications and sub single-digit percentage royalties on the net sales of licensed products for indications other than the Main Indications. Our royalty obligations continue on a product-by-product and country-by-country basis until the earlier of the date when there are no valid patent claims covering such licensed product in such country and 10 years following the date of first commercial sale of such licensed product in such country.

Advance Purchase Agreement for our First-Generation COVID-19 Vaccine Candidate

On November 30, 2020, we entered into an APA with the EC, acting on behalf and in the name of all Member States of the European Union, which provided for the advance purchase by the Member States of 225 million doses of the vaccine to be allocated among the Member States and the option to purchase up to an additional 180 million doses. Pursuant to the APA, we received an upfront payment of €450 million. Such upfront payment had to be used solely for the development and commercial supply of CVnCoV. We are required to return any unspent amounts of the upfront payment if, among others, we fail to successfully develop CVnCoV or if we successfully develop CVnCoV, but we do not receive EU marketing authorization or fail to supply any doses of CVnCoV to any of the Member States by late 2021, unless we and the EC mutually agree to a later date. In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which notification automatically terminated the APA. According to the APA, in such case of termination, CureVac would only return the unspent amount of the upfront payment. In the context of the APA, "spent" means either costs incurred or commitments made in connection with the purposes set forth in the APA. On March 8, 2022, we received a letter signed by the EC acknowledging and outlining that we will not be required to return any portion of the upfront payment. Due to the termination of the APA, we will not receive any further payments related to the APA.

In other respects, upon the EC's request, we will transfer any raw materials and/or primary components paid for with the upfront payment that were not used as of the termination date. Additionally, should the EC request, or should we successfully sell, any raw materials and/or primary components, then an applicable portion of such raw materials, primary components or proceeds, as the case may be, will be remitted to the EC. This repayment agreement expired at the end of 2022 and an amount of €4.1 million is accrued as of December 31, 2022, for the related amount due to be remitted to the EC.

Acquisition of Frame Pharmaceuticals

June 8, 2022, we entered into a Share Purchase Agreement ("SPA"), to acquire all of the issued and outstanding shares of Frame Pharmaceuticals B.V., domiciled in Amsterdam, the Netherlands, a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*), organized and existing under the laws of the Netherlands, focused on advanced genomics and bioinformatics to identify both unique and shared neoantigens across different cancer types. Under the SPA, the total consideration for the purchase was €34 million, conditioned on certain development milestone payments, as described therein. This acquisition serves to complement and strengthen our discovery capabilities to identify and validate promising neoantigens for our mRNA cancer vaccine programs and could strongly increase the likelihood of developing highly effective cancer vaccines for patients.

Results of Operations

Year Ended December 31, 2021 Compared to Year Ended December 31, 2022

We have based the following discussion of our financial condition and results of operations on our audited consolidated financial statements as of and for the years ended December 31, 2021 and 2022, and the notes thereto, included elsewhere in this Annual Report and which have been retrospectively adjusted to reflect the impact of the share split resulting from the Corporate Reorganization.

The following is a discussion of our consolidated results of operations for each of the years ended December 31, 2021 and December 31, 2022. This information is derived from our accompanying consolidated financial statements prepared in accordance with IFRS as issued by IASB.

The following table summarizes our results of operations for the fiscal year ended December 31, 2021 and 2022:

	For Years Ended December 31,	
	2021	**2022**
	(in thousands of euros, except per share data)	
Statement of Operations and Comprehensive Income (Loss) Data:		
Revenue	102,990	67,420
Cost of sales	(238,195)	(183,993)
Selling and distribution expenses	(1,743)	(2,817)
Research and development expenses	(815,907)	(62,550)
General and administrative expenses	(100,402)	(104,178)
Income from release of governmental contract liabilities	574,502	—
Other operating income	67,702	37,932
Other operating expenses	(1,210)	(1,271)
Operating loss	**(412,263)**	**(249,457)**
Finance income	10,103	4,009
Finance expenses	(10,338)	(3,707)
Loss before income tax	**(412,498)**	**(249,155)**
Income tax benefit	782	126
Net loss	**(411,716)**	**(249,029)**
Other comprehensive income/loss:		
Items that may be subsequently reclassified to profit or loss		
Foreign currency adjustments	(91)	(105)
Total comprehensive loss	**(411,807)**	**(249,134)**
Net loss per share (basic and diluted)	**(2.21)**	**(1.32)**

Revenue

Revenue was €67.4 million for the year ended December 31, 2022, representing a decrease of €35.6 million, or 35%, from €103.0 million for the year ended December 31, 2021. The decrease was primarily driven by the termination of the Boehringer Agreement in 2021, which led to a recognition of the remaining contract liability, option fee payment and development milestone in revenue amounting to €26.0 million for the full year ended December 31, 2021. For the full year ended December 31, 2022 and 2021, €62.3 million and €74.3 million, respectively, in revenue was recognized under the collaboration agreements with GSK, for both the 2020 GSK Agreement and the GSK COVID Agreement.

Cost of Sales

Cost of sales was €184.0 million for the year ended December 31, 2022, representing a decrease of €54.2 million, or 23%, from €238.2 million for the year ended December 31, 2021. The decrease was primarily attributable to less expenses on CMO services (fiscal year 2021 was highly impacted by significant expenses for the set-up of a CMO network), partially offset by increased write-offs and scrap of raw materials amounting to €80.0 million in 2022, which were procured for manufacturing of products to sell to GSK that are no longer expected to be sold to them or were determined to be excess materials on hand. We recognize in Cost of Sales costs related to all R&D-services that we provide to GSK and all other collaboration partners as well as costs from set-up and quality assurance activities for our production processes, including those relating to pharmaceutical products which are under development in our collaboration agreements and for which we have not yet generated revenues.

	For the Years Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Personnel	(22,159)	(27,185)
Materials	(46,250)	(88,891)
Third-party services	(139,975)	(32,331)
Maintenance and lease	(2,874)	(2,425)
Amortization and depreciation	(3,992)	(6,295)
Impairment of equipment	(22,810)	(24,948)
Other	(135)	(1,918)
Total	**(238,195)**	**(183,993)**

Selling and Distribution Expenses

Selling and distribution expenses were €2.8 million for the year ended December 31, 2022, representing an increase of €1.1 million, or 65%, from €1.7 million in the year ended December 31, 2021. The increase was primarily attributable to higher personnel expenses due to an increase in headcount.

	For the Years Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Personnel	(1,369)	(2,029)
Amortization and depreciation	(86)	(371)
Other	(288)	(417)
Total	**(1,743)**	**(2,817)**

Research and Development Expenses

Research and development costs were €62.6 million for the year ended December 31, 2022, representing a decrease of €753.3 million, or 92%, from €815.9 million in the year ended December 31, 2021. The decrease was primarily attributable to significantly lower research and development costs. Fiscal year 2021 was highly impacted from the start of our Phase 2/3 clinical trial for CVnCoV. As of December 2021, we had recognized a provision for all remaining costs related to the CVnCoV clinical trials. During 2022, we were able to renegotiate the existing contracts such that our estimated remaining costs decreased, and more participants exited the trials earlier than originally estimated. As a result of these changes, we recognized a gain from the reversal of €38.5 million of the provision. Additionally, during this period, we recognized a net gain of €25.1 million for a change of estimate in the contract termination provisions as a result of GSK taking over our committed capacity at a CMO. As a result of these gains, we experienced a net gain in third-party services costs.

	For the Years Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Materials	(232,292)	(32,982)
Personnel	(33,733)	(33,944)
Amortization and depreciation	(4,259)	(8,650)
Patents and fees to register a legal right	(3,199)	(3,813)
Third-party services	(539,786)	20,499
Maintenance and lease	(347)	(1,069)
Other	(2,291)	(2,591)
Total	**(815,907)**	**(62,550)**

The following table reflects our research and development costs for each of our programs for the year ended December 31, 2021 and 2022:

	For the Years Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Key Programs (CV8102, CV7202, CV2CoV and CVnCoV)		
CV8102	(6,591)	(2,781)
CV7202	(518)	(219)
Second Generation Covid (CV2CoV and CV0501)	(5,782)	(24,983)
CVnCoV	(753,627)	39,458
Other Research and Development Programs	(4,610)	(13,949)
Unallocated costs(1)	(44,779)	(60,076)
Total	**(815,907)**	**(62,550)**

(1) Unallocated costs primarily consist of costs associated with personnel expenses, patents and fees to register a legal right, amortization and depreciation, maintenance and lease expenses, certain third-party service expenses and certain material expenses.

We expect that our research and development expenses will constitute the most substantial part of our expenses in future periods in line with the advance and expansion of the development of our product candidates.

Considering that, our research and development expenses primarily relate to the following key programs:

- Our modified mRNA vaccine candidate against SARS-CoV-2, CV0501, a monovalent construct, developed in collaboration with GSK. A Phase 1 study was initiated in August 2022. We reported positive preliminary data in early 2023. A Phase 2 clinical study, expected to start later in 2023, will assess monovalent and/or bivalent vaccine candidates designed to target clinically relevant variants. Novel cancer vaccine candidates based on differentiated antigen discovery technologies and bioinformatics to target antigens that are overexpressed in tumor tissues with no or little expression on healthy tissues. Within this strategy, we follow two approaches. The first approach assesses tumor antigens shared by different cancer patients for the development of off-the-shelf cancer vaccines. The second approach is tailored to the individual tumor setup of a patient for personalized therapy. We plan to advance new antigens for both approaches based on our second-generation mRNA backbone. To assess the safety and immunogenicity of our second-generation backbone in an oncology setting, we expect to initiate a proof-of-principle study in the second quarter of 2023, assessing an mRNA construct encoding eight epitopes from tumor associated antigens in patients with surgically resected Glioblastoma Multiforme.

- Our oncology program, CV8102, which is currently in a Phase 1 dose escalating clinical trial for four types of solid tumors as a monotherapy and in combination with anti-PD1 and an expansion of the Phase 1 study to evaluate the safety, tolerability and efficacy of CV8102 at a 600µg dose in patients with PD-1 refractory melanoma – also as a monotherapy and in combinations with anti-PD-1 antibodies.

- Our vaccine program, CV7202, which is currently in a Phase 1 clinical trial as a vaccine candidate for rabies.

General and Administrative Expenses

General and administrative expenses were €104.2 million for the year ended December 31, 2022, representing an increase of €3.8 million, or 4%, from €100.4 million in the year ended December 31, 2021. The increase was primarily attributable to increased amortization and depreciation expenses due to increased depreciation expense of right-of-use assets.

	For the Years Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Personnel	(37,393)	(36,765)
Maintenance and lease costs	(4,306)	(5,853)
Third-party services	(28,875)	(27,669)
Legal and other professional services	(9,230)	(10,394)
Amortization and depreciation	(8,895)	(11,360)
Other	(11,703)	(12,137)
Total	**(100,402)**	**(104,178)**

Income from release of governmental contract liabilities

Due to the withdrawal of the EMA regulatory approval application for CVnCoV in October 2021, CureVac recorded in 2021 an "Income from release of governmental contract liabilities" amounting to €574.5 million (refer to the "Year Ended December 31, 2020 Compared to Year Ended December 31, 2021" section for additional information regarding this prior year event). There was no such event occurring in 2022.

Other Operating Income

Other operating income was €37.9 million in the year ended December 31, 2022, representing a decrease of €29.8 million or 44%, from €67.7 million for the year ended December 31, 2021.

In March 2022, CureVac SE (as the surviving entity from the merger of CureVac AG and CureVac Beteiligungsverwaltungs AG) and GlaxoSmithKline Biologicals SA amended and restated the 2020 GSK Agreement and the GSK COVID Agreement in connection with GSK entering into a direct Agreement with Novartis relating to the use of Novartis as CMO at the same time as CureVac exits its CMO agreement with Novartis and is released from its pre-existing capacity commitments under the agreement. As a result, the Company avoided an outflow of resources. Additionally, under the restated agreement, CureVac was entitled to further compensation by GSK. The compensation mainly consists of consideration for set-up activities undertaken by CureVac (€20.5 million) and for reimbursement of prepayments (€12.0 million).

In 2021 the other operating income was primarily attributable to amounts recognized from grants from government agencies and similar bodies, primarily the German Federal Ministry of Education and Research, or BMBF.

Other Operating Expense

Other operating expense was €1.3 million in the year ended December 31, 2022 representing an increase of €0.1 million, or 8%, from €1.2 million for the year ended December 31, 2021. Other operating expense related primarily to compensation expense of our supervisory board.

Finance Income

Finance income was €4.0 million for the year ended December 31, 2022, representing an decrease of €6.1 million, or 60%, from €10.1 million for the year ended December 31, 2021. The decrease was mainly attributable to less foreign exchange gains partially compensated by positive interest on cash investments.

Finance Expenses

Finance expenses were €3.7 million for the year ended December 31, 2022, representing an decrease of €6.6 million, or 64%, from €10.3 million for the year ended December 31, 2021. The decrease was mainly related to less foreign exchange losses and less negative interest on cash.

Income Tax Benefit (Expense)

An income tax benefit of €0.1 million for the year ended December 31, 2022, representing a decrease of €0.7 million, or 88%, from €0.8 million for the year ended December 31, 2021. The change was primarily attributable to decreased deferred tax benefits.

Year Ended December 31, 2020 Compared to Year Ended December 31, 2021

We have based the following discussion of our financial condition and results of operations on our audited consolidated financial statements as of and for the years ended December 31, 2020 and 2021, and the notes thereto, included elsewhere in this Annual Report and which have been retrospectively adjusted to reflect the impact of the share split resulting from the Corporate Reorganization.

The following is a discussion of our consolidated results of operations for each of the years ended December 31, 2020 and December 31, 2021. This information is derived from our accompanying consolidated financial statements prepared in accordance with IFRS as issued by IASB.

The following table summarizes our results of operations for the fiscal year ended December 31, 2020 and 2021:

	For Years Ended December 31,	
	2020	2021
	(in thousands of euros, except per share data)	
Statement of Operations and Comprehensive Income (Loss) Data:		
Revenue	48,871	102,990
Cost of sales	(14,173)	(238,195)
Selling and distribution expenses	(733)	(1,743)
Research and development expenses	(113,808)	(815,907)
General and administrative expenses	(53,554)	(100,402)
Income from release of governmental contract liabilities	—	574,502
Other operating income	24,150	67,702
Other operating expenses	(568)	(1,210)
Operating loss	**(109,815)**	**(412,263)**
Finance income	2,070	10,103
Finance expenses	(22,103)	(10,338)
Loss before income tax	**(129,848)**	**(412,498)**
Income tax benefit	726	782
Net loss	**(129,122)**	**(411,716)**
Other comprehensive income/loss:		
Items that may be subsequently reclassified to profit or loss		
Foreign currency adjustments	35	(91)
Total comprehensive loss	**(129,087)**	**(411,807)**
Net loss per share (basic and diluted)	**(0.98)**	**(2.21)**

Revenue

Revenue was €103.0 million for the year ended December 31, 2021, representing an increase of €54.1 million, or 110.6 %, from €48.9 million for the year ended December 31, 2020. The increase was primarily driven by increased revenues from our collaborations with GSK and the termination of the Boehringer Agreement. In total, for both the 2020 GSK Agreement and the GSK COVID Agreement, for the year ended December 31, 2021, revenue of €74.3 million was recognized, compared to €8.8 million in the same period of the prior year. Due to the termination of the Boehringer Agreement, the remaining contract liability, related to the upfront payment, was being recognized over a shorter period through November 17, 2021, the termination date. In addition, an option fee payment of €5 million and the additional €7 million development milestone were recognized. For the year ended December 31, 2021, €26.0 million was recognized, compared to €1.9 million in the same period of the prior year.

In the year ended December 31, 2020, revenue primarily consisted of €34.9 million recognized from the collaboration with Eli Lilly, including €33.1 million in contract liabilities from an upfront payment which was recognized in revenue upon termination of the collaboration as no further performance obligation remained.

Cost of Sales

Cost of sales was €238.2 million for the year ended December 31, 2021, representing an increase of €224.0 million, or 1,577%, from €14.2 million for the year ended December 31, 2020. The increase was primarily attributable to recognition of expenses related to ineffective set-up activities of several contracted CMOs and, to a lesser extent, write-offs related to inventory in the period preceding the withdrawal of the EMA application for CVnCoV.

	For the Years Ended December 31,	
	2020	2021
	(in thousands of euros)	
Personnel	(2,896)	(22,159)
Materials	(1,598)	(46,250)
Third-party services	(2,652)	(145,515)

Maintenance and lease	(1,016)	(2,874)
Amortization, depreciation and derecognition	(5,913)	(21,262)
Other	(98)	(135)
Total	**(14,173)**	**(238,195)**

Selling and Distribution Expenses

Selling and distribution expenses were €1.7 million for the year ended December 31, 2021, representing an increase of €1.0 million, or 143%, from €0.7 million in the year ended December 31, 2020. The increase was primarily attributable to the recruiting of personnel for business development.

	For the Years Ended December 31,	
	2020	**2021**
	(in thousands of euros)	
Personnel	(631)	(1,369)
Amortization and depreciation	(98)	(86)
Other	(4)	(288)
Total	**(733)**	**(1,743)**

Research and Development Expenses

Research and development costs were €815.9 million for the year ended December 31, 2021, representing an increase of €702.1 million, or 617%, from €113.8 million in the year ended December 31, 2020. The increase was primarily attributable to significantly higher research and development costs from our Phase 2/3 clinical trial for CVnCoV. The increase mainly consists of costs incurred through use of clinical research organizations, including an onerous contract provision for the remaining unavoidable and anticipated costs for completing the CVnCoV clinical trials, as we have an obligation to continue monitoring trial participants, and the cost of compensating personnel involved in the development of CVnCoV.

In addition, the increase was also driven by recognition of expenses related to settlement costs related to the termination of several CMO contracts and to write-offs of CVnCoV-related prepayments and inventory.

	For the Years Ended December 31,	
	2020	**2021**
	(in thousands of euros)	
Materials	(29,834)	(232,292)
Personnel	(21,313)	(33,733)
Amortization and depreciation	(2,578)	(4,259)
Patents and fees to register a legal right	(7,337)	(11,157)
Third-party services	(51,306)	(531,827)
Maintenance and lease	(717)	(347)
Other	(723)	(2,292)
Total	**(113,808)**	**(815,907)**

The following table reflects our research and development costs for each of our programs for the year ended December 31, 2020 and 2021:

	For the Years Ended December 31,	
	2020	**2021**
	(in thousands of euros)	
Key Programs (CV8102, CV7202, CV2CoV and CVnCoV)		
CV8102	(11,129)	(6,591)
CV7202	(5,726)	(518)
CV2CoV	—	(5,782)
CVnCoV	(52,701)	(753,627)

Other Research and Development Programs	(14,389)	(4,610)
Unallocated costs(1)	(29,863)	(44,779)
Total	**(113,808)**	**(815,907)**

(1) Unallocated costs primarily consist of costs associated with personnel expenses, patents and fees to register a legal right, amortization and depreciation, maintenance and lease expenses, certain third-party service expenses and certain material expenses.

Our research and development expenses increased significantly compared to our expenses in 2020. Such increased research and development expenses primarily relate to the following key programs:

- Our mRNA vaccine program, CVnCoV against SARS-CoV-2.
- Our second-generation mRNA vaccine program, CV2CoV against SARS-CoV-2, which is being co-developed with GSK. The Phase 1 clinical trial for CV2CoV started in the first quarter of 2022.
- Our lead oncology program, CV8102, which is currently in a Phase 1 dose escalating clinical trial for four types of solid tumors as a monotherapy and in combination with anti-PD-1 and an expansion of the Phase 1 study to confirm the safety, tolerability and efficacy of CV8102 at a 600µg dose, the selected dose to be advanced in a Phase 2 clinical trial.

General and Administrative Expenses

General and administrative expenses were €100.4 million for the year ended December 31, 2021, representing an increase of €46.8 million, or 87%, from €53.6 million in the year ended December 31, 2020. The increase was primarily attributable to consulting services for product launch readiness, personnel related costs from an increased headcount and higher expense recognized on share-based payments awards made subsequent to the year ended December 31, 2020.

	For the Years Ended December 31,	
	2020	**2021**
	(in thousands of euros)	
Personnel	(29,884)	(37,393)
Maintenance and lease costs	(2,505)	(4,306)
Third-party services	(6,914)	(28,875)
Legal and other professional services	(3,531)	(9,230)
Amortization and depreciation	(6,020)	(8,895)
Other	(4,700)	(11,703)
Total	**(53,554)**	**(100,402)**

Income from release of governmental contract liabilities

On November 30, 2020, we entered into an Advance Purchase Agreement (APA) with the European Commission (EC), acting on behalf and in the name of all Member States of the European Union. The APA provided for the advance purchase by the Member States of 225 million doses of our SARS-CoV-2 vaccine. In order to support our accelerated efforts to develop a safe and effective vaccine, the APA provided for support to our operations in the form of upfront payments. The first upfront payment of €450 million was paid by the EC on behalf of the Member States and was, as of December 31, 2020, included in contract liabilities.

In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which notification automatically terminated the APA. According to the APA, in such case of termination, CureVac would only return the unspent amount of the upfront payment. In the context of the APA, "spent" means either costs occurred, or commitments made in relation to the purpose as set out in the APA. We were able to demonstrate that the upfront payment was used in accordance with the contract and no repayment was required. As a result, the contract liability amounting to €450 million is be released and recognized as income in the fourth quarter of 2021.

Due to the material magnitude of the amount, its non-recurring nature and to better enable comparability to past performance and predictability of future performance, CureVac recognized the €450 million as income and presented it in an additional line item in the statement of operations under "Income from release of governmental contract liabilities."

In 2020, the Company announced with the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung), or BMBF, a German government-related entity, established a grant to support the development and production of its COVID-19 vaccine candidates. In July 2020, CureVac applied for this grant as part of a special program to accelerate the research and development of urgently needed vaccines against SARS-CoV-2. The grant amounted up to €252 million and the payments were contingent on reaching predefined milestones. Based on the terms and conditions of the arrangement, the Company assessed the arrangement as having two components: a grant component and a supply component. Both were separated. The amount attributed to the supply of future deliveries was determined based on the relative stand-alone selling price of the vaccine observed in similar arrangements and is presented in contract liabilities.

The Company reached all the predefined milestones for 2020 and therefore received €103 million in the year then ended. Due to the withdrawal of the EMA regulatory approval application for CVnCoV, CureVac was not able to reach all predefined milestones in 2021. From 2020 to December 2021, CureVac received a total of €196.3 million. In November 2021, CureVac notified BMG of the inability to supply CVnCoV, triggering the automatic termination of the supply agreement. As a result, the contract liability of €124 million also was released and was recognized as income in the fourth quarter of 2021.

Consistent with the rationale and treatment described above under the APA with the EC, CureVac recognized the €124 million as income and presented it in an additional line item "Income from release of governmental contract liabilities."

Other Operating Income

Other operating income was €67.7 million in the year ended December 31, 2021 representing an increase of €43.5 million or 180%, from €24.2 million for the year ended December 31, 2020. The increase was primarily attributable to an increase in amounts recognized from grants from government agencies and similar bodies, primarily the German Federal Ministry of Education and Research, or BMBF.

Other Operating Expense

Other operating expense was €1.2 million in the year ended December 31, 2021 representing an increase of €0.6 million, or 100%, from €0.6 million for the year ended December 31, 2020. Other operating expense related primarily to compensation expense of our supervisory board.

Finance Income

Finance income was €10.1 million for the year ended December 31, 2021, representing an increase of €8.0 million, or 381%, from €2.1 million for the year ended December 31, 2020. The increase was mainly attributable to higher foreign exchange gains.

Finance Expenses

Finance expenses were €10.3 million for the year ended December 31, 2021, representing a decrease of €11.8 million, or 53%, from €22.1 million for the year ended December 31, 2020. The increase was mainly related to less negative interest on cash, which is being held in liquid funds to be available for use for CVnCoV wind-down activities and CV2CoV development and manufacturing activities. The financial expenses from the year ended December 31, 2020, were mainly related to interest recognized on convertible loans which were fully repaid in August 2020.

Income Tax Benefit (Expense)

An income tax benefit of €0.8 million for the year ended December 31, 2021, representing an increase of €0.1 million, or 14%, from €0.7 million for the year ended December 31, 2020. The increase was primarily attributable to deferred tax benefits on temporary differences.

3.2 Liquidity and Capital

Resources

Overview

Since inception, we have incurred significant operating losses. For the year ended December 31, 2021 and 2022, we incurred net losses of €411.7 million and €249.0 million, respectively. To date, we have financed our operations primarily through the IPO in August 2020, follow-on public offerings, private placements of equity securities, issuance of convertible debt, grants from government agencies and similar bodies and payments for collaborative research and development services. Our cash and cash equivalents as of December 31, 2022, were €495.8 million. Our primary cash needs are to fund our non-clinical and clinical development programs, for working capital requirements and for capital expenditures. The expected cost of completion for GMP IV is €162.3 million, and as of December 31, 2022, we have spent €130.6 million on completing the GMP IV facility. We believe that our existing cash, cash equivalents and short-term investments will enable us to fund our operating expenses and capital expenditure requirements at least through mid-2025. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect.

In February 2023, we sold an additional 27,027,028 common shares in an underwritten public offering at an offering price of $9.25 per share raising $234.2 million in net proceeds, after deducting underwriting discounts and commissions and offering expenses payable by us.

In September 2021, we entered into a sales agreement, the Open Sale Agreement, with Jefferies LLC and SVB Leerink LLC, as sales agents, to establish an at-the-market offering (ATM) program, pursuant to which we may sell, from time to time, ordinary shares for aggregate gross proceeds of up to $600.0 million. As of December 31, 2022, we had issued 6,908,493 common shares through the ATM program, resulting in $67 million in net proceeds to us. Following these issuances, the remaining value authorized for sale under the at-the-market program is $533 million.

Our financial condition and liquidity is and will continue to be influenced by a variety of factors, including our ability to generate cash flows from our operations, future indebtedness and the interest we are obligated to pay on this indebtedness, the availability of public and private debt and equity financing, changes in exchange rates which will impact our generation of cash flows from operations when measured in euros and our capital expenditure requirements, which are described in more detail at section 2.4 Property, Plant and Equipment.

The following table summarizes our contractual obligations as of December 31, 2022, and the effects, including estimated interest payments, that such obligations are expected to have on our liquidity and cash flows in future periods:

	Total (in thousands of euros)	**2023**	**2024**	**2025**	**2026**	**2027**	**Thereafter**
Contractual commitments	**74,300**	49,923	16,877	7,500	—	—	—
Lease liabilities	**54,723**	7,247	7,162	7,002	5,920	5,610	21,782
Leases not yet commenced	**30,770**	134	1,897	1,897	1,982	1,982	22,878
Total	**159,793**	**57,304**	**25,936**	**16,399**	**7,902**	**7,592**	**44,660**

We have entered into various agreements with collaborators, including licensing agreements. These agreements provide for us to make milestone and royalty payments that are conditional on the achievement of certain development, regulatory and commercial milestones and certain of these agreements provide us an option to obtain further licenses which could additionally require us to make such milestone and royalty payments. As of December 31, 2022, the aggregate amount of such potential milestone payments, including those relating to licenses acquired from exercised options, under all such collaboration agreements, was up to $176.9 million. The timing of these payments, and whether they become due, is conditional on achieving the applicable milestones.

We have not included milestone or royalty payments or other contractual payment obligations in the table above if the timing and amount of such obligations are unknown or uncertain.

Convertible Loans

We entered into a convertible loan agreement on May 3, 2019, with Mr. Dietmar Hopp, managing director of dievini, under which Mr. Hopp disbursed to us the amount of €50 million, referred hereto as Convertible Loan I. On October 24, 2019, we entered into an additional convertible loan agreement with Mr. Hopp, as amended, under which we have the right to call for disbursements in two tranches of €20 million each and an additional final tranche of approximately €24 million, until December 31, 2021, referred hereto as Convertible Loan II, and together with Convertible Loan I, referred hereto as the Convertible Loans. The Convertible Loans bore an interest rate of 8.00% per annum. On June 26, 2020, Mr. Hopp disbursed to us an additional $26.8 million. On July 24, 2020, the First Loan and Second Loan were terminated and on August 7, 2020, the total principal of €94.8 million and total accrued interest of €5.6 million were repaid in full.

European Investment Bank Loan

In June 2020, we signed a financing arrangement with the European Investment Bank, or EIB, under which EIB agreed to provide us with a line of credit in an amount of up to €75 million for the partial financing of our clinical developments and large-scale production of our infectious diseases vaccine candidates including our vaccine against SARS-CoV-2, or the Investment, provided that the amount of financing does not exceed 50% of the cost of the Investment.

As of December 31, 2020, we had drawn €25 million under the first of the three tranches. In November 2020, a land charge (mortgage) amounting to €75 million was registered in favor of the EIB to secure the loan.

In November 2021, we issued a prepayment request and cancellation notice to the EIB, pursuant to which we voluntarily repaid the €25 million in principal in addition to accrued interest in December 2021 and canceled the remaining €50 million available under the EIB loan. The mortgage was deleted from the land register in 2022.

BMBF Grant

We received from BMBF a grant to support the development of our first-generation COVID-19 vaccine candidate, CVnCoV of up to €252 million. In July 2020, we had applied to that grant as part of a special program to accelerate the research and development of urgently needed vaccines against SARS-CoV-2. In addition to the further development of our first-generation COVID-19 vaccine candidate, CVnCoV, against COVID-19, the grant was used for the rapid expansion of the vaccine production. Payments were contingent on reaching predefined milestones. Amounts incurred in 2020 and 2021 were eligible for reimbursement through the grant. Due to the withdrawal of the regulatory approval application for CVnCoV, we were not able to reach all predefined milestones for 2021 under the grant. We received funding of €103 million in 2020 and funding of €93 million in 2021. As of December 31, 2021, we had drawn €196 million of the grant. In November 2021, we notified BMG of our inability to supply CVnCoV, thereby triggering automatic termination of the supply arrangement.

Advance Purchase Agreement for our First-Generation COVID-19 Vaccine Candidate

On November 30, 2020, we entered into an APA with the EC, acting on behalf and in the name of all Member States of the European Union, which provides for the advance purchase by the Member States of 225 million doses of the vaccine to be allocated among the Member States, and the option to purchase up to an additional 180 million doses. Pursuant to the APA, we received an upfront payment of €450 million. Such upfront payment had to be used solely for the development and commercial supply of CVnCoV. We are required to return any unspent amounts of the upfront payment if, among others, we fail to successfully develop CVnCoV or if we successfully develop CVnCoV, but we do not receive EU marketing authorization or fail to supply any doses of CVnCoV to any of the Member States by late 2021, unless we and the EC mutually agree to a later date. In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which notification automatically terminated the APA. According to the APA, in such case of termination, we would only return the unspent amount of the upfront payment. In the context of the APA, "spent" means either costs occurred, or commitments made in relation to the purpose as set out in the APA. We were able to demonstrate that the upfront payment was used in accordance with the contract and no repayment was required.

Comparative Cash Flows

Comparison of the years ended December 31, 2021 and 2022

	For the Year Ended December 31,	
	2021	**2022**
	(in thousands of euros)	
Net cash flow provided by (used in):		
Operating activities	(733,128)	(286,177)
Investing activities	(127,901)	(93,499)
Financing activities	344,964	63,173
Effect of currency translation gains on cash and cash equivalents	4,936	836
Overall cash inflow/(outflow)	**(511,129)**	**(315,667)**

Operating Activities

Net cash used in operating activities for the year ended December 31, 2022, was €286.2 million as compared to net cash provided by operating activities of €733.1 million for the year ended December 31, 2021. The decrease in net cash used in operating activities was primarily attributable to less payments for service agreements with contract research organizations and contract manufacturing organizations, including related settlements which were driving the cash outflows in the year ended December 31, 2021.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2022, was €93.5 million as compared to net cash used in investing activities of €127.9 million for the year ended December 31, 2021. The change in cash flows used in investing activities was primarily attributable to decreased purchases of property, plant and equipment for use in contract manufacturing facilities.

Financing Activities

Net cash provided by financing activities was €63.2 million for the year ended December 31, 2022, as compared to €345.0 million for the year ended December 31, 2021. The decrease in cash flows provided by financing activities was mainly attributable to the proceeds in 2022 from the at-the-market offering program being lesser than those from the follow-on public offering, which closed in February 2021.

Comparison of the years ended December 31, 2020 and 2021

	For the Year Ended December 31,	
	2020	**2021**
	(in thousands of euros)	
Net cash flow provided by (used in):		
Operating activities	522,403	(733,128)
Investing activities	(45,274)	(127,901)
Financing activities	819,833	344,964
Effect of currency translation gains on cash and cash equivalents	(5,053)	4,936
Overall cash inflow/(outflow)	**1,291,909**	**(511,129)**

Operating Activities

Net cash used in operating activities for the year ended December 31, 2021, was €733.1 million as compared to net cash provided by operating activities of €522.4 million for the year ended December 31, 2020. The increase in net cash used in operating activities was primarily attributable to payments for service agreements with contract research organizations and contract manufacturing organizations, including related settlements, and the absence of a €450 million upfront payment received under the EC APA in 2020. We do not expect this trend of increasing use of cash in operating activities to continue at the same level.

Investing Activities

Net cash used in investing activities for the year ended December 31, 2021, was €127.9 million as compared to net cash used in investing activities of €45.3 million for the year ended December 31, 2020. The increase in cash flows used in investing activities was primarily attributable to increased purchases of property, plant and equipment for manufacturing facilities and intangible assets.

Financing Activities

Net cash provided by financing activities was €345.0 million for the year ended December 31, 2021, as compared to €819.8 million for the year ended December 31, 2020. The decrease in cash flows provided by financing activities was mainly attributable to the raising of cash in the follow-on public offering, which closed in February 2021 and was lower compared to the aggregate cash raised in a financing round in July 2020 and in our initial public offering in August 2020. In addition, the repayment of the EIB loan amounting to €26.3 million (included interest) and the payment of a tax liability relating to the transfer of our shares in 2021 contributed to this decrease.

3.3 Research and Development, Patents and Licenses, etc.

Research and development expenses consist primarily of costs incurred for our research and preclinical and clinical development activities, including our product discovery efforts and certain activities relating to the design of GMP-manufacturing facilities. Research and development expenses contain wages and salaries, share-based compensation, fringe benefits and other personnel costs, the costs of clinical testing and the associated clinical production costs, research material production costs, fees for contractual partners, consultants and other third parties, fees to register legal rights, amortization of licensed software and intellectual property as well as costs for plant and facilities. Research and development expenses contain costs for independent research and development work as well as work carried out in the context of collaboration and licensing agreements; such expenses include all costs related to research and development services delivered under our collaboration arrangements. Additionally, prior to initial regulatory approval, if any, costs relating to production of products are expensed as research and development expenses in the period incurred. If pre-launch products are sold, the respective product gross margin may be higher compared to the expected recurring margin as the underlying costs will not be included in cost of sales as they will have been recognized in research and development expense in the period incurred.

We also have partnered programs as further described under section 2.2 Business Overview — Collaborations and section 2.2. Business Overview — Advance Purchase Agreements,for which we incur additional expenses. In addition, our research and development expenses relate to our preclinical studies of further product candidates and discovery activities. These expenses mainly consist of salaries, share based-compensation, costs for production of preclinical compounds and costs paid to contract research organizations.

We expense research and development expenses as incurred. We recognize costs for certain development activities, such as preclinical studies and clinical trials, based on an evaluation of the progress to completion of specific tasks. We use information provided to us by our vendors such as patient enrollment or clinical site activations for services received and efforts expended. We expect research and development costs, including manufacturing, to support these activities, to increase significantly for the foreseeable future as our current development programs progress and new programs are added.

3.3 Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources, except for those noncancellable contractual obligations from certain of our arrangements with contract manufacturing organizations disclosed in section 3.2 Liquidity and Capital.

4. Risk Management and Risk Factors

4.1 Risk management and control systems

In the ordinary course of our business activities, we are exposed to various market risks that are beyond our control, including fluctuations in foreign exchange rates, which may have an adverse effect on the value of our financial assets and liabilities, future cash flows and profit. As a result of these market risks, we could suffer a loss due to adverse changes in foreign exchange rates in the countries in which we operate. Our policy with respect to these market risks is to assess the potential of experiencing losses and the consolidated impact thereof and to mitigate these market risks. We are not currently exposed to significant interest rate risk because we do not currently hold long-term debt that is exposed to market rates. See note 16 to our consolidated financial statements contained elsewhere in this Annual Report for further information on our risk management policies and exposure to market risks.

Credit Risk

Our credit risk arises primarily from cash and cash equivalents and other financial assets, including deposits with banks and financial institutions, as well as credit exposures to customers, including outstanding receivables and contract assets. These financial instruments approximate fair value due to short-term maturities. We maintain our cash and cash equivalents and short-term investments with high credit quality financial institutions. We believe that our credit policies reflect normal industry terms and business risk.

Foreign Currency Risk

Foreign currency risk is the risk that the fair value or future cash flows of an exposure will fluctuate because of changes in foreign exchange rates. Our exposure to the risk of changes in foreign exchange rates relates primarily to our operating activities (when revenue or expense is denominated in a foreign currency) and the amounts held as cash and cash equivalents. Our consolidated financial statements are reported in euros. We generate a significant portion of our revenue and incur a significant portion of our expenditures in certain non-euro currencies, principally U.S. dollars. We are exposed to fluctuations in foreign currency exchange rates primarily on revenue generated from sales in these foreign currencies. Our results of operations can be affected if the U.S. dollar appreciates or depreciates against the euro. As of December 31, 2022, if the euro had weakened 10% against the U.S. dollar with all other variables held constant, pre-tax loss for the year would have been €8.1 million (2021: €0.4 million) lower and post-tax loss would have been €5.7 million lower (2021: €0.3 million). Conversely, if the euro had strengthened 10% against the U.S. dollar with all other variables held constant, pre-tax loss would have been €6.6 million (2021: €0.4 million) higher and post-tax loss would have been €4.7 million (2021: €0.3 million) higher. The effects on pre- and post-tax loss and (accumulated) other comprehensive income due to fact that our subsidiary CureVac Inc.'s functional currency is the U.S. dollar would still have been immaterial at December 31, 2021 and 2022.

To the extent that we need to convert U.S. dollars into foreign currencies for our operations, appreciation of such foreign currencies against the U.S. dollar would adversely affect the amount of such foreign currencies we receive from the conversion. Sensitivity analysis is used as a primary tool in evaluating the effects of changes in foreign currency exchange rates on our business operations. The analysis quantifies the impact of potential changes in these rates on our earnings, cash flows and fair values of assets and liabilities during the forecast period, most commonly within a one-year period. The ranges of changes used for the purpose of this analysis reflect our view of changes that are reasonably possible over the forecast period. Fair values are the present value of projected future cash flows based on market rates and chosen prices.

Interest Rate Risk

Interest rate risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in market interest rates. Our exposure to the risk of changes in market interest rates relates primarily to our cash and cash equivalents with floating interest rates. Due to persistent low interest rates we may be exposed to the risk of being charged negative interest rates on our bank deposits. If interest rates as of December 31, 2021 and 2022, had been 1% higher while all other variables had remained the same, the net loss for the year (before and after tax) would have been €5.0 million (2021: €8.1 million) lower, because the higher interest income would have been generated from floating rates on invested cash and cash equivalents.

Disclosure Controls and Procedures

As required by Rule 13a-15 under the Exchange Act, our management, including our Chief Executive Officer (CEO) and our Chief Financial Officer (CFO), has performed an evaluation of the effectiveness of our disclosure controls and procedures. Disclosure controls and procedures refer to controls and other procedures designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. Disclosure controls and procedures include, without limitations, controls and procedures designed to ensure that information required to be disclosed by us in our reports that we file or submit under the Exchange Act is accumulated and communicated to management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding our required disclosures.

Based on the foregoing, our chief executive officer and our chief financial officer, together with our other members of management, have concluded that, as of December 31, 2022, due to the material weakness in internal control over financial reporting described below, our disclosure controls and procedures were not effective.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting and has assessed the effectiveness of our internal control over financial reporting as of December 31, 2022. In making this assessment, our management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in "Internal Control – Integrated Framework" (2013 framework).

Our management has excluded Frame Pharmaceuticals B.V. ("Frame", now CureVac Netherlands B.V.) from its assessment of internal control over financial reporting as of December 31, 2022 because Frame was acquired by us in a business combination on July 1, 2022. The total assets, excluding goodwill and intangible assets, total revenue and total operating loss of Frame excluded from our management's assessment represented approximately 0.4%, 0% and 0.5%, respectively, of our related consolidated financial statement amounts as of and for the year ended December 31, 2022.

Our management has concluded, based on its assessment, that our internal control over financial reporting was not effective as of December 31, 2022 due to a material weakness resulting from an IT system's functionalities having not been configured to support segregation of duties in the recording of manual journal entries as well as in the authorization of purchase orders.

Notwithstanding the material weakness identified as of December 31, 2022, we have concluded that the financial statements and other financial information included in this Annual Report, fairly present in all material respects our financial condition, results of operations and cash flows as of, and for, the periods presented. The material weakness did not result in any identified material misstatements. Our auditors have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's consolidated financial statements and their report dated April 25, 2023 expressed an unqualified opinion thereon.

Remediation Plan

As previously disclosed, in connection with the preparation of our financial statements for the year ended December 31, 2021, we concluded that we had material weaknesses related to (a) ineffective information technology general controls (ITGCs) in the area of user access over certain information technology (IT) systems and the reports generated from these systems used in the execution of controls that support the Company's financial reporting processes and (b) business controls which were not adequately designed and operating effectively as a result of gaps in the identification of risks, precision of review controls and documentation to evidence control performance. During 2022, we have remediated these IT and business process material weaknesses identified the previous year.

Management strives to implement measures designed to ensure that control deficiencies resulting in material weaknesses are avoided. Despite these efforts, such material weaknesses may occur. Management's planned remediative measures for the material weakness identified in 2022 include implementation of IT system-enforced segregation of duties in the recording of manual journal entries and in the authorization of purchase orders.

Management believes the foregoing plans will effectively remediate the deficiencies constituting the material weakness. However, there is no assurance as to when such remediation will be successful. As the remediation plans are implemented, management may take additional measures or modify the plan described above. See section 4.3 Risk

Factors — We have identified a material weakness in our internal control related to ineffective configuration of segregation of duties in an IT system which, if not remediated appropriately or timely, could result in loss of investor confidence and adversely impact our stock price. If we are unable to remediate the material weakness, or if other control deficiencies are identified, we may not be able to report our financial results accurately, prevent fraud or file our periodic reports as a public company in a timely manner.

Attestation Report of the Registered Public Accounting Firm

The effectiveness of our internal control over financial reporting as of December 31, 2022 has been audited by Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft ("Ernst&Young"), an independent registered public accounting firm. Their report is included on page F-3. Ernst & Young is a member of the Chamber of Public Accountants (*Wirtschaftsprüferkammer*), Berlin, Germany.

Changes in Internal Control over Financial Reporting

Other than the changes described above and an upgrade of the enterprise resource planning software underlying our financial reporting, there were no changes to our internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) under the Securities and Exchange Act of 1934), which occurred during the period covered by this annual report that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

4.2 In control statement

On the basis of reports and information provided to the Management Board and its committees, the Management Board is of the opinion that:

a. this Annual Report provides sufficient insight into any failings in the effectiveness of the Company's risk management and control systems;

b. notwithstanding the material weakness in our internal controls over financial reporting identified above, the Company's risk management and control systems provide reasonable assurance that the Company's financial reporting does not contain material inaccuracies;

c. based on the Company's state of affairs as at the date of this Annual Report, it is justified that the Company's financial reporting is prepared on a going concern basis; and

d. this Annual Report states those material risks and uncertainties that are relevant to the expectation of the Company's continuity for a period of twelve months after the date of this Annual Report.

The Company has established an internal audit function in December 2021. Parts of our internal audit tasks with regards to the commercial and financial perspective have been outsourced to a third party (PwC) acting as external service supplier to the Company and responsible for our internal audit function until its transition to internal resources. Among others, services related to the implementation of Internal Controls over financial reporting have been conducted. The plan to set-up and transfer the internal audit function in-house and co-source with third parties if needed has been approved. The internal audit function with regards to the clinical and technical perspective has been already established inhouse by the function of corporate quality. In view of the foregoing, our management board is of the opinion that given the size, resources, personnel and experience of the Company, adequate alternative measures have been taken.

Furthermore, the Management Board confirms that:

a. to the best of its knowledge, the statutory annual accounts included in this Annual Report give a true and fair view of the assets, liabilities, financial position and profit or loss of the Company and its consolidated subsidiaries taken as a whole; and

b. this Annual Report includes a fair review concerning the position, on the balance sheet date, and the development and performance of the business of the Company and its consolidated subsidiaries taken as a whole, together with a description of the principal risks and uncertainties that they face.

4.3 Risk factors

Summary of Risk Factors

The following is a summary of the risk factors our business faces. The list below is not exhaustive, and investors should read this "Risk Factors" section in full. Some of the risks we face include:

- Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.
- We may face continued business disruption and related risks resulting from inflationary pressures, supply chain issues, labor shortages and increases in commodity prices (including as result of the war in Ukraine) and the lingering effects of the COVID-19 pandemic, which could have a material adverse effect on our business plan or clinical trials.
- We depend on strategic partnerships with other companies to assist in the research, development and commercialization of our platform and product candidates. If our existing or future partners do not perform as expected, if we fail to maintain any of these collaborations or if these collaborations are not successful, our ability to commercialize our product candidates successfully and to generate revenues through technology licensing or otherwise may be materially adversely affected.
- Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of our product candidates or production of our product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our product candidates on a timely basis or at all.
- Our proprietary product candidates are still in preclinical or clinical development. We cannot give any assurance that any of our product candidates will receive regulatory approval, and if we are unable to obtain regulatory approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.
- We have no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.
- Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following regulatory approval, if any. Significant adverse events may occur during our clinical trials or even after receiving regulatory approval, which could delay or terminate clinical trials, delay or prevent regulatory approval or market acceptance of any of our product candidates.
- To date, a limited number of products that utilize mRNA as a prophylactic vaccine against COVID-19 have been approved in the United States, Europe and other countries, subject to certain limitations. In addition, no product that utilizes mRNA as a therapeutic vaccine has been approved in the United States or Europe. As such, mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.
- The regulatory approval processes of the FDA and comparable authorities are lengthy, time-consuming and inherently unpredictable and if we fail to obtain regulatory approval in any jurisdiction, we will not be able to

commercialize our products in that jurisdiction and our business, results of operations, financial condition and prospects, may be materially adversely affected.

- A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.
- The manufacture of mRNA-based medicines is complex and manufacturers often encounter difficulties in production, especially in the field of biologics. If we or any of our third-party manufacturers encounter difficulties, our ability to provide product candidates for clinical trials or products, if approved, to patients or future customers could be delayed or halted.
- Undetected errors or defects in our production could harm our reputation or expose us to product liability claims.
- We rely on third parties to conduct our nonclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.
- If we or any third-party manufacturer of our product candidates is unable to increase the scale of production of our product candidates, and/or increase the product yield of manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.
- At the start of the COVID-19 pandemic, we entered into contractual engagements with third-party manufacturers to have access additional capacity. The wind-down of these contracts entails risks of financial penalties and litigation.
- If we fail to comply with our obligations under any license, collaboration or other intellectual property agreements, disagree over contract interpretation, or otherwise experience disruptions to our business relationships with our collaborators or licensors, we could lose intellectual property rights that are necessary to our business.
- Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the successful commercialization of our product candidates will depend in part on the extent to which governmental authorities, private health insurers and other third-party payors provide coverage and adequate reimbursement levels and implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.
- Some of our product candidates are classified as gene therapies by the FDA and the EMA, and the FDA has indicated that products similar to our product candidates will be reviewed within its Center for Biologics Evaluation and Research, or CBER. Even though our mRNA product candidates are designed to have a different mechanism of action from gene therapies, the association of our product candidates with gene therapies could result in increased regulatory burdens, impair the reputation of our product candidates, or negatively impact our platform or our business.

Risks Related to Our Financial Position and Need for Additional Capital

We cannot assure you of the adequacy of our capital resources to successfully complete the development and commercialization of our product candidates, and a failure to obtain additional capital, if needed, could force us to delay, limit, reduce or terminate one or more of our product development programs or commercialization efforts.

As of December 31, 2022, we had cash and cash equivalents amounting to €495.8 million. We believe that we will continue to expend substantial resources for the foreseeable future developing our proprietary product candidates. These expenditures will include costs associated with research and development, conducting preclinical studies and clinical trials, seeking regulatory approvals, as well as launching and commercializing products approved for sale, if any, and costs associated with manufacturing products and maintaining manufacturing facilities. In addition, other unanticipated costs may arise. Because the outcomes of our anticipated clinical trials are highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our proprietary product candidates.

Our future funding requirements will depend on many factors, including but not limited to:

- the numerous risks and uncertainties associated with developing product candidates and maintaining our mRNA technology platform;
- the number and characteristics of product candidates that we pursue;
- the rate of enrollment, progress, cost and outcomes of our clinical trials, which may or may not meet their primary endpoints;
- the timing of, and cost involved in, conducting nonclinical studies that are regulatory prerequisites to conducting clinical trials of sufficient duration for successful product registration;
- the cost of manufacturing clinical supply and establishing commercial supply of our product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the timing of, and the costs involved in, obtaining regulatory approvals for our product candidates if clinical trials are successful;
- the timing of, and costs involved in, conducting post-approval studies that may be required by regulatory authorities;
- the cost of commercialization activities for our product candidates, if any of our product candidates are approved for sale, including product manufacturing, marketing and distribution of product candidates generated from our mRNA technology platform and any other product opportunity for which we receive marketing approval in the future;
- the terms and timing of any collaborative, licensing and other arrangements that we are currently party to or may establish, including any required milestone and royalty payments thereunder and any nondilutive funding that we may receive;
- the costs involved in preparing, filing, prosecuting, maintaining, defending and enforcing patent claims, including litigation costs, if any, and the outcome of any such litigation;
- the timing, receipt, and amount of sales of, or royalties or milestones on, our future products, if any;
- the costs to recruit and build the organization, including key executives needed to transform to a commercial organization; and

- the costs of operating as a public company, including hiring additional personnel.

In addition, our operating plan may change as a result of many factors currently unknown to us. As a result of these factors, we may need additional funds sooner than planned. We expect to finance future cash needs primarily through a combination of public or private equity offerings, strategic collaborations, revenues from future product sales and debt financing. If sufficient funds on acceptable terms are not available when needed, or at all, we could be forced to significantly reduce operating expenses and delay, limit, reduce or terminate one or more of our product development programs or commercialization efforts, which would have a negative impact on our business, prospects, operating results and financial condition.

We have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.

We have incurred significant losses since our inception. Our consolidated net loss for the years ended December 31, 2022 and 2021 were €249.1 million and €411.7 million, respectively. As of December 31, 2022, our accumulated deficit was €1,305.8 million. We expect to continue to incur losses in the future as we continue our research and development of, and seek regulatory approvals for, our product candidates and maintain and develop new technology platforms, prepare for and begin to commercialize any approved product candidates and add infrastructure and personnel to support our product development efforts and operations as a public company in the United States. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and clinical trials and development of our manufacturing technology. The net losses and negative cash flows from operations incurred to date, together with expected future losses, have had, and likely will continue to have, an adverse effect on our working capital. The amount of future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue.

Because of the numerous risks and uncertainties associated with biopharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. For example, our expenses could increase if we are required by the U.S. Food and Drug Administration, or the FDA, the European Medicines Agency, or the EMA, or other regulatory agencies to perform trials in addition to those that we currently expect to perform, or if there are any delays in completing our currently planned clinical trials, the partnering process for our proprietary product candidates or the development of any of our proprietary product candidates.

Our revenue to date has been primarily revenue from the license of our technology platform and from milestone payments for the development of product candidates against targets provided by our collaborators. Our ability to generate revenue and achieve profitability in the future depends in large part on our ability, alone or with our collaborators, to achieve milestones and to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, our product candidates and technology platform. This will require us to be successful in a range of challenging activities, including developing product candidates, obtaining regulatory approval for such product candidates, and manufacturing, marketing and selling those product candidates for which we may obtain regulatory approval. We may never succeed in these activities and may never generate revenue from product sales that is significant enough to achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our failure to become or remain profitable could depress our market value and could impair our ability to raise capital, expand our business, develop other product candidates or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

We require substantial financing, which may not be available on acceptable terms, or at all. Raising capital may cause dilution to our shareholders, restrict our operations or require us to relinquish rights to our technology or product candidates.

To the extent that we raise capital through the sale of common shares, convertible securities or other equity securities, the ownership interests of our shareholders may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect rights of our common shareholders. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring debt, making capital expenditures, creating liens, redeeming shares or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We cannot be certain that funding will be available on acceptable terms, or at all. If we are unable to raise capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Our current or future license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

We have limited financial and managerial resources, and therefore we intend to focus on developing product candidates for specific indications that we believe are most likely to succeed, in terms of both their potential for marketing approval and potential for successful commercialization, if approved. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

We depend on strategic partnerships with other companies to assist in the research, development and commercialization of our platform and product candidates. If our existing or future partners do not perform as expected, if we fail to maintain any of these collaborations or if these collaborations are not successful, our ability to commercialize our product candidates successfully and to generate revenues through technology licensing or otherwise may be materially adversely affected.

We have established strategic partnerships and intend to continue to establish strategic partnerships with third parties to research, develop and commercialize our platform and existing and future product candidates. We have entered into strategic partnerships with Genmab, Arcturus, Acuitas, CRISPR Therapeutics, GlaxoSmithKline Biologicals SA ("GSK"), the Bill & Melinda Gates Foundation, CEPI and Tesla Automation (formerly trading under the name of Tesla Grohmann Automation), among others. For certain of these programs, including our collaborations with Genmab, CRISPR

Therapeutics and GSK, we will depend on our partners to design and conduct their clinical studies. As a result, we may not be able to conduct these programs in the manner or on the time schedule we currently contemplate, which may negatively impact our business operations. While we have certain contractual rights to information about preclinical and clinical developments and results under certain of our collaboration agreements, including our agreements with Genmab, CRISPR Therapeutics and GSK, we cannot be certain that clinical trials conducted in connection with such collaboration programs will be conducted in a manner consistent with the best interests of our business. In addition, if any of these partners withdraw support for these programs or proposed products or otherwise impair their development, our business could be negatively affected. Also, our inability to find a partner for any of our product candidates may result in our termination of that specific product candidate program or evaluation of a product candidate in a particular indication. Even if we found a partner for one or more of our product candidates, there is no assurance that upon the approval of one or more of such product candidates we will be able to successfully co-commercialize such products.

In addition, our existing licenses and collaboration agreements, including our agreements with Genmab, Arcturus, Acuitas, the Bill & Melinda Gates Foundation, CRISPR Therapeutics, GSK and CEPI, impose, and any future licenses, collaborations or other intellectual property agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. Furthermore, our licenses and collaboration agreements impose, and any future agreement we enter into may also impose, restrictions on our ability to license certain of our intellectual property to third parties or to develop or commercialize certain product candidates or technologies. In spite of our best efforts, our collaborators may conclude that we have breached our obligations under our agreements, in which case, we may be required to pay damages and the collaborator may have the right to terminate the agreement. Any of the foregoing could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology, enable a competitor to gain access to the licensed technology or disrupt our right to receive funding or milestone or royalty payments. See section 2.2 Business Overview — Collaborations.

In the future, we may enter into additional collaborations to fund our development programs or to gain access to sales, marketing or distribution capabilities. Under certain of our collaboration agreements, including our collaborations with Genmab, CRISPR Therapeutics and GSK, we grant our partners an exclusive license to develop and commercialize certain classes of products containing our mRNA technology for specific targets and receive license fees, research and development funding, milestone payments and/or, if a product is approved for marketing, sales royalties in return. Following the discovery and preclinical testing phase, in certain cases, our partners are solely responsible for the further development of the product candidate and therefore exercise full control over its further development and potential commercialization. In certain cases, including under our collaboration with Genmab, we have a limited right to co-commercialize collaboration products. While certain of our existing licenses and collaboration agreements, including our agreements with Genmab, CRISPR Therapeutics and GSK, impose development or commercialization obligations on our collaborators, we cannot be certain that our collaboration partners will allocate sufficient resources or attention to our collaboration programs or that they will progress our collaboration programs consistent with the best interests of our business. Our existing collaborations, and any future collaborations we enter into, therefore, may pose a number of risks, including the following:

- collaborators may have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected by us or by health authorities, such as the FDA, the EMA or comparable foreign regulatory authorities;
- collaborators may dissolve, merge, be bought or may otherwise become unwilling to fulfill the initial terms of the collaboration with us;
- collaborators may fail to perform their obligations under the collaboration agreements or may be slow in performing their obligations;

- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities or change the actual or perceived competitive situation in a specific indication;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or may require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, licensors or licensees, including disagreements over proprietary rights, contract interpretation and breach of contract claims, payment obligations or the preferred course of development, might cause delays or termination of the research, development or commercialization of products or product candidates, might lead to additional responsibilities, including financial obligations for us with respect to products or product candidates, or delays or withholding of any payments due or might result in litigation or arbitration, any of which would be time-consuming and expensive, and could limit our ability to execute on our strategies;
- collaborators may not properly obtain, maintain, enforce or defend our intellectual property or may use our proprietary information in such a way that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation; and
- collaborators may infringe, misappropriate or otherwise violate the intellectual property of third parties, which may expose us to litigation and potential liability.

If our collaborations on research and development candidates do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop our proprietary product candidates. Moreover, our relationships with our partners may divert significant time and effort of our scientific staff and management team and require effective allocation of our resources to multiple internal and collaborative projects. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report also apply to the activities of our program collaborators.

Additionally, subject to its contractual obligations to us, if one of our collaborators is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators in a timely manner. For more information on our current collaboration agreements, see section 2.2 Business Overview — Collaborations.

We incur significant costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives. We are subject to financial reporting and other requirements for which our accounting and other management systems and resources may not be adequately prepared. We may fail to comply with the rules that apply to public companies, including Section 404 of the Sarbanes-Oxley Act of 2002, which could result in sanctions or other penalties that would harm the business.

As a public company, we incur significant legal, accounting and other expenses. The U.S. federal securities laws, including the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, and rules subsequently implemented by the SEC and the Nasdaq Stock Market LLC, or Nasdaq, have imposed various requirements on public companies, including requirements to file annual and event-driven reports with respect to our business and financial condition, and to establish and maintain effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations result in substantial legal and financial compliance costs and have made some activities time-consuming and costly. We may not be able to produce reliable financial statements or file these financial statements as part of periodic report in a timely manner with the SEC or comply with Nasdaq listing requirements. In addition, we could make errors in our financial statements that could require us to restate our financial statement.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting, including the attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To maintain compliance with Section 404, we document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we have needed to continue to dedicate internal resources, have engaged outside consultants, and have adopted a detailed work plan to assess and document the adequacy of internal control over financial reporting. We will continue to implement steps to improve control processes as appropriate, validate through testing that controls are functioning as documented, and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that in the future neither we nor our independent registered public account firm will be able to conclude that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Adverse developments affecting financial institutions, companies in the financial service industry or the financial service industry generally, such as actual events or concerns involving liquidity, defaults or non-performance, could adversely affect our operations and liquidity.

Actual events involving limited liquidity, defaults, non-performance or other adverse developments that affect financial institutions or other companies in the financial services industry or the financial services industry generally, or concerns or rumors about any events of these kinds, have in the past and may in the future lead to market-wide liquidity problems, which could adversely affect our operations and liquidity. For example, on March 10, 2023, Silicon Valley Bank, or SVB, a bank which we used to support operations in the U.S. was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation, or the FDIC, as receiver. CureVac had no material exposure to the SVB situation.

Risks Related to the Development, Clinical Testing and Commercialization of Our Product Candidates

Our approach to the discovery and development of product candidates based on mRNA is unproven, and we do not know whether we will be able to successfully develop any products.

We focus on delivering mRNA encoding functional versions of proteins into cells without altering the underlying DNA. Our future success depends on the successful development of this novel therapeutic or vaccine approach. Relatively few mRNA-based product candidates have been tested in animals or humans, and the data underlying the feasibility of developing mRNA-based products are both preliminary and limited. To date, a limited number of products that utilize mRNA as a prophylactic vaccine against COVID-19 have been approved in the United States and Europe, subject to certain limitations. In addition, no product that utilizes mRNA as a therapeutic vaccine has been approved in the United States or Europe. We have not yet succeeded and may not succeed in demonstrating to the FDA or EMA the efficacy and safety of any of our product candidates in clinical trials or in obtaining marketing approval thereafter. We completed Phase 1, Phase 2a and Phase 2b/3 clinical trials for our COVID-19 product candidate, CVnCoV, which has completed recruitment and dosing. The study is currently being closed. We decided in early October 2021 to withdraw CVnCoV from the regulatory approval process and focus our efforts on second-generation mRNA vaccines. We have also completed an interim data readout of safety and immunogenicity in an ongoing Phase 1 clinical trial for our CV7202 (rabies vaccine) product candidate and have reported interim Phase 1 clinical trials for our CV8102 (cMEL, ACC, SCC and HNSCC). Early in 2022, we and our partners GSK reported Phase 1 clinical results for second-generation COVID-19 and flu vaccines. Overall, there may be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time. As a result of these factors, it is more difficult for us to predict the time and cost of product candidate development, and we cannot predict whether the application of our technology platform, or any similar or competitive mRNA platforms, will result in the development and regulatory approval of any products. There can be no assurance that any development problems we experience in the future related to our technology platform or any of our research programs will not cause significant delays or unanticipated costs, or that such development problems can be solved. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate or commercializing any product candidates we may develop on a timely or profitable basis, if at all.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier studies and trials may not be predictive of future trial results. If clinical trials of our product candidates or production of our product candidates are prolonged or delayed, we may be unable to obtain required regulatory approvals, and therefore be unable to commercialize our product candidates on a timely basis or at all.

Our business is dependent on the successful development, regulatory approval and commercialization of product candidates based on our technology platform. If we and our collaborators are unable to obtain approval for and effectively commercialize our product candidates, our business would be significantly harmed. Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain, and we may not be able to obtain approvals for the commercialization of any product candidates we may develop.
To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our products are safe and effective in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. For example, our Phase 2b clinical trial with CV9104, one of our first-generation vaccines based on protamine formulation that was designed to evaluate the investigational mRNA-based cancer vaccine in patients with asymptomatic or minimally symptomatic metastatic castrate resistant prostate cancer, failed to meet the primary endpoint of improving overall survival despite proceeding through preclinical and Phase 1 studies. While we have assessed the results of past trials and these have informed our approach going forward, we can provide no assurance that future clinical trials will not be discontinued or fail to meet their specified endpoints. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed

through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our future clinical trial results may not be successful.

We are subject to significant regulatory oversight with respect to manufacturing and developing our product candidates. Our manufacturing facilities or the manufacturing facilities of our third-party manufacturers or suppliers may not meet regulatory requirements. Failure to meet GMP requirements set forth in regulations promulgated by the FDA, the EMA and other comparable regulatory authorities could result in significant delays in and costs of our products.

Clinical trials must be conducted in accordance with the FDA, EMA and comparable foreign regulatory authorities' legal requirements, regulations or guidelines and are subject to oversight by these governmental agencies and Institutional Review Boards, or IRBs, at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced in accordance with current good manufacturing practices, or cGMPs, and other requirements. We depend on medical institutions and clinical research organizations, or CROs, to conduct our clinical trials in compliance with good clinical practice, or GCP, standards. Failure to follow and document adherence to such regulations or other regulatory requirements may lead to significant delays in the availability of a product for our clinical trials, result in the termination of, or a clinical hold being placed on, one or more of our clinical trials, or delay or prevent submission or approval of marketing applications for our product candidates.

To the extent our CROs fail to enroll participants for our clinical trials, fail to conduct the trial in accordance with GCP requirements or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both, which may harm our business. Our product candidates, CV2CoV (SARS-CoV-2), CV0501 (modified nucleotides, SARS-CoV-2), CVSQIV (multivalent seasonal influenza), Flu SV mRNA (modified nucleotides, single antigen seasonal influenza) CV7202 (rabies), CV8102 (melanoma, adenoidcystic carcinoma, squamous cell cancer of skin and head and neck), are in early clinical development. All other of our research programs are in the preclinical development stage.

The completion of clinical trials for our clinical product candidates may be delayed, suspended or terminated as a result of many factors, including but not limited to:

- shortage of materials required for the production of our product candidates including due to inflationary pressures, supply chain issues, labor shortages and increases in commodity prices (including as result of the war in Ukraine) and the lingering effects of COVID-19;
- inability of our manufacturing facilities or the manufacturing facilities of our third-party manufacturers or suppliers to meet regulatory requirements;
- transfer of manufacturing processes to larger-scale facilities operated by a CMO or by us, and delays or failure by our CMOs or us to make any necessary changes to such manufacturing process;
- the delay or refusal of regulators or IRBs to authorize us to commence a clinical trial at a prospective trial site and changes in regulatory requirements, policies and guidelines;
- delays or failure to reach agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- the inability to enroll a sufficient number of patients in trials to ensure adequate statistical power to detect statistically significant treatment effects;
- negative or inconclusive results, which may require us to conduct additional preclinical or clinical trials or to abandon projects that we expect to be promising;

- safety or tolerability concerns causing us to suspend or terminate a trial if it is determined that the participants are being exposed to unacceptable health risks;
- regulators or IRBs requiring that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or safety concerns, among others;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- our CROs or clinical trial sites failing to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all, deviating from the protocol or dropping out of a trial;
- delays relating to adding new clinical trial sites;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- delays in establishing the appropriate dosage levels;
- the quality or stability of the product candidate falling below acceptable standards;
- the inability to produce or obtain sufficient quantities of the product candidate to complete clinical trials on time, or delays in sufficiently developing, characterizing or controlling a manufacturing process suitable for clinical trials;
- exceeding budgeted costs due to difficulty in accurately predicting costs associated with clinical trials;
- lack of adequate funding to continue the clinical trial;
- developments observed in trials conducted by competitors for related technology that raise general FDA or foreign regulatory authority concerns about risk to patients of gene therapy technology;
- determination that the product will not be producible at the manufacturing stage; and
- Disruptions caused by the inflationary pressures, supply chain issues, labor shortages and increases in commodity prices (including result of the war in Ukraine) and the lingering effects of the COVID-19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a Data Safety Monitoring Board for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. In addition, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial.

In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. The FDA, the EMA and comparable foreign regulatory authorities have substantial discretion in the approval process and in determining when or whether regulatory

approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, the EMA or any other regulatory authority.

In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants.

If we are required to conduct additional clinical trials or other testing of our product candidates that we develop beyond the trials and testing that we contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are unfavorable or are only modestly favorable, or if there are safety concerns associated with our other product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- remove the product from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or receiving marketing approvals and we may be required to obtain additional funds to complete clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which may harm our business and results of operations. In addition, some of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of regulatory approval of our product candidates.

Interim, "top-line," and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or top-line data from our preclinical studies and clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line or preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available.

From time to time, we may also disclose interim data from our preclinical studies and clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially

change as patient enrollment continues and more patient data become available or as patients from our clinical trials continue other treatments for their disease. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed and result in increased costs and longer development periods or otherwise be adversely affected.

We will be required to identify and enroll a sufficient number of patients for our planned clinical trials. Trial participant enrollment could be limited in future trials given that many potential participants may be ineligible because of preexisting conditions, medical treatments or other reasons. We may not be able to initiate or continue clinical trials required by the FDA, EMA or other foreign regulatory agencies or any of our other product candidates that we pursue if we are unable to locate and enroll a sufficient number of eligible patients or volunteers to participate in these clinical trials.

Patient enrollment is affected by other factors, including:

- severity of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under trial;
- perceived safety and tolerability of the product candidate;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including standard-of-care and any new drugs that may be approved for the indications we are investigating;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- our ability to monitor patients adequately during and after treatment.

We also may encounter difficulties in identifying and enrolling such patients with a stage of disease appropriate for our ongoing or future clinical trials. In addition, the process of finding and diagnosing patients may prove costly. Our inability to enroll a sufficient number of patients for any of our clinical trials would result in significant delays or may require us to abandon one or more clinical trials.

We may face continued business disruption and related risks resulting from inflationary pressures, supply chain issues, labor shortages and increases in commodity prices (including as result of the war in Ukraine) and the lingering effects of the COVID-19 pandemic, which could have a material adverse effect on our business plan or clinical trials.

The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, increases in inflation rates, higher interest rates and uncertainty about economic stability. For example, the COVID-19 pandemic resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. Similarly, the ongoing military conflict between Russia and Ukraine has created extreme volatility in the global capital markets and is expected to have further global economic consequences, including disruptions of the global supply chain and energy markets. Any such volatility and disruptions may have adverse consequences on us or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, it may make any necessary debt or equity financing more difficult to obtain in a timely manner or on favorable terms, more costly or more dilutive. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs. Any significant increases in inflation and related increase in interest rates could have a material adverse effect on our business, results of operations and financial condition.

Moreover, if COVID-19 would restart, we may experience disruptions that could severely impact our business, preclinical studies and clinical trials, including:

- delays in receiving authorization from local regulatory authorities to initiate our planned clinical trials;
- changes in local regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue the clinical trials altogether;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others, or interruption of clinical trial subject visits and study procedures, the occurrence of which could affect the integrity of clinical trial data;
- risk that participants enrolled in our clinical trials will acquire COVID-19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events;
- interruptions in preclinical studies due to restricted or limited operations at our research and development laboratory facility;
- delays in necessary interactions with local regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furlough of government employees;
- limitations in employee resources that would otherwise be focused on the conduct of our clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people;
- refusal of the FDA to accept data from clinical trials in affected geographies; and
- interruption or delays to our sourced discovery and clinical activities.

These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

In addition, quarantines, travel restrictions, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our product candidates. We have taken a series of actions aimed at safeguarding our employees and business associates, including regular PCR-based COVID-19 testing, implementing a work-from-home policy for employees except for those related to our production and laboratory operations, and these arrangements may cause reduced productivity of our employees and/or delays or disruptions of our business operations.

Our suppliers, licensors or collaborators could also be disrupted by conditions related to COVID-19, possibly resulting in disruption to our supply chain, clinical trials, partnerships or operations. If our suppliers, licensors, CMOs, CROs or collaborators are unable or fail to fulfill their obligations to us for any reason, our ability to continue meeting clinical supply demand for our product candidates or otherwise advancing development of our product candidates may become impaired.

Our proprietary product candidates are still in preclinical or clinical development. We cannot give any assurance that any of our product candidates will receive regulatory approval, and if we are unable to obtain regulatory approval and ultimately commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

Our proprietary product candidates are still in preclinical or clinical development. Although we may receive certain payments from our collaboration partners, including upfront payments, payments for achieving certain development, regulatory or commercial milestones and royalties, our ability to generate revenue from our product candidates' sales is dependent on receipt of regulatory approval for, and successful commercialization of, such product candidates, which may never occur. Our business and future success is in particular dependent on our ability to develop, either alone or in partnership, successfully, receive regulatory approval for and then successfully commercialize our proprietary product candidates. Each of our product candidates will require additional preclinical and/or clinical development, regulatory approval in multiple jurisdictions, manufacturing supply, substantial investment and significant marketing efforts before we generate any revenue from product sales or royalties. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities. The success of our product candidates will depend on several factors, including the following:

- successful completion of preclinical and/or clinical studies;
- negative or inconclusive results from our clinical trials, the clinical trials of our collaborators or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- successful enrollment of patients in, and completion of, clinical trials;
- strategic commitment to particular product candidates and indications by us and our collaborators;
- receipt of regulatory authorizations from applicable regulatory authorities for future clinical trials;
- receipt of product approvals, including marketing approvals, from applicable regulatory authorities;
- successful completion of all safety studies required to obtain regulatory approval in the United States, the European Union and other jurisdictions for our product candidates;

- obtaining and maintaining patent and trade secret protection or regulatory exclusivity for our product candidates;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of the product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining coverage and adequate reimbursement from third-party payors;
- obtaining, maintaining, enforcing and defending intellectual property and intellectual property-related claims;
- maintaining a continued acceptable safety and quality profile of the product candidates following approval; and
- maintaining a continued, sufficient supply of drug substance in acceptable quality.

If we do not achieve one or more of these factors in a complete and timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially adversely affect our business, financial condition, results of operations and prospects and, in case of product candidates, technologies and licenses we have acquired, which may result in a significant impairment of assets.

Although we expect to submit biologics license applications, or BLAs, for our mRNA-based product candidates in the United States, and in the European Union, mRNA-based medicines have been classified as gene therapy medicinal products, other jurisdictions may consider our mRNA-based product candidates to be new drugs, not biologics or gene therapy medicinal products, and require different marketing applications. In addition, we have not previously submitted a BLA to the FDA, or similar regulatory approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trials or receive regulatory approval. Further, our product candidates may not receive regulatory approval even if they are successful in clinical trials. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations. Even if we successfully obtain regulatory approvals to market one or more of our product candidates, our revenues will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval and have commercial rights. If the markets for patient subsets that we are targeting are not as significant as we estimate, we may not generate significant revenues from sales of such products, if approved.

We plan to seek regulatory approval to commercialize our product candidates both in the United States and the EU, and potentially in additional foreign countries. While the scope of regulatory approval is similar in other countries, to obtain separate regulatory approval in many other countries, we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions.

We have no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We commenced operations in 2000 and have a long track record of performing clinical trials with multiple product candidates since 2008. Our operations to date have been limited to establishing our company, raising capital, developing our proprietary mRNA technology platform, identifying and testing potential product candidates and conducting clinical trials. We have not yet demonstrated an ability to obtain marketing approvals, manufacture a commercial-scale product,

or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our product candidates may cause undesirable side effects that could delay or prevent their regulatory approval, limit the commercial profile of an approved label or result in significant negative consequences following regulatory approval, if any. Significant adverse events may occur during our clinical trials or even after receiving regulatory approval, which could delay or terminate clinical trials, delay or prevent regulatory approval or market acceptance of any of our product candidates.

Undesirable side effects that may be caused by our product candidates could cause us, our collaboration partners or the regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA, EMA or comparable foreign regulatory authorities. Results of our trials could reveal a high and unacceptable severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA, EMA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

Clinical trials assess a sample of the potential patient population. With a limited number of patients and duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate. If our product candidates receive regulatory approval and we or others identify undesirable side effects caused by such product candidates (or any other similar products) after such approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw or limit their approval of such product candidates and require us to take our approved product(s) off the market;
- regulatory authorities may require the addition of labeling statements, such as a “boxed” warning or a contraindication, or submission of field alerts to physicians and pharmacies;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we may be required to change the way such product candidates are distributed or administered, conduct additional clinical trials or change the labeling of the product candidates;
- actual or potential drug-related side effects could negatively affect patient recruitment or the ability of enrolled patients to complete a trial for our products or product candidates;

- market acceptance of our products by patients and physicians may be reduced and sales of the product may decrease significantly;
- regulatory authorities may require a Risk Evaluation and Mitigation Strategy, or a REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide or be required to remove such product candidates from the marketplace;
- we could be sued and potentially held liable for injury caused to individuals exposed to or taking our product candidates;
- sales of the product(s) may decrease substantially; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidates and could substantially increase the costs of commercializing our product candidates, if approved, and therefore could have a material adverse effect on our business, financial condition, results of operations and prospects.

To date, a limited number of products that utilize mRNA as a prophylactic vaccine against COVID-19 have been approved in the United States, Europe and other countries, subject to certain limitations. In addition, no product that utilizes mRNA as a therapeutic vaccine has been approved in the United States or Europe. As such, mRNA drug development has substantial clinical development and regulatory risks due to the novel and unprecedented nature of this new category of medicines.

No product that utilizes mRNA as a therapeutic vaccine has been approved in the United States or Europe. In addition, a limited number of products that utilize mRNA as a prophylactic vaccine against COVID-19 have been approved by the FDA, EMA and other regulatory agencies. Such approvals were provided after parallelized clinical trials, and certain of the products may be subject to ongoing review by the FDA, EMA or other regulatory agencies, and in some cases may be canceled, expire or subject to lengthy renewal. Successful discovery, development and continued market presence of mRNA-based (and other) products by either us or our collaborators is highly uncertain and depends on numerous factors, many of which are beyond our or their control. Our product candidates that appear promising in the early phases of development may fail to advance, experience delays in the clinic or clinical holds, or fail to reach the market or stay in the market for many reasons, including:

- discovery efforts aimed at identifying potential immunotherapies may not be successful;
- nonclinical or preclinical study results may show product candidates to be less effective than desired or have harmful or problematic side effects;
- clinical trial results may show the product candidates to be less effective than expected, including a failure to meet one or more endpoints or have unacceptable side effects or toxicities;
- manufacturing failures, insufficient supply of GMP materials for clinical trials, or higher than expected cost could delay or set back clinical trials, or make our product candidates commercially unattractive;
- our improvements in the manufacturing processes may not be sufficient to satisfy the clinical or commercial demand of our product candidates or regulatory requirements for clinical trials;

- changes that we make to optimize our manufacturing, testing or formulating of GMP materials could impact the safety, tolerability and efficacy of our product candidates;
- pricing or reimbursement issues or other factors could delay clinical trials or make any immunotherapy uneconomical or noncompetitive with other therapies;
- the failure to timely advance our programs or receive the necessary regulatory approvals, or a delay in receiving such approvals, due to, among other reasons, slow or failure to complete enrollment in clinical trials, withdrawal by trial participants from trials, failure to achieve trial endpoints, additional time requirements for data analysis, data integrity issues, BLA, MAA or the equivalent application, discussions with the FDA or the EMA, a regulatory request for additional nonclinical or clinical data, or safety formulation or manufacturing issues may lead to our inability to obtain sufficient funding; and
- the proprietary rights, products and technologies of our competitors may prevent our immunotherapies from being commercialized.

Although we expect to submit biologics license applications, or BLAs, for our mRNA-based product candidates in the United States and in the European Union, mRNA-based medicines have been classified as gene therapy medicinal products. Unlike certain gene therapies that irreversibly alter cell DNA and may cause certain side effects, mRNA-based medicines are designed not to irreversibly change cell DNA. Side effects observed in other gene therapies, however, could negatively impact the perception of immunotherapies despite the differences in mechanism. Due to the circumstances surrounding the approval of mRNA-based vaccines against COVID-19, the regulatory pathway for future mRNA products in the United States and other jurisdictions for approval is uncertain. The length of time necessary to complete clinical trials and submit an application for marketing approval by a regulatory authority varies significantly from one pharmaceutical product to the next and may be difficult to predict.

The regulatory approval processes of the FDA and comparable authorities are lengthy, time-consuming and inherently unpredictable and if we fail to obtain regulatory approval in any jurisdiction, we will not be able to commercialize our products in that jurisdiction and our business, results of operations, financial condition and prospects, may be materially adversely affected.

The time required to obtain approval by the FDA, EMA and comparable authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval laws, regulations, policies or the type and amount of clinical data or other information necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the designs or our execution of clinical trials might not be considered adequate, or the results of clinical trials may not meet the level of statistical significance required, by the FDA, EMA or comparable foreign regulatory authorities for approval;

- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected may not be sufficient to support the submission of a BLA or other submission, or to obtain regulatory approval in the United States, the European Union or elsewhere;
- the FDA, EMA or comparable foreign regulatory authorities may fail to approve our manufacturing processes or facilities or those of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the laws, regulations or policies of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data or other regulatory submissions insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market any of our product candidates, which would significantly harm our business, results of operations and prospects. The FDA, the EMA and other regulatory authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be obtained for any of our product candidates. Even if we believe the data collected from clinical trials of our product candidates are promising, such data may not be sufficient to support approval by the FDA, the EMA or any other regulatory authority.

In order to commercialize our products in more than one jurisdiction, we will be required to obtain separate regulatory approvals in each market and to comply with numerous and varying regulatory requirements. The approval procedures vary from country to country and may require additional testing, administrative review periods, agreements with pricing authorities or other steps. Satisfying these and other regulatory requirements is costly, time-consuming, uncertain and subject to unanticipated delays. In addition, in many countries outside the United States and in particular in many of the Member States of the European Union, a product must undergo health economic assessments to agree on pricing and/or be approved for reimbursement before it can be approved for sale in that country, or before it becomes commercially viable. The FDA and the EMA may come to different conclusions regarding approval of a marketing application. Approval by the FDA or EMA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA or EMA. In addition, our failure to obtain regulatory approval in any country may delay or have negative effects on the process for regulatory approval in other countries. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. We may not obtain regulatory approvals on a timely basis, if at all. We may not be able to submit applications for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. We may be required to conduct additional preclinical studies or clinical trials, which would be costly and time-consuming. If we or any future partner are unable to obtain regulatory approval for our product candidates in one or more significant jurisdictions, then the commercial opportunity for our product candidates, and our business, results of operations, financial condition and prospects, may be materially adversely affected.

The regulatory landscape that will govern our product candidates is uncertain. Regulations relating to more established gene therapy and cell therapy products are still developing, and changes in regulatory requirements could result in delays or discontinuation of development of our product candidates or unexpected costs in obtaining regulatory approval.

The regulatory requirements to which our product candidates will be subject are not entirely clear. Even with respect to more established products that fit into the categories of gene therapies or cell therapies, the regulatory landscape is still developing. For example, regulatory requirements governing gene therapy products and cell therapy products have changed frequently and may continue to change in the future. Moreover, there is substantial, and sometimes uncoordinated, overlap in those responsible for regulation of existing gene therapy products and cell therapy products. Although the FDA decides whether individual gene therapy protocols may proceed, the review process and determinations of other reviewing bodies can impede or delay the initiation of a clinical study, even if the FDA has reviewed the study and authorizes its initiation. Conversely, the FDA can place an Investigational New Drug Application, or an IND, on clinical hold even if such other entities have provided a favorable review. Furthermore, gene therapy clinical trials may also require evaluation and assessment by an institutional biosafety committee, or an IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at the institution participating in the clinical trial. The IBC assesses the safety of the research and identifies any potential risk to the public health or the environment, and such assessment may result in some delay before initiation of a clinical trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

Complex regulatory environments exist in other jurisdictions in which we might consider seeking regulatory approvals for our product candidates, further complicating the regulatory landscape. For example, in the European Union a special committee called the Committee for Advanced Therapies, or the CAT, was established within the EMA in accordance with Regulation (EC) No 1394/2007 on advanced-therapy medicinal products, or ATMPs, to assess the quality, safety and efficacy of ATMPs, and to follow scientific developments in the field. ATMPs include gene therapy products as well as somatic cell therapy products and tissue-engineered products.

These various regulatory review committees and advisory groups and new or revised guidelines that they promulgate from time to time may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our product candidates or lead to significant post-approval limitations or restrictions. As the regulatory landscape for our product candidates is new, we may face even more cumbersome and complex regulations than those emerging for gene therapy products and cell therapy products. Furthermore, even if our product candidates obtain required regulatory approvals, such approvals may later be withdrawn as a result of changes in regulations or the interpretation of regulations by applicable regulatory agencies.

Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product sales revenue to maintain our business.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may materially adversely affect our business, prospects, financial condition and results of operations. We have not previously submitted a BLA to the FDA, or similar regulatory approval filings to comparable foreign authorities, for any product candidate and never received regulatory approval for any of our product candidates. Even if the FDA, EMA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, product sampling, adverse event reporting, storage, advertising, marketing, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize such products. There also are continuing, annual program user fees for any marketed products. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and

documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing and surveillance to monitor the safety and efficacy of the product. For example, the FDA has the authority to require a REMS as part of a BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved product, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory;
- product recalls;
- fines, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA, EMA or a comparable foreign regulatory authority to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- requirements to conduct additional clinical trials, change our product labeling or submit additional applications or application supplements;
- product seizure or detention, or refusal to permit the import or export of products;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

In addition, regulatory policies may change or additional government regulations or legislation may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we fail to comply with existing requirements, are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any regulatory approval that we may have obtained or face regulatory or enforcement actions, which may materially adversely affect our business, prospects, financial condition and results of operations.

In addition, if any of our product candidates is approved, our product labeling, advertising and promotion will be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product

candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize our product candidates.

Further, the policies of FDA, EMA and other comparable regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or to adopt new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including the FDA's pre-approval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

A breakthrough therapy designation by the FDA for a product candidate may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the product candidate will receive marketing approval.

We may in the future seek a breakthrough therapy designation for one or more product candidates. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

Because we are developing product candidates for the treatment or prevention of diseases in which there is little clinical experience using new technologies, there is increased risk that the FDA, the EMA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results and that these results may be difficult to analyze.

As we are developing novel treatments and preventative measures for diseases in which we believe there is limited clinical experience with new endpoints and methodologies, there is heightened risk that the FDA, EMA or comparable foreign regulatory bodies may not consider the clinical trial endpoints to provide clinically meaningful results, and the resulting clinical data and results may be more difficult to analyze. It is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in the United States, the European Union or other jurisdictions, if ever. Further, approvals by one regulatory agency may not be indicative of what other regulatory agencies may require for approval.

During the regulatory review process, we will need to identify success criteria and endpoints such that the FDA, the EMA or other regulatory authorities will be able to determine the clinical efficacy and safety profile of any product candidates we may develop. Because our initial focus is to identify and develop product candidates to treat or prevent diseases in which there is little clinical experience using new technologies, there is heightened risk that the FDA, the EMA or other regulatory authorities may not consider the clinical trial endpoints that we propose to provide clinically meaningful results. In addition, the resulting clinical data and results may be difficult to analyze. Even if the FDA determines that our success criteria is sufficiently validated and clinically meaningful, we may not achieve the prespecified endpoints to a sufficient degree of statistical significance.

This may be a particularly significant risk for many of the genetically defined diseases for which we plan to develop product candidates because many of these diseases have small patient populations, and designing and executing a rigorous clinical trial with appropriate statistical power is more difficult than with diseases that have larger patient populations. Further, even if we do achieve the prespecified criteria, the results may be unpredictable or inconsistent with the results of the non-primary endpoints or other relevant data. The FDA also weighs the benefits of a product against its risks, and the FDA may view the efficacy results in the context of safety as not being supportive of regulatory approval. The EMA and other regulatory authorities may make similar comments with respect to these endpoints and data. Any product candidate we may develop will be based on a novel technology that makes it difficult to predict the time and cost of development and of subsequently obtaining regulatory approval.

We and our collaboration partners have conducted and intend to conduct additional clinical trials for selected product candidates at sites outside the United States, and the FDA may not accept data from trials conducted in such locations or may require additional U.S.-based trials.

We and our collaboration partners have conducted, currently are conducting and intend in the future to conduct, clinical trials outside the United States, particularly in the European Union where we are headquartered. In addition, in February 2022, we and our partner GSK, initiated a Phase 1 clinical trial for our multivalent second-generation seasonal influenza vaccine candidate, CVSQIV, in Panama.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be conducted by qualified investigators in accordance with GCPs, and the FDA must be able to validate the trial data through an on-site inspection, if necessary. Generally, the patient population for any clinical trial conducted outside of the United States must be representative of the population for which we intend to seek approval in the United States. There can be no assurance that the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from

any clinical trials that we or our collaboration partners conduct outside the United States, it would likely result in the need for additional clinical trials, which would be costly and time-consuming and delay or permanently halt our ability to develop and market these or other product candidates in the United States. In other jurisdictions, for instance, in Japan, there is a similar risk regarding the acceptability of clinical trial data conducted outside of that jurisdiction.

In addition, there are risks inherent in conducting clinical trials in multiple jurisdictions, inside and outside of the United States, such as:

- regulatory and administrative requirements of the jurisdiction where the trial is conducted that could burden or limit our ability to conduct our clinical trials;
- foreign exchange fluctuations;
- manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- the risk that the patient populations in such trials are not considered representative as compared to the patient population in the target markets where approval is being sought.

If any of our product candidates receive regulatory approval, the approved products may not achieve broad market acceptance among physicians, patients, the medical community and third-party payors, in which case revenue generated from their sales would be limited.

The commercial success of our product candidates will depend upon their acceptance among physicians, patients and the medical community. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- limitations or warnings contained in the approved labeling for a product candidate;
- changes in the standard of care for the targeted indications for any of our product candidates;
- limitations in the approved clinical indications for our product candidates;
- demonstrated clinical safety and efficacy compared to other products;
- lack of significant adverse side effects;
- sales, marketing and distribution support;
- availability of coverage and extent of reimbursement from managed care plans and other third-party payors;
- timing of market introduction and perceived effectiveness of competitive products;
- the degree of cost-effectiveness of our product candidates;
- availability of alternative therapies at similar or lower cost, including generic and over-the-counter products;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular diseases;
- whether the product can be used effectively with other therapies to achieve higher response rates;
- adverse publicity about our product candidates or favorable publicity about competitive products;
- convenience and ease of administration of our products; and

- potential product liability claims.

If any of our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, patients and the medical community, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

Our product candidates for which we may seek approval as biologic products may face competition sooner than anticipated.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or the BPCIA, which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product.

To the extent any of our product candidates approved as a biological product under a BLA qualifies for a 12-year period of exclusivity, for which we make no assurances, there is a risk that such exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for nonbiological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If any approved products are subject to biosimilar competition sooner than we expect, we will face significant pricing pressure and our commercial opportunity will be limited.

Disruptions at the FDA and other government agencies caused by inflation, funding shortages, labor shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, or approved or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, inflation, labor shortages, statutory, regulatory, and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for our product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities.

Risks Related to the Manufacturing of Our Product Candidates

The manufacture of mRNA-based medicines is complex and manufacturers often encounter difficulties in production, especially in the field of biologics. If we or any of our third-party manufacturers encounter difficulties, our ability to provide product candidates for clinical trials or products, if approved, to patients or future customers could be delayed or halted.

The manufacture of mRNA-based medicines is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and analytics. We and our third-party manufacturers must comply with cGMP, regulations and guidelines for the manufacturing of our product candidates used in preclinical studies and clinical trials and, if approved, marketed products. Manufacturers of biotechnology products often encounter difficulties in production, particularly in scaling up and validating initial production.

Before 2020, the mRNA quantities produced globally were very limited compared to the quantities produced since mRNA vaccines were approved as prophylactic vaccines to protect from SARS-CoV-2. Large-scale mRNA vaccine production requires a high level of (i) equipment to build and run new facilities and (ii) raw materials to produce mRNA and to formulate the drug substance in the required volumes. The current demand for mRNA vaccines is unprecedented and bears the risk of overloading and hence delaying regular supply chains. This risk is further extended by export restrictions imposed by countries to protect their own supplies, some of which can only be resolved on a political level.

Furthermore, if microbial, viral or other contaminations are discovered in our product candidates or in the manufacturing facilities where our product candidates are made, such manufacturing facilities may be closed for an extended period of time to investigate and remedy the contamination. Shortages of raw materials may also extend the period of time required to develop our product candidates.

Manufacturing these products requires facilities specifically designed for and validated for this purpose and sophisticated quality assurance and quality control procedures are necessary. Slight deviations anywhere in the manufacturing process, including filling, labeling, packaging, storage and shipping and quality control and testing, may result in lot failures, product recalls or spoilage. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. The use of biologically derived ingredients can also lead to allegations of harm, including infections or allergic reactions, or closure of product facilities due to possible contamination.

In addition, there are risks associated with large-scale manufacturing for clinical trials or commercial-scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if we obtain marketing approval for any of our product candidates, there is no assurance that we or our manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other comparable foreign regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential commercial launch of the product or to meet potential future demand. If we or our manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, our development and commercialization efforts would be impaired, which would have an adverse effect on our business, financial condition, results of operations and growth prospects.

We cannot assure you that any disruptions or other issues relating to the manufacture of any of our product candidates will not occur in the future. Any delay or interruption in the supply of clinical trial supplies could delay the completion of planned clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely. Any adverse developments affecting clinical or commercial manufacturing of our product candidates or

products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the supply of our product candidates or products. We may also have to take inventory write-offs and incur other charges and expenses for product candidates or products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. Accordingly, failures or difficulties faced at any level of our supply chain could delay or impede the development and commercialization of any of our product candidates or products and could have an adverse effect on our business, prospects, financial condition and results of operations.

We and our third-party manufacturers and suppliers could be subject to liabilities, fines, penalties or other sanctions under federal, state, local and foreign environmental, health and safety laws and regulations if we or they fail to comply with such laws or regulations or otherwise incur costs that could have a material adverse effect on our business.

We manufacture and produce mRNA-based active ingredients for our product pipeline. We also currently rely on and expect to continue to rely on third parties for the manufacturing and supply of active pharmaceutical ingredients, or API, and drug products of our product candidates. We and these third parties are subject to various federal, state, local and foreign environmental, health and safety laws and regulations, including those governing laboratory procedures and the generation, handling, labeling, transportation, use, manufacture, storage, treatment and disposal of hazardous materials and wastes and worker health and safety. We do not have control over a manufacturer's or supplier's compliance with environmental, health and safety laws and regulations. Liabilities they incur pursuant to these laws and regulations could result in significant costs or, in certain circumstances, an interruption in operations, any of which could adversely affect our business and financial condition.

With respect to any hazardous materials or waste which we are currently, or in the future will be, generating, handling, transporting, using, manufacturing, storing, treating or disposing of, we cannot eliminate the risk of contamination or injury from these materials or waste, including at third-party disposal sites. In the event of such contamination or injury, we could be held liable for any resulting damages and liability. We also could be subject to significant civil or criminal fines and penalties, cessation of operations, investigation or remedial costs or other sanctions for failure to comply with applicable environmental, health and safety laws. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts or otherwise have a material adverse effect on our business.

At the start of the COVID-19 pandemic, we had entered in contractual engagements with third-party manufacturer to have access additional capacity. The wind-down of these contracts entail risks of financial penalties and risk of litigation.

Undetected errors or defects in our production could harm our reputation or expose us to product liability claims.

Defects in the cGMP materials we produce may damage the third parties' businesses we work with and could harm their and our reputation. If that occurs, we may incur significant costs, the attention of our key personnel could be diverted, or other significant problems may arise. We may also be subject to warranty and liability claims for damages related to errors or defects in products made with our cGMP materials. In addition, if we do not meet industry or quality standards, if applicable, such products may be subject to recall. A material liability claim, recall or other occurrence that harms our reputation or decreases market acceptance of such products could harm our business and operating results.

Risks Related to Our Reliance on Collaborators and Other Third Parties

We rely on third parties to conduct our nonclinical and clinical trials and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines, or comply with regulatory requirements,

we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third-party CROs to monitor and manage data for our ongoing nonclinical and clinical programs. We rely on these parties for execution of our nonclinical and clinical studies and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with cGMP, GCP, Good Laboratory Practice, or GLP, and other regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Union and comparable foreign regulatory authorities for all of our product candidates in nonclinical and clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, trial sites and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the data generated in our nonclinical and clinical trials may be deemed unreliable and the EMA, FDA, or other regulatory authorities may require us to perform additional nonclinical and clinical trials before approving our marketing applications. In addition, even if, for example, the EMA finds our data generated in our nonclinical and clinical trials reliable for approving a marketing application, there is no assurance that other regulatory authorities like the FDA will find such data reliable and sufficient for approving a similar market application. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that all of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If any of our relationships with these third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our ongoing nonclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations, meet expected deadlines, conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, if they need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed, or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. CROs may also generate higher costs than anticipated. As a result, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase, and our ability to generate revenue could be delayed.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

If we or any third-party manufacturer of our product candidates is unable to increase the scale of production of our product candidates, and/or increase the product yield of manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of our product candidates in our pipeline or that we may develop, our third-party manufacturers will be required to increase their production and optimize their manufacturing processes while maintaining the quality of the

product. The transition to larger-scale and more robust production could prove difficult or costly. Further, any claims in our manufacturing process as a result of scaling up or optimization of the manufacturing, supply and fill and finish process may result in the need to obtain regulatory approvals. If we or our third-party manufacturers are not able to optimize the manufacturing process to increase the product yield for our product candidates or the cGMP production requirement for clinical studies, or if we or our third-party manufacturers are unable to produce increased amounts of our product candidates while maintaining the quality of the product or generally unable to produce the right quality, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits. Difficulty in achieving commercial scale-up production or production optimization or the need for additional regulatory approvals as a result could have a material adverse impact on our business and results of operations.

Risks Related to Our Intellectual Property Rights

If we are unable to obtain, maintain and enforce intellectual property protection for our products or product candidates, or if the scope of our intellectual property protection is not sufficiently broad, our ability to commercialize our product candidates successfully and to compete effectively may be materially adversely affected.

Our success depends on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our current and future proprietary product candidates. We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technology, manufacturing processes, products and product candidates. We and our collaborators have primarily sought to protect our proprietary positions by filing patent applications in the United States and abroad related to our proprietary technology, manufacturing processes, and product candidates that are important to our business. Despite our efforts to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we may fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. In addition, we or our collaborators, may only pursue, obtain or maintain patent protection in a limited number of countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found. We may be unaware of prior art that could be used to invalidate or narrow the scope of an issued patent or prevent our pending patent applications from issuing as patents. Because patent applications in the United States, Europe and many other non-U.S. jurisdictions are typically not published until 18 months after filing, or in some cases not at all, and because publications of discoveries in scientific literature lag behind actual discoveries, we cannot be certain that we or our licensors were the first to make the inventions claimed in any of our owned or any in-licensed issued patents or pending patent applications, or that we or our licensors were the first to file for protection of the inventions set forth in our patents or patent applications. As a result, we may not be able to obtain or maintain protection for certain inventions. Even if patents do successfully issue, our owned or in-licensed patents may not adequately protect our intellectual property, provide exclusivity for our products or product candidates, prevent others from designing around our claims or otherwise provide us with a competitive advantage. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents or whether any issued patents will be found invalid or unenforceable or will be threatened by third parties. In addition, third parties may challenge the validity, enforceability, ownership, inventorship or scope of any of our patents. Any successful challenge to any of our patents could deprive us of rights necessary for the successful commercialization of any product candidate that we may develop and could impair or eliminate our ability to collect future revenues and royalties with respect to such products or product candidates. If any of our patent applications with respect to our product candidates fail to issue as patents, if their breadth or strength of protection is narrowed or threatened, or if they fail to

provide meaningful exclusivity or competitive position, it could dissuade companies from collaborating with us or otherwise adversely affect our competitive position.

The patent position of pharmaceutical companies is generally uncertain because it involves complex legal, scientific and factual considerations for which legal principles remain unsolved. The standards applied by the United States Patent and Trademark Office, or the USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably, and can change. Additionally, the laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property rights, particularly those relating to biotechnology, which could make it difficult for us to stop the infringement, misappropriation, or other violation of our patents or other intellectual property, including the unauthorized reproduction of our manufacturing or other know-how or the marketing of competing products in violation of our intellectual property rights generally. Any of these outcomes could impair our ability to prevent competition from third parties, which may have a material adverse effect on our business, financial condition, results of operations and prospects.

Further, the existence of issued patents does not guarantee our right to practice the patented technology or commercialize the patented product candidate. Third parties may have or obtain rights to patents which they may use to prevent or attempt to prevent us from practicing our patented technology or commercializing any of our patented product candidates. If any of these other parties are successful in obtaining valid and enforceable patents, and establishing our infringement of those patents, we could be prevented from selling our products unless we were able to obtain a license under such third-party patents, which may not be available on commercially reasonable terms or at all. In addition, third parties may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or agency of competent jurisdiction may find our patents invalid or unenforceable. Our competitors and other third parties may also be able to circumvent our patents by developing similar or alternative product candidates in a non-infringing manner. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, competitors may use our technologies in jurisdictions where we have not obtained or are unable to adequately enforce patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States and Europe. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing with us. Proceedings to enforce our patent rights, whether or not successful, could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or held unenforceable, or interpreted narrowly and our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop, acquire or license.

Our owned and in-licensed patents may be subject to a reservation of rights by one or more third parties. For example, the research resulting in certain of our patents and technology, including patents and technology relating to our yellow fever product candidate, was funded in part by the U.S. government. As a result, the U.S. government has certain rights to such patent rights and technology, which include march-in rights. When new technologies are developed with government funding, in order to secure ownership of such patent rights, the recipient of such funding is required to comply with certain government regulations, including timely disclosing the inventions claimed in such patent rights to the U.S. government and timely electing title to such inventions. Additionally, the U.S. government generally obtains certain rights

in any resulting patents, including a nonexclusive license authorizing the government to use the invention or to have others use the invention on its behalf. Accordingly, we have granted the U.S. government a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States, the inventions described in the patents and patent applications relating to our technology or one or more of our product candidates. If the U.S. government decides to exercise these rights, it is not required to engage us as its contractor in connection with doing so. The government's rights may also permit it to disclose our confidential information to third parties and to exercise march-in rights to use or allow third parties to use such government-funded technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the government-funded technology, or because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations, or to give preference to U.S. industry. In addition, our rights in such inventions may be subject to certain requirements to manufacture products embodying such inventions in the United States. If we fail to comply with those requirements, we could lose our ownership of, or other rights to, any patents subject to such regulations.

In Germany, the German federal government, and the Federal Ministry of Health and downstream authorities, in the event of a national epidemic, have the right to order the use of our owned and in-licensed patents in the interest of the public welfare or the security of the Federal Republic. The German government may issue such an order with respect to our owned or in-licensed patents and we may lose exclusivity with respect to the technologies and product candidates covered by such patents. For example, if the German government determines that we are unable to develop our COVID-19 vaccine candidates on a timeline or at a scale that is necessary to respond to the COVID-19 pandemic, it may issue a use order for the patents covering our development of COVID-19 vaccines. We would be entitled to compensation in the event a use order is issued with respect to our owned or in-licensed patents; however, such compensation may be less than what we could otherwise receive and any such use order could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

In Russia, the United States and foreign government actions related to Russia's invasion of Ukraine may limit or prevent filing, prosecution and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications in Russia, resulting in a partial or complete loss of patent rights in Russia. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit, without consent or compensation, inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in countries that Russia has deemed unfriendly. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be materially adversely affected.

In addition, it is uncertain whether the World Trade Organization, or the WTO, will waive certain intellectual property protections now or in the future on certain technologies related to COVID-19. We cannot be certain that any of our current or future product candidates or technologies would not be subject to an intellectual property waiver by the WTO. We also cannot be certain that any of our current or future intellectual property rights, whether patents, trade secrets, or other confidential information would be eliminated, narrowed, or weakened by such a waiver. Given the uncertain future actions by the WTO and other countries and jurisdictions around the world, including the United States, it is unpredictable how our current or future intellectual property rights or how our current or future business would be impacted.

Additionally, the research resulting in certain of our patents and technology, including patents and technology relating to our CV8102 and RSV product candidates, was funded in part by the German Ministry of Education and Research, or the BMBF. Results of such government-funded research projects must, subject to certain conditions, be made available free of charge for academic research and teaching in Germany and must be published in half-yearly interim reports and a

final report following completion of the funded work. Information relating to intellectual property generated, commercial expectations, scientific chances of success and next steps and certain additional information must be disclosed to the German government and must be disclosed to third parties for academic research and teaching upon request under a written confidentiality agreement. The BMBF additionally has, in the case of a special public interest, a nonexclusive and transferable right to use intellectual property generated as part of the funded work. Contracts with third parties relating the exploitation of the results of the funded work must be disclosed to the BMBF and any such contracts with parties outside of the European Union require the prior consent of the BMBF to the extent they deviate from an exploitation plan previously approved by the BMBF. Additionally, if we fail to use or commercialize the results of the funded work we may be required to grant third parties licenses to use such results. In certain scenarios, including if we come under the decisive influence of foreign investors, the funded results are exclusively or predominantly used outside Germany without the prior consent of the BMBF or if we are in breach of our obligations under the grant, the grant funding, including funding already received, can be revoked.

Furthermore, certain of our patents and technology, including patents and technology relating to our rotavirus, malaria, Lassa virus and SARS-CoV-2 product candidates, were funded in part by grants from nonprofit third parties, including the Bill & Melinda Gates Foundation and CEPI. We are required to fulfill certain contractual obligations with respect to products created using such grant funding, including making certain products available at an affordable price in a list of clearly defined low- and lower-middle income countries and ensuring that certain products are available in geographic regions where there has been an outbreak of an infectious disease at certain reduced economic rates. See section 2.2 Business Overview — Collaborations.

Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its effective filing date. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing, regulatory review and approval of new product candidates, our patents protecting such candidates might expire before or shortly after such candidates are commercialized. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be further reduced. Even if patents covering our product candidates are obtained, once such patents expire, we may be vulnerable to competition from similar or biosimilar products. The launch of a similar or biosimilar version of one of our products would likely result in an immediate and substantial reduction in the demand for our product, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we fail to comply with our obligations under any license, collaboration or other intellectual property agreements, disagree over contract interpretation, or otherwise experience disruptions to our business relationships with our collaborators or licensors, we could lose intellectual property rights that are necessary to our business.

We rely, in part, on license, collaboration and other intellectual property agreements. These may not provide exclusive rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our product candidates in the future.

In addition, our existing licenses and collaboration agreements, including our agreements with Genmab, Arcturus, Acuitas, GSK, the Bill & Melinda Gates Foundation, CRISPR Therapeutics and CEPI, impose, and any future licenses, collaborations or other intellectual property agreements we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement or other obligations on us. Our licenses and collaboration agreements, including our agreement with Genmab, impose, and any future agreement we enter into may also impose, restrictions on our ability to license certain of our intellectual property to third parties or to develop or commercialize certain product candidates or technologies. In spite of our best efforts, our licensors, licensees and collaborators may conclude that we have breached our obligations under our

agreements, or that we have used the intellectual property licensed to us in an unauthorized manner, in which case, we may be required to pay damages and the licensor, licensee or collaborator may have the right to terminate the agreement. Any of the foregoing could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology, enable a competitor to gain access to the licensed technology or disrupt our right to milestone or royalty payments. We might not have the necessary rights or the financial resources to develop, manufacture or market our current or future product candidates without the rights granted under our licenses, and the loss of sales or potential sales in such product candidates could have a material adverse effect on our business, financial condition, results of operations and prospects.

Disputes have arisen and may in the future arise regarding intellectual property subject to licensing, collaboration or other intellectual property agreements, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- our financial obligations under the license agreement;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we currently license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or expand the rights of our licensors or partners to the relevant intellectual property or technology, including their ability to use or license such intellectual property or technology to third parties. In addition, such resolution may also increase what we believe to be our financial or other obligations under the relevant agreement. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

In some circumstances, we may not have the right to control the preparation, filing, prosecution, maintenance, enforcement, and defense of patents and patent applications covering the technology that we license from third parties. We cannot be certain that these patents and applications will be prepared, filed, prosecuted, maintained, enforced, and defended in a manner consistent with the best interests of our business. If our licensors fail to prosecute, maintain, enforce, and defend such intellectual property, or lose rights to such intellectual property, the rights we have licensed and our exclusivity may be reduced or eliminated and our right to develop and commercialize any of our products that are subject to such licensed rights could be adversely affected.

Moreover, our rights to our in-licensed patents and patent applications may depend, in part, on inter-institutional or other operating agreements between the joint owners of such in-licensed patents and patent applications. If one or more of such joint owners breaches such inter-institutional or operating agreements, our rights to such in-licensed patents and patent applications may be adversely affected. In addition, while we cannot currently determine the amount of the

royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability. In addition, the development of certain of our product candidates is funded by grants that impose certain pricing limitations on such product candidates and limit our ability to commercialize such product candidates and to achieve or maintain profitability. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have on reasonable terms or at all, we may have to abandon development of the relevant program or product candidate and our business, financial condition, results of operations and prospects could suffer.

We are and may in the future become involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful and could result in a court or administrative body finding our patents to be invalid or unenforceable.

Even if the patent applications we own or license are issued, third parties may infringe our patents. To counter infringement, we have been and may in the future be required to file infringement claims, which can be expensive and time-consuming. If we initiate legal proceedings against a third-party to enforce a patent covering any of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including novelty, nonobviousness (or inventive step), written description or enablement. In addition, patent validity challenges may, under certain circumstances, be based upon nonstatutory obviousness-type double patenting, which, if successful, could result in a finding that the claims are invalid for obviousness-type double patenting or the loss of patent term if a terminal disclaimer is filed to obviate a finding of obviousness-type double patenting. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld information material to patentability from the USPTO, or made a misleading statement, during prosecution. In an infringement proceeding, a court may decide that one or more of our patents is not valid, is unenforceable or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. Third parties also may raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include reexamination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation or cancellation of or amendment to our patents in such a way that they no longer cover our product candidates or provide any competitive advantage. For example, one of our manufacturing related U.S. patents was invalidated in an *inter partes* review proceeding and certain of our European patents relating to RNA-based adjuvants/immunostimulants, RNA-coded antibodies, mRNA vaccination of the elderly, intratumoral (m)RNA treatments, polyvalent mRNA production, and mRNA vaccination in combination with an anti-PD-L1 antibody have been revoked in European opposition proceedings. Further European patents have been amended after opposition proceedings. For example, European patents related to an mRNA injection solution, mRNA vaccination of newborns and infants, combination of an mRNA vaccine and an anti-PD1 antibody, combination of mRNA-based vaccination and agonistic OX40 antibodies and method of RNA analysis have been amended. Further European patents have been maintained after opposition proceedings. One of these patents relates to an mRNA injection solution and the other relates to sequence optimization of a coding sequence. Some of these decisions are currently on appeal and continuation or divisional applications of certain of the maintained, revoked and amended patents have been filed and are currently under examination, although there can be no assurance that any such appeal will be successful or that any such patent applications will issue as patents that provide us with any competitive advantage. Additionally, several of our

European and Australian patents relating to prime-boost regimens, lyophilization of RNA, spray-drying of RNA, spray-freeze-drying of RNA, and an improved method for plasmid production for in vitro transcription of mRNA are currently subject to opposition proceedings. The outcome following legal assertions of invalidity and unenforceability is unpredictable. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we could lose part or all of the patent protection on one or more of our product candidates, which could result in our competitors and other third parties using our technology to compete with us. Such a loss of patent protection could have a material adverse impact on our business.

Interference proceedings, or other similar enforcement and revocation proceedings, provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications. We may not be able to prevent, alone or with our licensors, infringement, misappropriation or other violation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

In June 2022, we filed a lawsuit against BioNTech SE and its wholly owned subsidiaries, BioNTech Manufacturing GmbH and BioNTech Manufacturing Marburg GmbH (collectively, "BioNTech"), in the Düsseldorf Regional Court, for infringement of one European patent, EP1857122B1, ("EP'122 Patent"), and three utility patents, DE202015009961U1, DE202015009974U1, and DE202021003575U1, as a result of the manufacture, use and sale of Comirnaty, BioNTech and Pfizer's mRNA COVID-19 vaccine. Later in July 2022, BioNTech and Pfizer filed a complaint for a declaratory judgment in the U.S. District Court for the District of Massachusetts, seeking a judgment of non-infringement by Comirnaty of U.S. Patent Nos. 11,135,312, 11,149,278 and 11,241,493. Subsequently we filed to have the case transferred to the Eastern District of Virginia.

In August 2022, we added European Patent EP3708668B1, ("EP'688 Patent") to the German lawsuit. Subsequently, BioNTech additionally filed a nullity action in the Federal Patent Court of Germany seeking a declaration that the EP'122 Patent is invalid, and we are defending this action.

In September 2022, BioNTech and Pfizer filed a declaration of non-infringement and revocation action against the EP'122 Patent and the EP'668 Patent in the Patents Court of the Business and Property Courts of England and Wales. In October 2022, we counterclaimed seeking an order that the EP '122 Patent and EP '688 Patent are infringed and are valid. Lastly, on November 11, 2022, BioNTech SE filed cancellation actions seeking the cancellation of the three German utility patents in the German Patent and Trademark Office, and we are defending these actions.

All of the proceedings are currently pending. In the course of pursuing our case for infringement and defending against the challenges to our patent estate from Pfizer and BioNTech, should we ultimately not be successful, we will be liable for our own and may be liable for BioNTech and Pfizer's legal costs in at least Germany and the UK.

An unfavorable outcome could also require us to cease using the related technology or attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

Additionally, an adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against competitors, affect our ability to receive royalties or other licensing consideration from our licensees, and may curtail or preclude our ability to exclude third parties from making, using and selling similar or competitive products. Any of these occurrences could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are sued for infringing, misappropriating, or otherwise violating intellectual property rights of third parties, such litigation could be costly and time-consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing, misappropriating, or otherwise violating the intellectual property and other proprietary rights of third parties.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights of third parties with respect to our product candidates, including interference and post-grant proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, formulation, use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that we may or may not be aware of which may later result in issued patents that our product candidates may be accused of infringing. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates. After issuance, the scope of patent claims remains subject to construction based on interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we are sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims at issue are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. Some claimants may have substantially greater resources than we do and may be able to sustain the costs of complex intellectual property litigation to a greater degree and for longer periods of time than we could. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us, especially as we gain greater visibility and market exposure as a public company.

Third parties have, and may in the future have, U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds or methods of use for the treatment of the disease indications for which we are developing our product candidates that may cover our product candidates. For example, we are aware of certain third-party U.S. and non-U.S. issued patents and patent applications, including those of our competitors, that relate to mRNA production, mRNA optimization, modification of mRNA, LNP technology, RNA-based tumor vaccination, LNP-based mRNA delivery to the eye, lung or liver, mRNA encoding gene-editing enzymes, RNA-encoded antibodies or antigens in LNPs and LNP-formulated RNA that may be construed to cover the LNP-formulated RNA technology used in our vaccines and protein and antibody therapies. We are also aware of certain third-party U.S. and non-U.S. patents and patent applications, including those of our competitors, that relate to coronavirus vaccines, influenza virus vaccines, Respiratory Syncytial Virus (RSV) vaccines and treatments and vaccines against other infectious diseases

and we expect such third parties to have filed additional patent applications, which have not yet been published, and to file additional patent applications in the future.

In the event that any of these patent rights were asserted against us, we believe that we have defenses against any such action, including that such patents would not be infringed by our product candidates and/or that such patents are not valid. However, if any such patent rights were to be asserted against us and our defenses to such assertion were unsuccessful, unless we obtain a license to such patents, we could be liable for damages, which could be significant and include treble damages and attorneys' fees if we are found to willfully infringe such patents, and we could be precluded from commercializing any product candidates that were ultimately held to infringe such patents, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are required to obtain a license from any third-party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate, we may not be able to obtain such required license on commercially reasonable terms or at all. In particular, any of our competitors that control intellectual property that we are found to infringe may be unwilling to provide us a license under any terms. Even if we were able to obtain a license, it could be nonexclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. Further, if a patent infringement suit is brought against us or our third-party service providers and if we are unable to successfully obtain rights to required third-party intellectual property, we may be required to expend significant time and resources to redesign our product candidates, or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis, and may delay or require us to abandon our development, manufacturing or sales activities relating to our product candidates. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation and other proceedings could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, intellectual property litigation or other legal proceedings relating to our, our licensor's or other third parties' intellectual property claims may cause us to incur significant expenses and could distract our personnel from their normal responsibilities. Patent litigation and other proceedings may also absorb significant management time. If not resolved in our favor, litigation may require us to pay any portion of our opponents' legal fees. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Our competitors or other third parties may be able to sustain the cost of such litigation and proceedings more effectively than we can because of their substantially greater resources. Uncertainties resulting from our participation in patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Furthermore, because of the substantial amount of discovery required in certain jurisdictions in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the perceived value of our product candidates or intellectual property could be diminished. Accordingly, the market price of our common shares may decline. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our business, financial condition, results of operations and prospects.

Changes to the patent law in the United States and other jurisdictions could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, thereby impairing our ability to protect our technologies and product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time-consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. For example, the Leahy-Smith America Invents Act, or the America Invents Act, was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Specifically, the America Invents Act reforms United States patent law in part by changing the U.S. patent system from a "first to invent" system to a "first inventor to file" system. Under a "first inventor to file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to the patent on an invention regardless of whether another inventor was the first to invent the invention. This will require us to be cognizant going forward of the time from invention to filing of a patent application and be diligent in filing patent applications. Circumstances may arise that could prevent us from promptly filing patent applications on our inventions and allow third parties to file patents claiming our inventions before we are able to do so. The America Invents Act also includes a number of significant changes that affect the way patent applications will be prosecuted and may also affect patent litigation. These include allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by the USPTO administered post-grant proceedings, including reexamination proceedings, *inter partes* review, post-grant review and derivation proceedings. These adversarial proceedings at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than in a litigation in a U.S. federal court. One of our manufacturing-related patents has been invalidated in an *inter partes* proceeding and if any of our other patents are challenged by a third-party in a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which would result in a loss or narrowing of the challenged patent right to us.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents, once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways. In addition, the complexity and uncertainty of European patent laws have also increased in recent years. Complying with these laws and regulations could have a material adverse effect on our existing patent portfolio and our ability to protect and enforce our intellectual property in the future.

We may be subject to claims by third parties asserting that our employees, consultants, independent contractors or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property and proprietary technology.

Many of our current and former employees, consultants, and independent contractors including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including

some which may be competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees, consultants or independent contractors have used or disclosed intellectual property, including trade secrets or other proprietary information, of such individual's current or former employers, or that patents and applications we have filed to protect inventions of these individuals, even those related to one or more of our product candidates, are rightfully owned by their former or concurrent employer. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain damages. Such intellectual property rights could be awarded to a third-party, and we could be required to obtain a license from such third-party to commercialize our technology or products. Such a license may not be available on an exclusive basis or on commercially reasonable terms, or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and independent contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, or such agreements may be breached or alleged to be ineffective, and the assignment may not be self-executing, which may result in claims by or against us related to the ownership of such intellectual property or may result in such intellectual property becoming assigned to third parties. If we fail in enforcing or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Obtaining and maintaining our patent protection, including patents licensed from third parties, depends on compliance with various procedural, documentary, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and patent applications will be due to be paid to the USPTO and various government patent agencies outside the United States over the lifetime of our patents and patent applications and any patent rights we may own or license in the future. Additionally, the USPTO and various government patent agencies outside the United States require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. In certain cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we or our licensors fail to maintain the patents and patent applications covering or otherwise protecting our product candidates, it could have a material adverse effect on our business. In addition, to the extent that we have responsibility for taking any action related to the prosecution or maintenance of patents or patent applications in-licensed from a third party, any failure on our part to maintain the in-licensed intellectual property could jeopardize our rights under the relevant license and may have a material adverse effect on our business, financial condition, results of operations and prospects.

If we do not obtain patent term extensions and data exclusivity for each of our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates we may develop, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman

Amendments permit a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. In the European Union, a maximum of five and a half years of supplementary protection can be achieved for an active ingredient or combinations of active ingredients of a medicinal product protected by a basic patent, if a valid marketing authorization exists (which must be the first authorization to place the product on the market as a medicinal product) and if the product has not already been the subject of supplementary protection. However, we may not receive an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. If we are unable to obtain patent term extension or if the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our business, financial condition, results of operations and prospects could be materially harmed.

Certain employees and patents are subject to German law.

A significant number of our personnel work in Germany and are subject to German employment law. Inventions which may be the subject of a patent or of protection as a utility model as well as technical improvement proposals for other technical innovations that may not be the subject of a patent or of protection as a utility model made by such employees are subject to the provisions of the German Act on Employees' Inventions (*Gesetz über Arbeitnehmererfindungen*), which regulates the ownership of, and compensation for, inventions made by employees. We face the risk that disputes may occur between us and our current or former employees pertaining to the sufficiency of compensation paid by us, allocation of rights to inventions under this act, or alleged nonadherence to the provisions of this act, any of which may be costly to resolve and take up our management's time and efforts whether we prevail or fail in such dispute. In addition, under the German Act on Employees' Inventions, certain employees retain rights to patents they invented or co-invented and disclosed to us prior to October 1, 2009 if the employee inventions were not actively claimed by us after notification by the employee inventors. While we believe that all of our current and past German employee inventors have assigned to us their interest in inventions and patents they invented or co-invented, there can be no assurance that all such assignments are fully effective. Therefore, there can be no assurance that present or former employees do not hold rights to intellectual property used by us or that such employees will not demand the registration of intellectual property rights in their name or demand damages pursuant to the German Act on Employees' Inventions or other applicable laws. Even if we lawfully own all inventions of our employee inventors who are subject to the German Act on Employees' Inventions, we are required under German law to reasonably compensate such employees for the use of the inventions. If we are required to pay increased compensation or face other disputes under the German Act on Employees' Inventions, our business, financial condition, results of operations and prospects could be adversely affected.

The German Act on Employees' Inventions does not generally apply to managing directors, supervisory directors, freelancers or agents who are not employees under German labor law. Unless the German Act on Employees' Inventions has been referred to in the respective services agreements, inventions and intellectual property rights created by such inventors must be assigned to us by contract. While we believe that all of our managing directors, supervisory directors, freelancers or agents which are not employees have assigned to us their interest in inventions and patents required for our course of business, there can be no assurance that all such assignments are fully effective. If any of our current or past employees, managing directors, supervisory directors, freelancers or agents obtain or retain ownership of any inventions or related intellectual property rights that we believe we own, we may lose valuable intellectual property rights and be required to obtain and maintain licenses from such persons to such inventions or intellectual property rights, which may not be available on commercially reasonable terms or at all, or may be nonexclusive. If we are unable to obtain and maintain a license to any such person's interest in such inventions or intellectual property rights, we may need to cease the development, manufacture, and commercialization of one or more of our product candidates or the product

candidates we may develop. In addition, any loss of exclusivity of our intellectual property rights could limit our ability to stop others from using or commercializing similar or identical technologies and products. Any of the foregoing events could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we are unable to protect the confidentiality of our proprietary information, the value of our technology and products could be materially adversely affected.

In addition to patent protection, we also rely on trade secrets and confidentiality agreements to protect other proprietary information that is not patentable or that we elect not to patent. To maintain the confidentiality of trade secrets and proprietary information, we enter into confidentiality agreements with our employees, consultants, independent contractors, collaborators, CMOs, CROs and others upon the commencement of their relationships with us. These agreements require that all confidential information developed by the individual or entity or made known to the individual or entity by us during the course of the individual's or entity's relationship with us be kept confidential and not disclosed to third parties. Our agreements with employees as well as our personnel policies also generally provide that any inventions conceived by the individual in the course of rendering services to us shall be our exclusive property (to the extent not covered by the German Act on Employees' Inventions) or that we may obtain full rights to such inventions at our election. However, we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology and processes and cannot guarantee that individuals with whom we have these agreements will comply with their terms. We also face the risk that present or former employees could continue to hold rights to intellectual property used by us, may demand the registration of intellectual property rights in their name and demand damages pursuant to the Patent Act. In addition, present or former employees may demand damages due to violation of obligations under the German Act on Employees' Invention. In the event of unauthorized use or disclosure of our trade secrets or proprietary information, these agreements, even if obtained, may not provide meaningful protection, particularly for our trade secrets.

We may not have adequate remedies in the event of unauthorized use or disclosure of our proprietary information in the case of a breach of any such agreements and our trade secrets and other proprietary information could be disclosed to third parties, including our competitors. Many of our partners also collaborate with our competitors and other third parties. The disclosure of our trade secrets to our competitors, or more broadly, would impair our competitive position and may materially harm our business, financial condition, results of operations and prospects. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to maintain trade secret protection could adversely affect our competitive business position. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. Courts outside the United States are sometimes less willing to protect proprietary information, technology and know-how. In addition, others may independently discover or develop substantially equivalent or superior proprietary information and techniques, and the existence of our own trade secrets affords no protection against such independent discovery.

We may not be successful in obtaining necessary intellectual property rights to product candidates for our development pipeline through acquisitions and in-licenses.

Although we intend to develop product candidates through our own internal research, we may need to obtain additional licenses from others to advance our research or allow commercialization of our product candidates and it is possible that we may be unable to obtain additional licenses at a reasonable cost or on reasonable terms, if at all. However, we may be unable to acquire or in-license intellectual property rights relating to, or necessary for, any product candidates from third parties on an exclusive basis or commercially reasonable terms or at all. In that event, we may be unable to develop or commercialize such product candidates. We may also be unable to identify product candidates that we believe are an appropriate strategic fit for our company and intellectual property relating to, or necessary for, such product candidates.

The in-licensing and acquisition of third-party intellectual property is a competitive area, and a number of more established companies are also pursuing strategies to in-license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. Furthermore, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. In addition, we expect that competition for the in-licensing or acquisition of third-party intellectual property rights for product candidates that are attractive to us may increase in the future, which may mean fewer suitable opportunities for us as well as higher acquisition or licensing costs. We may be unable to in-license or acquire the third-party intellectual property rights for product candidates on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to suitable product candidates, our business, financial condition, results of operations and prospects for growth could suffer.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting, and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Third parties may use our technologies in jurisdictions where we have not obtained or are unable to adequately enforce patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. Proceedings to enforce our intellectual property and proprietary rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

If our trademarks and trade names are not adequately protected, we may not be able to build name recognition in our markets of interest and our business, financial condition, results of operations and prospects may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names or marks which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business, financial condition, results of operations and prospects may be adversely affected.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our proprietary and intellectual property rights is uncertain because such rights offer only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- others may be able to develop products that are similar to, or better than, our product candidates in a way that is not covered by the claims of the patents we license or may own currently or in the future;
- we, or our licensing partners or current or future collaborators, might not have been the first to make the inventions covered by issued patents or pending patent applications that we license or may own currently or in the future;
- we, or our licensing partners or current or future collaborators, might not have been the first to file patent applications for certain of our or their inventions;
- our pending owned or in-licensed patent applications may not lead to issued patents;
- we may choose not to file a patent for certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property;
- our competitors or other third parties might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- it is possible that there are prior public disclosures that could invalidate our or our licensors' patents;
- the patents of third parties or pending or future applications of third parties, if issued, may have an adverse effect on our business;
- any patents that we obtain may not provide us with any competitive advantages or may ultimately be found not to be owned by us, invalid or unenforceable; or
- we may not develop additional proprietary technologies that are patentable.

Should any of these events occur, they could significantly harm our business, financial conditions, results of operations and prospects.

Risks Related to Our Business and Industry

Our current and future relationships with third-party payors, healthcare professionals and customers in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and

abuse, false claims, physician payment transparency and other healthcare laws and regulations, which could expose us to significant penalties.

Healthcare providers, physicians and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, including, without limitation, the federal Anti-Kickback Statute and the federal civil False Claims Act, that may constrain the business or financial arrangements and relationships through which we conduct clinical research, sell, market and distribute any products for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws and regulations that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs, such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation. Further, several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of a federal healthcare-covered business, the Anti-Kickback Statute has been violated;

- federal civil and criminal false claims laws, including, without limitation, the federal civil False Claims Act (that can be enforced through civil whistleblower or qui tam actions), and the civil monetary penalties law, which impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. Moreover, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

- the U.S. Federal Food, Drug, and Cosmetic Act, which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices;

- the U.S. Public Health Service Act, or the PHSA, which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;

- the Physician Payments Sunshine Act, created under Section 6002 of the Affordable Care Act, and its implementing regulations, which requires specified manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or the CMS, information related to payments or other "transfers of value" made to physicians, which is defined to include doctors, dentists, optometrists, podiatrists and chiropractors, and certain other healthcare providers beginning in 2022, and which requires teaching hospitals and applicable manufacturers to report annually to CMS ownership and investment interests held by physicians and their immediate family members by the 90th day of each calendar year. All such reported information is publicly available; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; and state and foreign laws that require drug

manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our relationships with physicians and other healthcare providers, some of whom may recommend, purchase or prescribe our product candidate, if approved, may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations.

If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of noncompliance with these laws and the curtailment or restructuring of our operations, which could have a material adverse effect on our business. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also materially affect our business.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the successful commercialization of our product candidates will depend in part on the extent to which governmental authorities, private health insurers and other third-party payors provide coverage and adequate reimbursement levels and implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement. The insurance coverage and reimbursement status of newly approved products for orphan diseases is particularly uncertain and failure to obtain or maintain adequate coverage and reimbursement for our product candidates could limit our ability to generate revenue. Third-party payors may not view our product candidates, if approved, as cost-effective, and coverage and reimbursement may not be available to our customers or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. If coverage and reimbursement are not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. Cost-control initiatives could also cause us to decrease any price we might establish for our product candidates, which could result in lower than anticipated product revenues. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including our costs related to research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. If the prices for our product candidates, if approved, decrease or if governmental and other third-party payors do not provide adequate coverage or reimbursement, our business, prospects, operating results and financial condition will suffer, perhaps materially.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products, including genetic treatments. In the United States, the Centers for Medicare & Medicaid Services, or the CMS, the federal agency responsible for administering the Medicare program, make the principal decisions about coverage and reimbursement for new treatments under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours. In addition, certain Affordable Care Act marketplace and other private payor plans are required to include coverage for certain preventative services, including vaccinations recommended by the U.S. Centers for Disease Control's, or the CDC's, Advisory Committee on Immunization Practices, or ACIP, without cost share obligations (i.e., co-payments, deductibles or co-insurance) for plan members. For Medicare beneficiaries, vaccines may be covered for reimbursement under either the Part B program or Part D depending on several criteria, including the type of vaccine and the beneficiary's coverage eligibility. If our vaccine candidates, once approved, are reimbursed only under the Part D program, physicians may be less willing to use our products because of the claims adjudication costs and time related to the claims adjudication process and collection of co-payment associated with the Part D program.

Outside the United States, certain countries, including a number of Member States of the European Union, set prices and reimbursement for pharmaceutical products, with limited participation from the marketing authorization holders. We cannot be sure that such prices and reimbursement will be acceptable to us or our collaborators. If the regulatory authorities in these jurisdictions set prices or reimbursement levels that are not commercially attractive for us or our collaborators, our revenues from sales by us or our collaborators, and the potential profitability of our product candidates, in those countries would be negatively affected. Additionally, some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then may experience delays in the reimbursement approval of our product or be subject to price regulations that would delay our commercial launch of the product, possibly for lengthy time periods, which could negatively impact the revenues we are able to generate from the sale of the product in that particular country.

Moreover, an increasing number of countries are taking initiatives to attempt to reduce large budget deficits by focusing cost-cutting efforts on pharmaceuticals for their state-run healthcare systems. These international price control efforts have impacted all regions of the world, but have been most drastic in the European Union. In some countries, in particular, in many Member States of the European Union, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. In addition, publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries.

If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially adversely affected. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Price controls may be imposed in certain markets, which may adversely affect our future profitability.

In some countries, particularly Member States of the European Union, the pricing of prescription drugs is subject to governmental control or control by associations of health insurers. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost-containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In some countries, in particular, in many Member States of the European Union, we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially adversely affected.

Exchange rate fluctuations or abandonment of the euro currency may materially affect our results of operations and financial condition.

Potential future expense and revenue may be incurred or derived from outside the European Union, particularly the United States. As a result, our business and share price may be affected by fluctuations in foreign exchange rates between the euro and other currencies, particularly the U.S. dollar, which may also have a significant impact on our reported results of operations and cash flows from period to period. In addition, the abandonment of the euro by one or more members of the European Union could lead to the re-introduction of individual currencies in one or more European Union Member States, or in more extreme circumstances, the dissolution of the European Union. The effects on our business of the abandonment of the euro as a currency, the exit of one or more European Union Member States from the European Union (such as Brexit) or a potential dissolution of the European Union, are impossible to predict with certainty, and any such events could have a material adverse effect on our business, financial condition and results of operations.

More generally, shifts in geopolitical balance, political crisis or wars may affect foreign exchange rates between the euro and other currencies, which may also have a significant impact on our reported results of operations and cash flows from period to period.

We could be subject to strict restrictions on the movement of cash and the exchange of foreign currencies.

In some countries, we could be subject to strict restrictions on the movement of cash and the exchange of foreign currencies, which would limit our ability to use this cash across our global operations. This risk could increase as we continue our geographic expansion, and in particular if we seek to expand into emerging markets, which are more likely to impose these restrictions than more established markets.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we, or they, may obtain.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

In March 2010, President Obama signed the Affordable Care Act into law. Among the provisions of the Affordable Care Act of potential importance to our business and our product candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription products and biologic products;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a requirement that certain Affordable Care Act marketplace and other private payor plans include coverage for preventative services, including vaccinations recommended by the ACIP without cost share obligations (i.e., co-payments, deductibles or co-insurance) for plan members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or an IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- the establishment of the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

Since its enactment, there have been judicial and congressional challenges to numerous aspects of the Affordable Care Act. By way of example, the 2017 Tax Reform Act included a provision repealing the individual mandate, effective January 1, 2019. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the Affordable Care Act is an essential and inseverable feature of the Affordable Care Act, and therefore because the mandate was repealed, the remaining provisions of the Affordable Care Act are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the Fifth Circuit upheld the District Court ruling that the individual mandate was unconstitutional, but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act are invalid as well. On March 2, 2020, the U.S. Supreme Court

granted the petitions for writs of certiorari to review the case. On June 17, 2021, the U.S. Supreme Court upheld the Affordable Care Act. However, there may be other efforts to challenge, repeal or replace the Affordable Care Act. Additionally, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the Affordable Care Act marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining policies that create unnecessary barriers to obtaining access to health insurance coverage through the Affordable Care Act. Further, on March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. We are continuing to monitor any changes to the Affordable Care Act that, in turn, may potentially impact our business in the future.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011 and subsequent laws, which began in 2013 and will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through December 31, 2021. In addition, in January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. New laws may result in additional reductions in Medicare and other healthcare funding, which may materially adversely affect customer demand and affordability for our product candidates, if approved, and, accordingly, the results of our financial operations.

Also, there has been heightened governmental scrutiny recently over the manner in which pharmaceutical companies set prices for their marketed products, which has resulted in several congressional inquiries and proposed federal legislation, as well as state efforts, designed to, among other things, bring more transparency to product pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. On November 20, 2020, CMS issued an Interim Final Rule implementing the Most Favored Nation, or the MFN, Model under which Medicare Part B reimbursement rates will be calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on August 6, 2021, the CMS announced a proposed rule to rescind the Most Favored Nations rule. Additionally, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point of sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, Congress has indicated that it will continue to seek new legislative measures to control drug costs.

The policies of the FDA or similar regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or the Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and spur innovation, but its ultimate implementation is unclear. If we or our collaborators are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or our collaborators are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability, which would adversely affect our business.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. It is difficult to predict how current and future legislation, executive actions, and litigation, including the executive orders, will be implemented, and the extent to which they will impact our business, our clinical development, and the FDA's and other agencies' ability to exercise their regulatory authority, including FDA's preapproval inspections and timely review of any regulatory filings or applications we submit to the FDA. To the extent any executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

We cannot predict whether future healthcare legislative or policy changes will be implemented at the federal or state level or in countries outside the United States in which we may do business, or the effect any future legislation or

regulation will have on us, but we expect there will continue to be legislative and regulatory proposals at the federal and state levels directed at containing or lowering the cost of healthcare.

Cyberattacks or other failures in our or our third-party vendors', contractors' or consultants' telecommunications or information technology systems could result in information theft, data corruption and significant disruption of our business operations.

We utilize information technology, or IT, systems and networks and cloud computing services to process, transmit and store electronic information in connection with our business activities. We manage and maintain our applications and data utilizing a combination of on-site systems, managed data centers and cloud-based data centers. We utilize external security and infrastructure vendors to manage our information technology systems and data centers. These applications and data encompass a wide variety of business-critical information, including research and development information, commercial information, and business and financial information. We face a number of risks relative to protecting this critical information, including loss of access risk, inappropriate use or disclosure, inappropriate modification, and the risk of our being unable to adequately monitor, audit and modify our controls over our critical information. This risk extends to the third-party vendors and subcontractors we use to manage this sensitive data. Despite the implementation of security measures, given the size and complexity of our internal IT systems and those of our third-party vendors, contractors and consultants, and the increasing amounts of confidential information that they maintain, such IT systems are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war, and telecommunication and electrical failures. Such IT systems are additionally vulnerable to security breaches from inadvertent or intentional actions by our employees, third-party vendors, contractors, consultants, business partners, and/or other third parties, or from cyberattacks by malicious third parties (including the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information). These threats pose a risk to the security of our systems and networks, the confidentiality and the availability and integrity of our data and these risks apply both to us, and to third parties on whose systems we rely for the conduct of our business.

Cyber threats are persistent and constantly evolving. Such threats have increased in frequency, scope and potential impact in recent years, which increase the difficulty of detecting and successfully defending against them. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. The techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates, terrorist organizations, or hostile foreign governments or agencies. There can be no assurance that we or our third-party service providers, contractors or consultants will be successful in preventing cyberattacks or successfully mitigating their effects. Similarly, there can be no assurance that such third-party service providers, contractors or consultants will be successful in protecting our clinical and other data that is stored on their systems. If the IT systems of our third-party vendors and other contractors and consultants become subject to disruptions or security breaches, we may have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. Any cyberattack or destruction or loss of data could have a material adverse effect on our business, financial condition, results of operations and prospects. For example, if such an event were to occur and cause interruptions in our operations, or those of our third-party vendors and other contractors and consultants, it could result in a material disruption or delay of the development of our product candidates. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyberattacks or other data security breaches and may incur significant additional expense to implement further data protection measures. As cyber threats continue to evolve, we may be required to incur material additional expenses in order to enhance our protective measures or to remediate any information security vulnerability.

Our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We are in the early stages of developing disaster recovery, business continuity plans and document retention plans designed to allow us to be operational despite unforeseen events, including natural disasters such as an earthquake, fire, hurricane, tornado, flood or significant power outage; political crises, such as terrorist attacks, war and other political instability, including the ongoing geopolitical tensions related to Russia's actions in Ukraine and associated international sanctions in response to such sanctions; or other catastrophic events. Without disaster recovery, business continuity and document retention plans, if we encounter difficulties or disasters with our manufacturing facilities, affiliates, corporate headquarters or those of third parties we rely on, our critical systems, operations and information may not be restored in a timely manner, or at all, and our business activities could be materially disrupted.

We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which could have a material adverse effect on our business.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical development and regulatory affairs, as well as to support our public company operations. We are currently constructing a new facility, designed for the development of a cGMP production process on a large industrial scale for market supply. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to a different geographic area of the country. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, and give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful development and commercialization of our product candidates. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

Engaging in acquisitions, joint ventures or collaborations may increase our capital requirements, dilute our shareholders, cause us to incur debt or assume contingent liabilities, and subject us to other risks. We may not realize the benefits of these acquisitions, joint ventures or collaborations.

We may evaluate various acquisitions and collaborations, including licensing or acquiring complementary products, intellectual property rights, technologies or businesses. Any potential acquisition, joint venture or collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and products of an acquired company, including difficulties associated with integrating new personnel;
- the diversion of our management's attention from our existing product programs and initiatives in pursuing such a strategic merger or acquisition;
- risk in the retention of key employees, the loss of key personnel, and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing products or product candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology or products sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

In addition, if we undertake acquisitions, we may utilize our cash, issue dilutive securities, assume or incur debt obligations, incur large one-time expenses and acquire intangible assets that could result in significant future amortization expense. Moreover, we may not be able to locate suitable acquisition or collaboration opportunities and this inability could impair our ability to grow or obtain access to technology or products that may be important to the development of our business.

Our employees, principal investigators and consultants may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could have an adverse effect on the results of our operations.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators and consultants, despite our robust efforts to prevent such misconduct through sponsor oversight. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the European Union and other jurisdictions, provide accurate information to the FDA, the EMA and other regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. Such misconduct also could involve the improper use of information obtained in the course of clinical trials or interactions with the FDA or other regulatory authorities, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from government investigations or other actions or lawsuits stemming from a failure to comply with laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

We are subject to stringent privacy laws, information security laws, regulations, policies and contractual obligations related to data privacy and security and changes in such laws, regulations, policies and contractual obligations could adversely affect our business, financial condition, results of operations and prospects.

We are subject to data privacy and protection laws and regulations that apply to the collection, transmission, storage and use of personally identifying information, which among other things, impose certain requirements relating to the privacy, security and transmission of personal information. The legislative and regulatory landscape for privacy and data protection continues to evolve in jurisdictions worldwide, and there has been an increasing focus on privacy and data protection issues with the potential to affect our business. Failure to comply with any of these laws and regulations could result in enforcement action against us, including fines, imprisonment of company officials and public censure, claims for damages by affected individuals, damage to our reputation and loss of goodwill, any of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Additionally, if we are unable to properly protect the privacy and security of personal information, including protected health information, we could be found to have breached our contracts.

There are numerous U.S. federal and state laws and regulations related to the privacy and security of personal information. In particular, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, establish privacy and security standards that limit the use and disclosure of individually identifiable health information, or protected health information, and require the implementation of administrative, physical and technological safeguards to protect the privacy of protected health information and ensure the confidentiality, integrity and availability of electronic protected health information. Determining whether protected health information has been handled in compliance with applicable privacy standards and our contractual obligations can be complex and may be subject to changing interpretation. If we fail to comply with applicable privacy laws, including applicable HIPAA privacy and security standards, we could face civil and criminal penalties. The HHS has the discretion to impose penalties without attempting to first resolve violations. HHS enforcement activity can result in financial liability and reputational harm, and responses to such enforcement activity can consume significant internal resources. Even when HIPAA does not apply, failing to take appropriate steps to keep consumers' personal information secure can constitute unfair acts or practices in or affecting commerce and be construed as a violation of Section 5(a) of the Federal Trade Commission Act, or the FTCA, 15 U.S.C § 45(a). The Federal Trade Commission, or the FTC, expects a company's data security measures to be reasonable and appropriate in light of the sensitivity and volume of consumer information it holds, the size and complexity of its business, and the cost of available tools to improve security and reduce vulnerabilities. Individually identifiable health information is considered sensitive data that merits stronger safeguards and the FTC's guidance for appropriately securing consumers' personal information is similar to what is required by the HIPAA Security Rule. In addition, state attorneys general are authorized to bring civil actions seeking either injunctions or damages in response to violations that threaten the privacy of state residents. We cannot be sure how these regulations will be interpreted, enforced or applied to our operations. In addition to the risks associated with enforcement activities and potential contractual liabilities, our ongoing efforts to comply with evolving laws and regulations at the federal and state level may be costly and require ongoing modifications to our policies, procedures and systems.

In addition, many states in which we operate have laws that protect the privacy and security of personal information. For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act, or the CCPA, increases privacy rights for California residents and imposes obligations on companies that process their personal information. Among other things, the CCPA requires covered companies to provide new disclosures to

California consumers and provide such consumers new data protection and privacy rights, including the ability to opt out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for certain data breaches that result in the loss of personal information. The CCPA also creates a new state agency that will be vested with authority to implement and enforce the CCPA. State laws are changing rapidly and there is discussion in Congress of a new federal data protection and privacy law to which we would become subject if it is enacted.

Internationally, laws, regulations and standards in many jurisdictions apply broadly to the collection, use, retention, security, disclosure, transfer and other processing of personal information. For example, in the European Union, the collection and use of personal data is governed by the provisions of the General Data Protection Regulation, or the GDPR, in addition to other applicable laws and regulations. The GDPR came into effect in May 2018, repealing and replacing the European Union Data Protection Directive, and imposing revised data privacy and security requirements on companies in relation to the processing of personal data of European Union and United Kingdom data subjects. The GDPR, together with national legislation, regulations and guidelines of the European Union Member States and the United Kingdom governing the processing of personal data, impose strict obligations with respect to, and restrictions on, the collection, use, retention, protection, disclosure, transfer and processing of personal data. The GDPR imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States. For example, in 2016, the European Union and United States agreed to a transfer framework for data transferred from the European Union to the United States, called the Privacy Shield, but the Privacy Shield was invalidated in July 2020 by the Court of Justice of the European Union. The standard contractual clauses issued by the European Commission, or the EC, for the transfer of personal data may be similarly invalidated by the Court of Justice of the European Union. On June 4, 2021, the EC adopted new standard contractual clauses, which impose on companies additional obligations relating to data transfers, including the obligation to conduct a transfer impact assessment and, depending on a party's role in the transfer, to implement additional security measures and to update internal privacy practices. If we elect to rely on the new standard contractual clauses for data transfers, we may be required to incur significant time and resources to update our contractual arrangements and to comply with new obligations. If we are unable to implement a valid mechanism for personal data transfers from the EU, we will face increased exposure to regulatory actions, substantial fines and injunctions against processing personal data from the EU. It remains to be seen whether these standard contractual clauses will remain available and whether additional means for lawful data transfers will become available. The GDPR authorizes fines for certain violations of up to 4% of the total global annual turnover of the preceding financial year or €20 million, whichever is greater. Such fines are in addition to any civil litigation claims by data subjects. Separately, Brexit could also lead to further legislative and regulatory changes and increase our compliance costs. As of January 1, 2021, and the expiry of transitional arrangements agreed to between the United Kingdom and the European Union, data processing in the United Kingdom is governed by a United Kingdom version of the GDPR (combining the GDPR and the Data Protection Act 2018), exposing us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. On June 28, 2021, the European Commission adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from European Union member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless the European Commission reassesses and renews or extends that decision. Other jurisdictions outside the European Union are similarly introducing or enhancing privacy and data security laws, rules and regulations, which could increase our compliance costs and the risks associated with noncompliance. We cannot guarantee that we are, or will be, in compliance with all applicable international regulations as they are enforced now or as they evolve.

It is possible that these laws may be interpreted and applied in a manner that is inconsistent with our practices and our efforts to comply with the evolving data protection rules may be unsuccessful. We must devote significant resources to understanding and complying with this changing landscape. Failure to comply with federal, state and international laws regarding privacy and security of personal information could expose us to penalties under such laws, orders requiring that we change our practices, claims for damages or other liabilities, regulatory investigations and enforcement action, litigation and significant costs for remediation, any of which could adversely affect our business. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which have a material adverse effect on our business, financial condition, results of operations and prospects.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face and will continue to face competition from third parties that use mRNA, gene editing or gene therapy development platforms and from third parties focused on other

therapeutic modalities, such as small molecules, antibodies, biologics and nucleic acid-based therapies. The competition is likely to come from multiple sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions.

Many of our potential competitors, alone or with their strategic partners, have substantially greater financial, technical and other resources, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even greater concentration of resources among a smaller number of competitors. Our commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approvals for their products faster or earlier than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. For example, some of our competitors have already received approval from the FDA and other regulatory agencies for their mRNA-based COVID-19 vaccines. Additionally, technologies developed by our competitors may render our product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors' products. In addition, the availability of our competitors' products could limit the demand and the prices we are able to charge for any products that we may develop and commercialize.

We depend heavily on our executive officers and managing directors, and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to retain the services of our current executive officers, managing directors, principal consultants and other service providers, and our ability to hire new highly qualified personnel. We are highly dependent on the management, development, clinical, financial and business development expertise of our executive officers, managing directors, principal consultants and other service providers. In addition, we have established relationships with universities and research institutions which have historically provided, and continue to provide, us with access to research laboratories, clinical trials, facilities and patients. Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel.

In most cases, our personnel may only terminate their employment upon first providing notice. A limited number of agreements provide for at-will termination. If we lose one or more of our executive officers or other key employees, our ability to implement our business strategy successfully could be seriously harmed. Furthermore, replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain marketing approval of and commercialize products successfully.

We may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

Our employees, independent contractors, consultants, collaborators and contract research organizations may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless or negligent conduct or disclosure of unauthorized activities to us that violates (i) FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities, (ii) manufacturing and clinical trial conduct standards, (iii) federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities and (iv) laws that require the reporting of financial information or data accurately. Activities subject to these laws also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation

in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment of our operations, any of which could have a material adverse effect on our ability to operate our business and our results of operations.

As a result of our geographically diverse operations, we are more susceptible to certain risks.

We have offices and operations in six cities and in five countries. If we are unable to manage the risks of our global operations, including fluctuations in foreign exchange and inflation rates, international hostilities, natural disasters, security breaches, failure to maintain compliance with our clients' control requirements and multiple legal and regulatory systems, our results of operations and ability to grow could be materially adversely affected.

Changes in our level of taxes, and audits, investigations and tax proceedings, could have a material adverse effect on our results of operations and financial condition.

Although limited in terms of magnitude due to ongoing losses incurred so far, we are subject to income taxes in Germany and the United States. We calculate and provide for income taxes in each tax jurisdiction in which we operate. Tax accounting often involves complex matters and judgment is required in determining our worldwide provision for income taxes and other tax liabilities. We are subject to ongoing tax audits in Germany. In the future, tax authorities may disagree with our judgments or may take increasingly aggressive positions with respect to the judgments we make. We regularly assess the likely outcomes of these audits in order to determine the appropriateness of our tax liabilities. However, our judgments might not be sustained as a result of these audits, and the amounts ultimately paid could be different from the amounts previously recorded. In addition, our effective tax rate in the future could be adversely affected by changes in the mix of earnings in countries with differing statutory tax rates, changes in the valuation of deferred tax assets and liabilities and changes in tax laws. Tax rates in the jurisdictions in which we operate may change as a result of macroeconomic or other factors outside of our control. Increases in the tax rate in any of the jurisdictions in which we operate could have a negative impact on our profitability. In addition, changes in tax laws, treaties or regulations, or their interpretation or enforcement, may be unpredictable, particularly in less developed markets, and could become more stringent, which could materially adversely affect our tax position. Any of these occurrences could have a material adverse effect on our results of operations and financial condition.

Uninsured losses arising from third-party claims brought against us could result in payment of substantial damages, which would decrease our cash reserves and could harm our profit and cash flow.

Our products are used in applications where the failure to use our products properly or their malfunction could result in serious bodily injury or death. We may not have adequate insurance to cover the payment of any potential claim related to such injuries or deaths. Insurance coverage may not continue to be available to us or, if available, may be at a significantly higher cost.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products.

The use of our investigational medicinal products in clinical trials and the sale of any approved products in the future may expose us to liability claims. These claims might be made by patients who use the product, healthcare providers, pharmaceutical companies or others selling such products. Any claims against us, regardless of their merit, could be difficult and costly to defend and could materially adversely affect the market for our product candidates or any prospects for commercialization of our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, it is always possible that a product, even after regulatory approval, may exhibit unforeseen side effects. If any of our product candidates were to cause adverse side effects during clinical trials or after approval of the product candidate, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates.

To cover such liability claims, we purchase clinical trial insurance in the conduct of each of our clinical trials. It is possible that our liabilities could exceed our insurance coverage or that our insurance will not cover all situations in which a claim against us could be made. We also intend to expand our insurance coverage to include the sale of commercial products if we receive marketing approval for any of our proprietary products. However, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise. If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business

operations could be impaired. Should any of the events described above occur, this could have a material adverse effect on our business, financial condition and results of operations, including, but not limited to:

- decreased demand for our future product candidates;
- adverse publicity and injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- compensation in response to a liability claim;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize our products or product candidates.

We could be adversely affected if we are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to patients. Any adverse publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our business, financial condition, results of operations or prospects.

Some of our product candidates are classified as gene therapies by the FDA and the EMA, and the FDA has indicated that products similar to our product candidates will be reviewed within its Center for Biologics Evaluation and Research, or CBER. Even though our mRNA product candidates are designed to have a different mechanism of action from gene therapies, the association of our product candidates with gene therapies could result in increased regulatory burdens, impair the reputation of our product candidates or negatively impact our platform or our business.

There have been few approvals of gene therapy products in the United States and other jurisdictions, and there have been well-reported significant adverse events associated with their testing and use. Gene therapy products have the effect of introducing new DNA and potentially irreversibly changing the DNA in a cell. In contrast, mRNA is highly unlikely to localize to the nucleus, integrate into cell DNA or otherwise make any permanent changes to cell DNA. Consequently, we expect that our product candidates will have a different potential side effect profile from gene therapies because they lack risks associated with altering cell DNA irreversibly. Further, we may avail ourselves of ways of mitigating side effects in developing our product candidates to address safety concerns that are not available to all gene therapies, such as lowering the dose of our product candidates during repeat dosing or stopping treatment to potentially ameliorate undesirable side effects.

Regulatory requirements governing gene and cell therapy products have evolved and may continue to change in the future, and the implications for mRNA-based medicines is unknown. For example, the FDA has established the Office of Tissues and Advanced Therapies within CBER to consolidate the review of gene therapy and related products, and convenes the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. In the European Union, mRNA has been characterized as a Gene Therapy Medicinal Product. In certain countries, mRNA therapies have not yet been classified or any such classification is not known to us. Specifically, in Japan, the Pharmaceuticals and Medical Devices Agency has not taken a position on the regulatory classification. Notwithstanding the differences between our mRNA product candidates and gene therapies, the classification of some of our mRNA product candidates as gene therapies in the United States, the European Union and potentially other countries could adversely impact our ability to develop our product candidates, and could negatively impact our platform and our business. For instance, a clinical hold on gene therapy products across the field due to risks associated with altering cell DNA irreversibly may apply to our mRNA product candidates irrespective of the mechanistic differences between gene therapies and mRNA.

Adverse events reported with respect to gene therapies or genome-editing therapies could adversely impact one or more of our programs. Although our mRNA product candidates are designed not to make any permanent changes to cell DNA, regulatory agencies or others could believe that adverse effects of gene therapy products caused by introducing

new DNA and irreversibly changing the DNA in a cell could also be a risk for our mRNA investigational therapies, and as a result, may delay one or more of our trials or impose additional testing for long-term side effects. Any new requirements and guidelines promulgated by regulatory review agencies may have a negative effect on our business by lengthening the regulatory review process, requiring us to perform additional or larger studies, or increasing our development costs, any of which could lead to changes in regulatory positions and interpretations, delay or prevent advancement or approval and commercialization of our product candidates or lead to significant post-approval studies, limitations or restrictions. As we advance our product candidates, we will be required to consult with these regulatory agencies and advisory committees and comply with applicable requirements and guidelines. If we fail to do so, we may be required to delay or discontinue development of some or all of our product candidates.

Risks Related to Our Common Shares

An active trading market for our common shares may not be sustainable. If an active trading market is not maintained, investors may not be able to resell their shares at or above the purchase price and our ability to raise capital in the future may be impaired.

Although our common shares are listed and trade on Nasdaq, an active trading market for our shares may not be maintained. If an active market for our common shares is not maintained, it may be difficult for you to sell shares you purchase without depressing the market price for the shares or at all. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration. In addition to the risks described above, the market price of our common shares may be influenced by many factors, some of which are beyond our control, including:

- the failure of financial analysts to continue to cover our common shares or changes in financial estimates by analysts;
- actual or anticipated variations in our operating results;
- changes in financial estimates by financial analysts, or any failure by us to meet or exceed any of these estimates, or changes in the recommendations of any financial analysts that elect to follow our common shares or the shares of our competitors;
- announcements by us or our competitors of significant contracts or acquisitions;
- future sales of our shares; and
- investor perceptions of us and the industries in which we operate.

These and other factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, the stock market in general has from time to time experienced extreme price and volume fluctuations, including in recent months, that have often been unrelated or disproportionate to the operating performance of particular companies affected. These broad market and industry factors may materially harm the market price of our common shares, regardless of our operating performance. In the past, following periods of volatility in the market price of certain companies' securities, securities class action litigation has been instituted against these companies. This litigation, if instituted against us, could adversely affect our financial condition or results of operations.

Sales of substantial amounts of our common shares in the public market, or the perception that these sales may occur, could cause the market price of our common shares to decline.

Sales of substantial amounts of our common shares in the public market, or the perception that these sales may occur, could cause the market price of our common shares to decline. This could also impair our ability to raise additional capital through the sale of our equity securities. We cannot predict the size of future issuances of our shares or the effect, if any, that future sales and issuances of shares would have on the market price of our common shares.

Considerable amounts of common shares are available for issuance under our equity incentive plans, and significant issuances in the future may adversely impact the market price of our common shares.

As of December 31, 2022, we had 386,250,000 authorized common shares, of which 194,954,225 shares were outstanding. In addition, 29,249,564 common shares were reserved for issuance pursuant to our equity incentive plans. The availability of substantial amounts of our common shares resulting from the exercise or settlement of equity awards

outstanding under our equity incentive plans, which would be dilutive to existing stockholders, could adversely affect the prevailing market price of our common shares and could impair our ability to raise additional capital through the sale of equity securities.

We have broad discretion in the use of our cash on hand and may invest or spend it in ways with which you do not agree and in ways that may not yield a return on your investment.

As of December 31, 2022, we had cash and cash equivalents amounting to € 495.8 million. Our management will have broad discretion in the use of such cash and could spend it in ways that do not improve our results of operations or enhance the value of our common shares. You will not have the opportunity to influence our decisions on how to use our cash on hand. The failure by our management to apply these funds effectively could result in financial losses that could harm our business, cause the price of our common shares to decline and delay the development of our product candidates. Pending its use, we may invest our cash on hand in a manner that does not produce income or that loses value.

Concentration of ownership by our principal shareholders may conflict with your interest and may prevent you from influencing significant corporate decisions.

As of March 31, 2023, our principal shareholders, dievini Hopp BioTech holding GmbH & Co. KG, or dievini, beneficially own 37.5% of our common shares, and Kreditanstalt für Wiederaufbau, or KfW, beneficially owns 13.3% of our common shares.

In addition, dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) has the right under our articles of association to make a binding nomination for the following number of supervisory directors until dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates as defined by our articles of association and ultimate beneficiaries as defined by our articles of association (individually or collectively) cease to own at least 10% of our issued share capital or an earlier change of control over dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) as defined by our articles of association, which period we refer to as the initial nomination period for dievini:

- four (4) supervisory directors for as long as dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates (as defined by our articles of association) and ultimate beneficiaries (as defined by our articles of association) (individually or collectively) own at least 70% of our issued share capital;
- three (3) supervisory directors for as long as dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates (as defined by our articles of association) and ultimate beneficiaries (as defined by our articles of association) (individually or collectively) own at least 50% (but less than 70%) of our issued share capital;
- two (2) supervisory directors for as long as dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates (as defined by our articles of association) and ultimate beneficiaries (as defined by our articles of association) (individually or collectively) own at least 30% (but less than 50%) of our issued share capital; and
- one (1) supervisory director for as long as dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates (as defined by our articles of association) and ultimate beneficiaries (as defined by our articles of association) (individually or collectively) own at least 10% (but less than 30%) of our issued share capital.

Dievini and Mr. Dietmar Hopp may be able to significantly influence all matters requiring shareholder approval. Even when dievini ceases to own common shares representing a majority of the total voting power, for so long as dievini continues to own a significant percentage of our common shares, dievini will still be able to significantly influence the composition of our supervisory board and the approval of actions requiring shareholder approval. Accordingly, for such period of time, dievini will continue to have significant influence with respect to our management, business plans and policies, including the appointment and removal of our managing directors, decisions on whether to raise future capital and any amending of our organizational documents, which govern the rights attached to our common shares. In particular, for so long as dievini continues to own a significant percentage of common shares, it will be able to cause or prevent a change of control of us or a change in the composition of our supervisory board and could preclude any unsolicited acquisition of us.

In addition, KfW (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) has the right, and has exercised the right under our articles of association, the KfW dievini Shareholders' Agreement

and the ISA to make a binding nomination for one (1) supervisory director until KfW or any KfW affiliates as defined by our articles of association (individually or together with any other KfW affiliate) cease to own at least 10% of our issued share capital, which period we refer to as the initial nomination period for KfW. Certain decisions require, and cannot be taken without, a resolution of our supervisory board that the KfW nominee, and a dievini nominee, have approved. These relate in particular to the location within the European Union of certain of our activities. The KfW dievini Shareholders' Agreement includes provisions relating to voting together and in a coordinated fashion on certain specified matters as further described under section 7 Related Party Transactions.

The concentration of ownership and these nomination rights could deprive you of an opportunity to receive a premium for your common shares as part of a sale of us and ultimately might affect the market price of our common shares. In addition, the concentration of voting power and these nomination rights could delay or prevent an acquisition of our company on terms that other shareholders may desire or result in the management of our company in ways with which other shareholders disagree.

We may be required to redeem for cash all, or to facilitate the purchase by a third-party of all, the shares of us held by the Bill & Melinda Gates Foundation as per the date of the ISA if we default under the Global Access Agreement, which could have an adverse impact on us and limit our ability to make distributions to our shareholders.

We entered into a Global Access Agreement with our shareholder, the Bill & Melinda Gates Foundation, in February 2015 pursuant to which we are required to take certain actions to support the Bill & Melinda Gates Foundation's mission. In the event that we commit a material breach of the Global Access Agreement or certain provisions of the ISA, following a cure period, we may be required to redeem for cash all, or to facilitate the purchase by a third-party of all, the shares of our company held by the Bill & Melinda Gates Foundation as per the date of the ISA at certain terms that may not be favorable to us. If this occurs, cash used for this purpose may adversely affect our liquidity, cause us to reduce expenditures in other areas of our business, or curtail our growth plans. If we do not have sufficient cash on hand to purchase the shares, we would have to seek financing alternatives in order to meet our obligations, and there is no certainty that financing would be available on reasonable terms or at all. For the period that we are unable to redeem the shares held by the Bill & Melinda Gates Foundation or arrange for a third-party to purchase such shares, we will generally not be allowed to pay dividends, redeem the shares of any other shareholder or otherwise make any other distribution to any of our shareholders in connection with their shares. Therefore, meeting this purchase obligation, if necessary, could have a material adverse effect on our business and financial results. For more information on the Bill & Melinda Gates Foundation's withdrawal rights, see section 7 Related Party Transactions.

Being a public company may continue to increase our costs and disrupt the regular operations of our business.

In August 2020, we completed our initial public offering. After the completion of our initial public offering we incurred and expect to continue to incur costs and expenses, including, but not limited to, managing directors' and supervisory directors' fees, increased directors and officers insurance, investor relations, and various other costs of a public company.

We also anticipate that we will continue to incur significant costs associated with corporate governance requirements, including requirements under the Sarbanes-Oxley Act of 2002, as amended, or the Sarbanes-Oxley Act, as well as rules implemented by the SEC and Nasdaq. We expect these rules and regulations to continue to increase our legal and financial compliance costs and make some management and corporate governance activities more time-consuming and costly. These rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. This could have an adverse impact on our ability to retain, recruit and bring on a qualified independent supervisory board. We expect that the additional costs we will incur as a public company, including costs associated with corporate governance requirements, will be considerable relative to our costs as a private company.

The additional demands associated with being a public company may disrupt regular operations of our business by diverting the attention of some of our senior management team away from revenue producing activities to management and administrative oversight, adversely affecting our ability to attract and complete business opportunities and increasing the difficulty in both retaining professionals and managing and growing our businesses. To date, such additional demands did not disrupt regular operations. Any of these effects could harm our business, financial condition and results of operations.

We are a foreign private issuer and, as a result, we are not subject to U.S. proxy rules and are subject to Exchange Act reporting obligations that, to some extent, are more lenient and less frequent than those of a U.S. domestic public company.

We report under the Securities Exchange Act of 1934, as amended, or the Exchange Act, as a non-U.S. company with foreign private issuer status. Because we qualify as a foreign private issuer under the Exchange Act, we are exempt from certain provisions of the Exchange Act that are applicable to U.S. domestic public companies, including (i) the sections of the Exchange Act regulating the solicitation of proxies, consents or authorizations in respect of a security registered under the Exchange Act, (ii) the sections of the Exchange Act requiring insiders to file public reports of their share ownership and trading activities and liability for insiders who profit from trades made in a short period of time and (iii) the rules under the Exchange Act requiring the filing with the SEC of quarterly reports on Form 10-Q containing unaudited financial and other specified information, or current reports on Form 8-K, upon the occurrence of specified significant events. In addition, foreign private issuers are not required to file their annual report on Form 20-F until four months after the end of each fiscal year, while U.S. domestic issuers that are accelerated filers are required to file their annual report on Form 10-K within 75 days after the end of each fiscal year. Foreign private issuers are also exempt from the Regulation Fair Disclosure, aimed at preventing issuers from making selective disclosures of material information. As a result of the above, you may not have the same protections afforded to shareholders of companies that are not foreign private issuers.

We may lose our foreign private issuer status which would then require us to comply with the Exchange Act's domestic reporting regime and cause us to incur significant legal, accounting and other expenses.

We are a foreign private issuer and therefore we are not required to comply with all of the periodic disclosure and current reporting requirements of the Exchange Act applicable to U.S. domestic issuers. If in the future we are not a foreign private issuer as of the last day of the second fiscal quarter in any fiscal year, we would be required to comply with all of the periodic disclosure, current reporting requirements and proxy solicitation rules of the Exchange Act applicable to U.S. domestic issuers. In order to maintain our current status as a foreign private issuer, either (a) a majority of our common shares must be either directly or indirectly owned of record by nonresidents of the United States or (b) (i) a majority of our managing directors, supervisory directors and executive officers may not be United States citizens or residents, (ii) more than 50% of our assets cannot be located in the United States and (iii) our business must be administered principally outside the United States. If we were to lose this status, we would be required to comply with the Exchange Act reporting and other requirements applicable to U.S. domestic issuers, which are more detailed and extensive than the requirements for foreign private issuers. We may also be required to make changes in our corporate governance practices in accordance with various SEC and stock exchange rules. The regulatory and compliance costs to us if we are required to comply with the reporting requirements applicable to a U.S. domestic issuer may be significantly higher than the costs we would incur as a foreign private issuer. As a result, we expect that a loss of foreign private issuer status would increase our legal and financial compliance costs and would make some activities highly time-consuming and costly. These rules and regulations could also make it more difficult for us to attract and retain qualified managing directors and supervisory directors.

As a foreign private issuer and as permitted by the listing requirements of Nasdaq, we follow certain home country governance practices rather than the corporate governance requirements of Nasdaq.

We are a foreign private issuer. As a result, in accordance with the listing requirements of Nasdaq, we rely on home country governance requirements and certain exemptions thereunder rather than relying on the corporate governance requirements of Nasdaq. In accordance with Dutch law and generally accepted business practices, our articles of association do not provide quorum requirements generally applicable to general meetings. To this extent, our practice varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting shares. Although we must provide shareholders with an agenda and other relevant documents for the general meeting, Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands, thus our practice varies from the requirement of Nasdaq Listing Rule 5620(b). As permitted by the listing requirements of Nasdaq, we have also opted out of the requirements of Nasdaq Listing Rule 5605(d), which requires, among other things, an issuer to have a compensation committee that consists entirely of independent directors, Nasdaq Listing Rule 5605(e), which requires independent director oversight of director nominations, and Nasdaq Listing Rule 5605(b)(1), which requires an issuer to have a majority of independent directors on its board. These rules require that a majority of our supervisory directors must be independent. In addition, we have opted out of shareholder approval requirements, as included in the Nasdaq Listing Rules, for the issuance of securities in connection with certain events such as the acquisition of shares or assets of another company, the establishment of or amendments to equity-based compensation plans for employees, a change of control of our company and certain

private placements. To this extent, our practice varies from the requirements of Nasdaq Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events. Accordingly, you may not have the same protections afforded to shareholders of companies that are subject to these Nasdaq requirements.

Although we do not believe that we were a "passive foreign investment company," or a PFIC, for U.S. federal income tax purposes for our 2022 taxable year, we may be a PFIC for 2023 or one or more future taxable years. A U.S. holder of common shares may suffer adverse U.S. federal income tax consequences if we are a PFIC for any taxable year.

Under the Internal Revenue Code of 1986, as amended, or the Code, we will generally be a PFIC for any taxable year in which, after the application of certain look-through rules with respect to subsidiaries, either (i) 75% or more of our gross income consists of "passive income," or (ii) 50% or more of the average quarterly value of our assets consists of assets that produce, or are held for the production of, "passive income." Passive income generally includes dividends, interest, certain nonactive rents and royalties, and capital gains. The value of a non-U.S. corporation's goodwill that is associated with activities that produce or are intended to produce active income is generally an active asset for purposes of the asset test unless, for U.S. federal income tax purposes, the non-U.S. corporation is a "controlled foreign corporation," or a CFC, that is not publicly traded "for the taxable year." If a non-U.S. corporation is a CFC that is not publicly traded for the taxable year, its PFIC status under the asset test is determined by using the U.S. tax basis of its assets rather than their fair market value and therefore the market value of its goodwill is generally disregarded. Generally, a non-U.S. corporation is a CFC if more than 50% of its shares' voting power or value is owned, directly, indirectly or constructively, by "United States shareholders" (as defined in Section 951(b) of the Code). Although it is not certain, we may be or may have been a CFC in the 2022 taxable year. However, under recently promulgated Treasury regulations, the fair market value of our assets (including goodwill) can be used for purposes of the asset test provided that (i) we are publicly traded on the majority of days during our taxable year or (ii) we would not be a CFC if certain constructive ownership rules were not applied. We believe, and the remainder of this discussion assumes, that we are eligible to use the fair market value of our assets for purposes of the asset test for our 2022 taxable year.

Based on the composition of our income and assets during 2022, we do not believe that we were a PFIC for our 2022 taxable year. However, there can be no assurance that the Internal Revenue Service, or the "IRS," will agree with our conclusion. Whether we will be a PFIC in 2023 or any future year is uncertain because, among other things, (i) we currently own a substantial amount of passive assets, including cash, (ii) the valuation of our assets that generate nonpassive income for PFIC purposes, including our intangible assets, is uncertain and may vary substantially over time, (iii) the treatment of grants as income for U.S. federal income tax purposes is unclear, and (iv) the composition of our income may vary substantially over time. Accordingly, there can be no assurance that we will not be a PFIC in 2023 or any future taxable year.

If we are a PFIC for any taxable year during which a U.S. investor holds common shares, we generally would continue to be treated as a PFIC with respect to that U.S. investor for all succeeding years during which the U.S. investor holds common shares, even if we ceased to meet the threshold requirements for PFIC status. Such a U.S. investor may be subject to adverse U.S. federal income tax consequences, including (i) the treatment of all or a portion of any gain on disposition as ordinary income, (ii) the application of a deferred interest charge on such gain and the receipt of certain dividends and (iii) compliance with certain reporting requirements. There is no assurance that we will provide information that will enable investors to make a qualified electing fund election, also known as a QEF Election, that could mitigate the adverse U.S. federal income tax consequences should we be classified as a PFIC.

Insiders have substantial control over us and could limit your ability to influence the outcome of key transactions, including a change of control.

As of April 25, 2023, our principal shareholders, managing directors, supervisory directors and executive officers and entities affiliated with them own 64% of the outstanding common shares. As a result, these shareholders, if acting together, would be able to influence or control matters requiring approval by our general meeting, including the appointment of managing directors and supervisory directors, changes to our articles of association and approval of mergers or other extraordinary transactions. They may also have interests that differ from yours and may vote in a way with which you disagree and which may be adverse to your interests. The concentration of ownership may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our shareholders of an opportunity to receive a premium for their common shares as part of a sale of our company and might ultimately affect the market price of our common shares.

If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common shares depends in part on the research and reports that securities or industry analysts publish about us or our business. If securities or industry analysts do not continue to cover our company, the market price for our common shares would likely be negatively impacted.

In addition, if one or more of the analysts who cover us downgrade our common shares or publish inaccurate or unfavorable research about our business, our share price may decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our shares could decrease, which might cause our share price and trading volume to decline.

We do not anticipate paying any cash dividends in the foreseeable future.

We currently intend to retain our future earnings, if any, for the foreseeable future, to fund the development and growth of our business. We do not intend to pay any dividends to holders of our common shares. As a result, capital appreciation in the price of our common shares, if any, will be your only source of gain on an investment in our common shares.

If we do pay dividends, we may need to withhold tax on such dividends payable to holders of our shares in both Germany and the Netherlands.

We do not intend to pay any dividends to holders of our common shares. See section 4.3 Risk Factors "— We do not anticipate paying any cash dividends in the foreseeable future." However, if we do pay dividends, we may need to withhold tax on such dividends both in Germany and the Netherlands.

As an entity incorporated under Dutch law, any dividends distributed by us are subject to Dutch dividend withholding tax on the basis of Dutch domestic law. However, on the basis of the 2012 Convention between the Federal Republic of Germany and the Kingdom of the Netherlands for the avoidance of double taxation with respect to taxes on income, or the "double tax treaty between Germany and the Netherlands," the Netherlands will be restricted in imposing these taxes if we are also a tax resident of Germany and our effective management is located in Germany, or the "withholding tax restriction." See also section 4.3 Risk Factors "— We may become taxable in a jurisdiction other than Germany and this may increase the aggregate tax burden on us." The withholding tax restriction does, however, not apply, and Dutch dividend withholding tax is still required to be withheld from dividends, if and when paid to Dutch resident holders of our common shares (and non-Dutch resident holders of our common shares that have a permanent establishment in the Netherlands to which their shareholding is attributable). As a result, upon a payment of dividends, we will be required to identify our shareholders in order to assess whether there are Dutch residents (or non-Dutch residents with a permanent establishment in the Netherlands to which the common shares are attributable) in respect of which Dutch dividend withholding tax has to be withheld. Such identification may not always be possible in practice. If the identity of our shareholders cannot be determined, withholding of both German and Dutch dividend withholding tax may occur upon a payment of dividends.

Furthermore, the withholding tax restriction referred to above is based on the current reservation made by Germany under the Multilateral Convention to Implement Tax Treaty Related Measures to Prevent Base Erosion and Profit Shifting, or the MLI, with respect to the tie-breaker provision included in Article 4(3) of the double tax treaty between Germany and the Netherlands, or the "MLI tie-breaker reservation." If Germany changes its MLI tie-breaker reservation, we will not be entitled to any benefits of the double tax treaty between Germany and the Netherlands, including the withholding tax restriction, as long as Germany and the Netherlands do not reach an agreement on our tax residency for purposes of the double tax treaty between Germany and the Netherlands, and, as a result, any dividends distributed by us during the period no such agreement has been reached between Germany and the Netherlands, may be subject to dividend withholding tax both in Germany and the Netherlands.

Our ability to use our net operating loss carryforwards and other tax attributes may be limited.

Our ability to utilize our net operating losses, or NOLs, is currently limited, and may be limited further, under Section 8c of the German Corporation Income Tax Act (*Korperschaftsteuergesetz*, or KStG) and Section 10a of the German Trade Tax Act (*Gewerbesteuergesetz*, or GewStG). These limitations apply if a qualified ownership change, as defined by Section 8c KStG, occurs and no exemption is applicable.

Generally, a qualified ownership change occurs if more than 50% of the share capital or the voting rights are directly or indirectly transferred to a shareholder or a group of shareholders within a period of five years. A qualified

ownership change may also occur in case of a transaction comparable to a transfer of shares or voting rights or in case of an increase in capital leading to a respective change in the shareholding.

In the case of such a qualified ownership change, tax loss carryforwards expire in full. To the extent that the tax loss carryforwards do not exceed the built-in gains (*stille Reserven*) in the assets and liabilities taxable in Germany, they may be further utilized despite a qualified ownership change. In case of a qualified ownership change within a group, tax loss carryforwards will be preserved if certain conditions are satisfied. In case of a qualified ownership change, tax loss carryforwards will be preserved (in the form of a "*fortfuhrungsgebundener Verlustvortrag*") if the business operations have not been changed and will not be changed within the meaning of Section 8d KStG.

According to an appeal filed by the fiscal court of Hamburg dated August 29, 2017, Section 8c, paragraph 1, sentence 1 KStG is not in line with the German Constitution. The appeal is still pending. It is unclear when the Federal Constitutional Court will decide this case.

As of December 31, 2022, there are NOLs for the German entities of CureVac for German corporate tax purposes of € 1,427.8 million: € 1,124.2 million for CureVac SE, € 243.3 million for CureVac Manufacturing GmbH, € 36.2 million for CureVac N.V., € 2.6 million for CureVac Corporate Service GmbH, and € 21.2 million for CureVac RNA Printer GmbH, and for German trade tax purposes of € 1,419.2 million: € 1,120.4 million for CureVac SE, € 239.2 million for CureVac Manufacturing GmbH, € 36.0 million for CureVac N.V., € 2.3 million for CureVac Corporate Service GmbH, and € 21.1 million for CureVac RNA Printer GmbH available.

Future changes in share ownership may also trigger an ownership change and, consequently, a Section 8c KStG or a Section 10a GewStG limitation. Any limitation may result in the expiration of a portion or the complete tax operating loss carryforwards before they can be utilized. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to reduce German income tax may be subject to limitations, which could potentially result in increased future cash tax liability to us.

Shareholders may not be able to exercise preemptive rights and, as a result, may experience substantial dilution upon future issuances of common shares.

In the event of an issuance of common shares, subject to certain exceptions, each shareholder will have a pro rata preemptive right in proportion to the aggregate nominal value of the common shares held by such holder. These preemptive rights may be restricted or excluded by a resolution of the general meeting or by another corporate body designated by the general meeting. Our management board, subject to approval of our supervisory board, has been authorized, for a period of five years, to issue shares or grant rights to subscribe for shares up to our authorized share capital from time to time and to limit or exclude preemptive rights in connection therewith. This could cause existing shareholders to experience substantial dilution of their interest in us.

We may become taxable in a jurisdiction other than Germany and this may increase the aggregate tax burden on us.

Since our incorporation, we have had, on a continuous basis, our place of "effective management" in Germany. We will therefore qualify as a tax resident of Germany on the basis of German domestic law. As an entity incorporated under Dutch law, however, we also qualify as a tax resident of the Netherlands on the basis of Dutch domestic law. However, based on our current management structure and the current tax laws of the United States, Germany and the Netherlands, as well as applicable income tax treaties, and current interpretations thereof, we should qualify solely as a tax resident of Germany for the purposes of the double tax treaty between Germany and the Netherlands due to the "effective management" tie-breaker included in Article 4(3) of the double tax treaty between Germany and the Netherlands and the current MLI tie-breaker reservation.

The test of "effective management" is largely a question of fact and degree based on all the circumstances, rather than a question of law. Nevertheless, the relevant case law and OECD guidance suggest that our company is likely to be regarded as having become a German tax resident from incorporation and remaining so if, as our company intends, (i) most meetings of its management board are prepared and held in Germany (and none will be held in the Netherlands) with a majority of managing directors present in Germany for those meetings; (ii) at those meetings there are full discussions of, and decisions are made regarding, the key strategic issues affecting our company and its subsidiaries; (iii) those meetings are properly minuted; (iv) a majority of our managing directors, together with supporting staff, are based in Germany; and (v) our company has permanent staffed office premises in Germany. We may, however, become subject to limited income tax liability in other countries with regard to the income generated in

the respective other country, for example, due to the existence of a permanent establishment or a permanent representative in such other country.

The applicable tax laws or interpretations thereof may change, including the MLI tie-breaker reservation. Furthermore, whether we have our place of effective management in Germany and are as such tax resident in Germany is largely a question of fact and degree based on all the circumstances, rather than a question of law, which facts and degree may also change. Changes to applicable laws or interpretations thereof, changes to applicable facts and circumstances (for example, a change of directors or the place where board meetings take place), or changes to applicable income tax treaties, including a change to the MLI tie-breaker reservation, may result in us becoming (also) a tax resident of the Netherlands or another jurisdiction. See "— If we do pay dividends, we may need to withhold tax on such dividends payable to holders of our shares in both Germany and the Netherlands." As a consequence, our overall effective income tax rate and income tax expense could materially increase, which could have a material adverse effect on our business, results of operations, financial condition and prospects, which could cause our share price and trading volume to decline. In addition, as a consequence, dividends distributed by us, and interest or royalty payments made by us, if any, may become subject to withholding taxes in more than one jurisdiction. The double taxation of income and the double withholding tax on dividends, interest and/or royalties may be reduced or avoided entirely under the double tax treaty between Germany and the Netherlands or under a double tax treaty between the Netherlands and the respective other country.

Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under the laws of the Netherlands and, as such, Dutch private international law governs the rights of our shareholders and the civil liability of our managing directors, supervisory directors and executive officers are governed in certain respects by the laws of the Netherlands. Our headquarters is located in Germany. Most of our assets are located outside the United States. The majority of our managing directors and supervisory directors reside outside the United States. The ability of our shareholders in certain countries other than the Netherlands to bring an action against us or our managing directors, supervisory directors and executive officers may be limited under applicable law. As a result, it may not be possible for shareholders to effect service of process within the United States upon such persons or to enforce judgments against them or us in U.S. courts, including judgments predicated upon the civil liability provisions of the federal securities laws of the United States. In addition, it is not clear whether a Dutch court would impose civil liability on us or any of our managing directors, supervisory directors and executive officers in an original action based solely upon the federal securities laws of the United States brought in a court of competent jurisdiction in the Netherlands.

As of the date of this Annual Report, there is no treaty in effect between the United States and the Netherlands providing for the reciprocal recognition and enforcement of judgments, other than arbitration awards, in civil and commercial matters. It is noted that, on today's date, the Hague Convention on Choice of Court Agreements of June 30, 2005 has entered into force for the Netherlands, but has not entered into force for the United States. The Hague Convention of 2 July 2019 on the Recognition and Enforcement of Foreign Judgments in Civil or Commercial Matters has not entered into force for either the Netherlands or the United States. Accordingly, a judgment rendered by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized and enforced by the competent Dutch courts. However, if a person has obtained a judgment rendered by a court in the United States that is enforceable under the laws of the United States and files a claim with the competent Dutch court, the Dutch court will in principle give binding effect to such judgment if (i) the jurisdiction of the U.S. court was based on a ground of jurisdiction that is generally acceptable according to international standards, (ii) the judgment by the U.S. court was rendered in legal proceedings that comply with the Dutch standards of proper administration of justice including sufficient safeguards (*behoorlijke rechtspleging*), (iii) binding effect of such U.S. judgment is not contrary to Dutch public order (*openbare orde*) and (iv) the judgment by the U.S. court is not incompatible with a decision rendered between the same parties by a Dutch court, or with a previous decision rendered between the same parties by a U.S. court in a dispute that concerns the same subject and is based on the same cause, provided that the previous decision qualifies for recognition in the Netherlands. However, even if such a U.S. judgment is given binding effect, a claim based on that U.S. judgment may still be rejected if the foreign judgment is not or no longer formally enforceable. Dutch courts may deny the recognition and enforcement of punitive damages or other awards. Moreover, a Dutch court may reduce the amount of damages granted by a U.S. court and recognize damages only to the extent that they are necessary to compensate actual losses or damages. Enforcement and recognition of judgments of U.S. courts in the Netherlands are solely governed by the provisions of the Dutch Code of Civil Procedure (*Wetboek van Burgerlijke Rechtsvordering*).

The United States and Germany currently do not have a treaty providing for the reciprocal recognition and enforcement of judgments, in civil and commercial matters. Consequently, a final judgment for payment or declaratory

judgments given by a court in the United States, whether or not predicated solely upon U.S. securities laws, would not automatically be recognized or enforceable in Germany. German courts may deny the recognition and enforcement of a judgment rendered by a U.S. court if they consider the U.S. court not to be competent or the decision to be in violation of German public policy principles. For example, judgments awarding punitive damages are generally not enforceable in Germany. A German court may reduce the amount of damages granted by a U.S. court and recognize damages only to the extent that they are necessary to compensate actual losses or damages.

In addition, actions brought in a German court against us, our managing directors, our supervisory directors, our senior management and the experts named herein to enforce liabilities based on U.S. federal securities laws may be subject to certain restrictions. In particular, German courts generally do not award punitive damages. Litigation in Germany is also subject to rules of procedure that differ from the U.S. rules, including with respect to the taking and admissibility of evidence, the conduct of the proceedings and the allocation of costs. German procedural law does not provide for pre-trial discovery of documents, nor does Germany support pre-trial discovery of documents under the 1970 Hague Evidence Convention. Proceedings in Germany would have to be conducted in the German language and all documents submitted to the court would, in principle, have to be translated into German. For these reasons, it may be difficult for a U.S. investor to bring an original action in a German court predicated upon the civil liability provisions of the U.S. federal securities laws against us, our managing directors, our supervisory directors, our senior management and the experts named in this Annual Report.

Based on the lack of a treaty as described above, there can be no assurance that U.S. investors will be able to enforce against us or managing directors, supervisory directors, executive officers or certain experts named herein who are residents of or possessing assets in the Netherlands, Germany, or other countries other than the United States any judgments obtained in U.S. courts in civil and commercial matters, including judgments under the U.S. federal securities laws.

The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions and may not protect investors in a similar fashion afforded by incorporation in a U.S. jurisdiction.

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We are a public company (*naamloze vennootschap*) organized under the laws of the Netherlands. Our corporate affairs are governed by our articles of association, the rules of our management board and those of our supervisory board and by the laws governing companies incorporated in the Netherlands. However, there can be no assurance that Dutch law will not change in the future or that it will serve to protect investors in a similar fashion afforded under corporate law principles in the United States, which could adversely affect the rights of investors.

The rights of shareholders and the responsibilities of managing directors and supervisory directors may be different from the rights and obligations of shareholders and directors in companies governed by the laws of U.S. jurisdictions. In the performance of their duties, our managing directors and supervisory directors are required by Dutch law to consider the interests of our company, its shareholders, its employees and other stakeholders, in all cases with due observation of the principles of reasonableness and fairness. It is possible that some of these parties will have interests that are different from, or in addition to, your interests as a shareholder.

The ability for our shareholders to alter the members of our management board or supervisory board may be limited by the Dutch cooling-off period in face of shareholder activism or hostile take-over

Our management board, with the approval of our supervisory board, can invoke a cooling-off period of up to 250 days when shareholders, using their right to have items added to the agenda for a general meeting or their right to request a general meeting, propose an agenda item for our general meeting to dismiss, suspend or appoint one or more managing directors or supervisory directors (or to amend any provision in our articles of association dealing with those matters) or when a public offer for our company is made or announced without our support, provided, in each case, that our management board believes that such proposal or offer materially conflicts with the interests of our company and its business. During a cooling-off period, our general meeting cannot dismiss, suspend or appoint managing directors and supervisory directors (or amend the provisions in our articles of association dealing with those matters) except at the proposal of our management board. During a cooling-off period, our management board must gather all relevant information necessary for a careful decision-making process and at least consult with shareholders representing 3% or more of our issued share capital at the time the cooling-off period was invoked, as well as with our Dutch works council (if we or, under certain circumstances, any of our subsidiaries would have one). Formal statements expressed by these stakeholders during such consultations must be published on our website to the extent these stakeholders have approved that publication. Ultimately one week following the last day of the cooling-off period, our management board must publish a report in respect of its policy and conduct of affairs during the cooling-off period on

our website. This report must remain available for inspection by shareholders and others with meeting rights under Dutch law at our office and must be tabled for discussion at the next general meeting. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber of the Amsterdam Court of Appeal, or the Enterprise Chamber (*Ondernemingskamer*), for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

- our management board, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business;
- our management board cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or
- other defensive measures, having the same purpose, nature and scope as the cooling-off period, have been activated during the cooling-off period and have not since been terminated or suspended within a reasonable period at the relevant shareholders' request (i.e., no "stacking" of defensive measures).

Provisions of our articles of association or Dutch corporate law might deter acquisition bids for us that might be considered favorable and prevent, delay or frustrate any attempt to replace or remove our managing directors or supervisory directors.

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Under Dutch law, various protective measures are possible and permissible within the boundaries set by Dutch law and Dutch case law. In this respect, our general meeting shall authorize our management board, subject to the approval by our supervisory board, to grant a call option to an independent foundation under Dutch law (if and when incorporated), or protective foundation, to acquire preferred shares pursuant to a call option agreement, or the call option agreement, that may be entered into between us and such protective foundation after the later of (a) dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates as defined by our articles of association and ultimate beneficiaries as defined by our articles of association (individually or collectively) no longer holding at least 25% of our issued share capital (or an earlier change of control over dievini, as defined in our articles of association), which we refer to as the initial period, or (b) the termination or expiry of the KfW dievini Shareholders' Agreement (see section 7 Related Party Transactions for further information on that agreement), which we refer to as the initial approval period.

This call option, if and when granted, shall be continuous in nature and can be exercised repeatedly on multiple occasions. If the protective foundation, if and when incorporated, would exercise such call option, if and when granted, a number of preferred shares up to 100% of our issued share capital held by others than the protective foundation, minus one share, will be issued to the protective foundation. These preferred shares would then be issued to the protective foundation under the obligation to pay 25% of their nominal value upon issuance. In order for the protective foundation to finance the issue price in relation to the preferred shares, the protective foundation may enter into a finance arrangement with a bank or other financial institution. As an alternative to securing this external financing, subject to applicable restrictions under Dutch law, the call option agreement, if and when entered into, will provide that the protective foundation may request us to provide, or cause our subsidiaries to provide, sufficient funding to the protective foundation to enable it to satisfy the payment obligation (or part thereof) in cash and/or to charge an amount equal to the payment obligation (or part thereof) against our profits and/or reserves in satisfaction of such payment obligation. The articles of association of the protective foundation, if and when incorporated, will provide that it will promote and protect the interests of the company, the business connected with the company and the company's stakeholders from time to time, and repress possible influences which could threaten the strategy, continuity, independence and/or identity of the company or the business connected with it, to such an extent that it could be considered to be damaging to the aforementioned interests. These influences may include a third-party acquiring a significant percentage of our common shares, the announcement of an unsolicited public offer for our common shares, shareholder activism, other concentration of control over our common shares or any other form of undue pressure on us to alter our strategic policies. The protective foundation, if and when incorporated, shall be structured to operate independently of us.

The voting rights of our shares are based on nominal value and, as we expect our common shares to trade substantially in excess of their nominal value, preferred shares issued at 25% of their nominal value can carry significant voting power for a substantially reduced price compared to the price of our common shares and thus can be used as a defensive measure. These preferred shares, if and when issued, will have both a liquidation and dividend preference over our common shares and will accrue cash dividends at a fixed rate calculated over the amount paid-up on those preferred shares *pro rata tempore* for the period during which they were outstanding. The protective foundation would be expected to require us to cancel its preferred shares, if and when issued to the protective foundation, once the

perceived threat to the company and its stakeholders has been removed or sufficiently mitigated or neutralized. However, subject to the same limitations described above, the protective foundation would, in that case, continue to have the right to exercise the call option in the future in response to a new threat to the interests of us, our business and our stakeholders from time to time.

In addition, certain provisions of our articles of association may make it more difficult for a third party to acquire control of us or effect a change in the composition of our management board and supervisory board. These include:

- a provision that our managing directors and supervisory directors are appointed on the basis of a binding nomination, the binding nature of which can only be overruled by a simple majority of votes cast representing at least one-third of our issued share capital;
- a provision that our managing directors and supervisory directors may only be dismissed by the general meeting by a two-thirds majority of votes cast representing more than 50% of our issued share capital (unless the dismissal is proposed by the supervisory board or, with respect to supervisory directors nominated by dievini or KfW, by dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for dievini or by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for KfW, respectively, in which case a simple majority of the votes would be sufficient);
- a provision that certain provisions of our articles of association can only be amended with the affirmative vote of (i) during the nomination period for dievini, dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) and (ii) during the nomination period for KfW, KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement);
- a provision that if a supervisory director is no longer in office or is unable to act, he or she may be replaced temporarily by a person who the supervisory board has designated for that purpose and, where a supervisory director who has been appointed upon a nomination of dievini or KfW, as applicable, is no longer in office or unable to act, such supervisory director may only be temporarily replaced by a person designated for such purposes by dievini or KfW, as applicable. Such person shall become a full member of the supervisory board with the rights of the relevant supervisory director appointed upon a nomination of dievini or KfW, as applicable, as soon as a written designation to that effect has been received by the chairman or vice-chairman of our supervisory board, subject to limitations, under applicable law regarding dievini's rights under this provision;
- a provision allowing, among other matters, a former chairman of our supervisory board, a former nominee of dievini, and a former nominee of KfW to jointly take on the supervisory functions, which persons jointly may designate one or more other persons to be charged with the supervision of our company (instead of or together with the former chairman of our supervisory board), as applicable, to supervise our affairs if all of our supervisory directors are removed from office and to appoint others to be charged with the supervision of our affairs, until new supervisory directors are appointed by the general meeting on the basis of a binding nomination discussed above;
- a provision allowing the management board to temporarily replace a managing director who is no longer in office or unable to act, with another person or persons designated for this purpose by the management board and attributing the management of the company to the supervisory board in case all managing directors are no longer in office or unable to act; and
- a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our management board with the approval of our supervisory board.

In addition, Dutch law allows for staggered multiyear terms of our managing directors and supervisory directors, as a result of which only part of our managing directors and supervisory directors may be subject to appointment or reappointment in any one year.

We are not obligated to, and do not, comply with all best practice provisions of the Dutch Corporate Governance Code.

For the fiscal year ended December 31, 2022, the Dutch Corporate Governance Code 2016 (the "**DCGC**") applied to the Company. The DCGC has been updated in the course of 2022, with effect from January 1, 2023 and will be reflected in our 2023 annual report. The DCGC contains both principles and best practice provisions on corporate

governance that regulate relations between the management board, the supervisory board and the general meeting and matters in respect of financial reporting, auditors, disclosure, compliance and enforcement standards. The DCGC is based on a "comply or explain" principle. Accordingly, companies are required to disclose in their annual reports, filed in the Netherlands, whether they comply with the provisions of the DCGC. If they do not comply with those provisions (for example, because of a conflicting Nasdaq requirement), the company is required to give the reasons for such noncompliance. The DCGC applies to Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, including Nasdaq. We do not comply with all best practice provisions of the DCGC. See section 5.1 Dutch Corporate Governance Code. This may affect your rights as a shareholder and you may not have the same level of protection as a shareholder in a Dutch company that fully complies with the DCGC.

We have identified a material weakness in our internal control related to ineffective configuration of segregation of duties in an IT system which, if not remediated appropriately or timely, could result in loss of investor confidence and adversely impact our stock price. If we are unable to remediate the material weakness, or if other control deficiencies are identified, we may not be able to report our financial results accurately, prevent fraud or file our periodic reports as a public company in a timely manner.

Our management is responsible for establishing and maintaining internal control over financial reporting, disclosure controls, and compliance with the other requirements of the Sarbanes-Oxley Act and the rules promulgated by the SEC thereunder. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with international financial reporting standards. A "material weakness" is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

We reported in our Annual Report 20-F for the year ended December 31, 2021, material weaknesses in internal control over financial reporting primarily related to (a) ineffective information technology general controls (ITGCs) in the area of user access over certain information technology (IT) systems and the reports generated from these systems used in the execution of controls that support the Company's financial reporting processes and (b) business controls which were not adequately designed and operating effectively as a result of gaps in the identification of risks, precision of review controls and documentation to evidence control performance as of December 31, 2021.

During 2022, we implemented measures to remediate this material weakness, and even though progress was made to strengthen our control environment, management concluded that at December 31, 2022, there was a material weakness in internal control related to an IT system's functionalities that were not configured to support segregation of duties in the recording of manual journal entries as well as in the authorization of purchase orders. As a result, management concluded that our internal control over financial reporting was not effective as of December 31, 2022. While we are working to remediate the weakness as quickly and efficiently as possible, we cannot at this time provide an estimate of the time frame we expect in connection with implementing our plan to remediate this material weakness. These remediation measures may be time consuming, costly and might place significant demands on our financial and operational resources. If we are unable to remediate the material weakness, or are otherwise unable to maintain effective internal control over financial reporting or disclosure controls and procedures, our ability to record, process and report financial information accurately, and to prepare financial statements within required time periods, could be adversely affected, which could subject us to litigation or investigations requiring management resources and payment of legal and other expenses, result in material misstatements in our financial statements that could require a restatement of financial statements, negatively affect investor confidence in our financial statements and adversely impact our stock price.

Notwithstanding the material weakness identified as of December 31, 2022, we have concluded that the financial statements and other financial information included in this Annual Report, fairly present in all material respects our financial condition, results of operations and cash flows as of, and for, the periods presented.

Our management has and continues to take measures to remediate these material weaknesses, as discussed in more detail under section 4.1 Risk Management and Control Systems of this Report and is committed to continue investing significant time and resources and taking actions to remediate the material weakness in segregation of duties as we work to further strengthen our internal control over financial reporting. Any failure to maintain or implement required new or improved controls, or any difficulties we encounter in their implementation, could result in additional significant deficiencies or material weaknesses, and result in material misstatements in our financial statements that could result in a restatement of financial statements.

Risks Related to ESG

Our ability to effectively monitor and respond to the rapid and ongoing developments and expectations relating to environmental, social and governance, or "ESG," matters, including related social expectations and concerns, may impose unexpected costs or result in reputational or other harm that could have a material adverse effect on our business, financial condition, cash flows and results of operations and could cause the market value of our common shares to decline.

There are rapid and ongoing developments and changing expectations relating to ESG matters and factors such as the impact of our operations on the environment, corporate governance, management of business ethics, human rights diligence in our supply chain, and human resource development, which may result in increased regulatory, social or other scrutiny on us. Regarding climate risks, we are expected to address climate risks due to our own contribution to climate change (inside-out perspective), risks due to physical effects of climate change as well as transition risks (outside-in perspective), and interactions between both perspectives ("dual materiality"). If we are unable to adequately recognize and respond to such developments and governmental, societal, investor and NGO expectations relating to such ESG matters, we may miss corporate opportunities, become subject to additional scrutiny, incur unexpected costs or experience damage to our reputation or our various brands. If any of these events were to occur, there may be a material adverse effect on our business, financial condition, cash flows and results of operations and the market value of our common shares may decline. We have observed that in addition to the importance of their financial performance, companies are increasingly being judged by their performance on ESG matters. A variety of organizations measure the performance of companies on such ESG topics, and the results of these assessments are widely publicized. We may fail to comply with standards or best practices put forth by such organizations or by governmental or regulatory bodies. In addition, investment in funds that specialize in companies that perform well in such assessments are increasingly popular, and major institutional investors have publicly emphasized the importance of such ESG measures to their investment decisions. In light of investors' increased focus on ESG matters, there can be no certainty that we will manage such issues successfully. Any failure or perceived failure by us in this regard could have a material adverse effect on our reputation and on our business, share price, financial condition, or results of operations, including the sustainability of our business over time.

If we or our third-party suppliers fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also may produce hazardous waste products. We generally anticipate contracting with third parties for the disposal of these materials and wastes. We will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by us of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

5. Corporate Governance

5.1 Dutch corporate governance code

For the fiscal year ended December 31, 2022, the Dutch Corporate Governance Code 2016 (the "**DCGC**") applied to the Company. The text of the DCGC is publicly available on the website of the Dutch Corporate Governance Code Monitoring Committee: http://www.mccg.nl. The DCGC has been updated in the course of 2022, with effect from January 1, 2023 and will be reflected in our 2023 annual report.

Except as set out below, during the fiscal year to which this Annual Report relates, the Company complied with the principles and best practice provisions of the DCGC, to the extent that these are directed at the Management Board and the Supervisory Board.

The Company has established an internal audit function in December 2021. Our internal audit tasks with regards to the commercial and financial perspective have been outsourced to a third party acting as external service supplier to the Company and responsible for our internal audit. The management board and supervisory board have considered whether setting up an internal audit department would be advisable and believes that given the size, resources,

personnel and experience of the Company, adequate alternative measures have been taken as outlined elsewhere in this Annual Report (see also section 4.2).

Under our articles of association, managing directors and supervisory directors can only be dismissed by the general meeting by simple majority, if the supervisory board or, with respect to supervisory directors nominated by dievini or KfW, by dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for dievini or by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for KfW, respectively, proposes the dismissal. In other cases, the general meeting can only pass such resolution by a at least a two-thirds majority of the votes cast, representing at least half of the issued share capital. However, the DCGC recommends that the general meeting can pass a resolution to dismiss a managing director or supervisory director by a simple majority of the votes cast, representing no more than one-third of the issued share capital.

The DCGC recommends that, for each shareholder or group of affiliated shareholders, who directly or indirectly hold more than ten percent of our issued share capital, there should be no more than one member of our supervisory board who is affiliated with that shareholder or group of shareholders. During the initial nomination period, dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) has the right under our articles of association to make a binding nomination for one or more supervisory directors, depending on its shareholding at that time (as described above) who may be affiliated with dievini. As of the date of this Annual Report, two members of our supervisory board are not independent within the meaning of the DCGC.

The DCGC recommends against providing equity awards as part of the compensation of a supervisory director. However, consistent with U.S. market practice, the trading jurisdiction of our common shares, and in order to further support our ability to attract and retain the right highly qualified candidates for our management board and supervisory board:

- our equity incentive plan (the "Plan") allows us to set the terms and conditions of equity awards granted thereunder. Under the Plan, we may grant common shares that are not subject to a lock-up period of at least five years after the date of grant, and we may grant options without restricting the exercisability of those options during the first three years after the date of grant; and

- we have granted and intend to grant restricted stock units, or RSUs, to our supervisory directors as part of their compensation. Such RSUs could (subject to the terms and conditions of the award) vest and automatically settle during the first three years after the date of grant.

Though certain performance criteria, as further described in Note 10 of our Consolidated Financial Statement (section 9), were considered when granting any variable pay, no scenario analyses have been performed in relation to variable pay. Also given the size, resources and personnel of our Company and our focus to devote significant resources to the wind down of activities related to CMOs and the restructuring of our HR department, we have not yet determined the pay ratios within our Company and its affiliated enterprise. Our Management Board, audit committee and Supervisory Board envisage to comply with such recommendations in the financial year 2023.

5.2 Code of conduct and ethics and other corporate governance practices

The Company has adopted a code of conduct and ethics, which has been revised in December 2022 and which can be accessed at https://www.curevac.com. The Company does not voluntarily apply other formal codes of conduct or corporate governance practices.

5.3 Risk management and control systems

See section 4.1 of this Annual Report for an overview of the main characteristics of the Company's risk management and control systems relating to the process of financial reporting by the Company and the Company's group companies whose financial information is included in the Company Financial Statements.

5.4 General meeting of shareholders

5.4.1 Functioning of the General Meeting

Annually, at least one general meeting of the Company (the "**General Meeting**") must be held. This annual General Meeting must be held within six months after the end of the Company's fiscal year. A General Meeting must also be held within three months after the Management Board has decided that it is likely that the Company's equity has decreased to or below 50% of its paid up and called up share capital. In addition, without prejudice to the best practice provisions of the DCGC with respect to invoking a 'response period' or the provisions under Dutch law with respect to invoking a 'cooling-off period', a General Meeting must be held when requested by one or more shareholders and/or others with meeting rights under Dutch law collectively representing at least 10% of the Company's issued share capital, provided that certain criteria are met. Any additional General Meeting shall be convened whenever the Management Board or the Supervisory Board would so decide. Each General Meeting must be held in Arnhem, Assen, The Hague, Haarlem, 's-Hertogenbosch, Groningen, Leeuwarden, Lelystad, Maastricht, Middelburg, Rotterdam, Schiphol (Haarlemmermeer), Utrecht or Zwolle, the Netherlands.

For purposes of determining who have voting rights and/or meeting rights under Dutch law at a General Meeting, the Management Board may set a record date. The record date, if set, shall be the 28th day prior to that of the General Meeting. Those who have voting rights and/or meeting rights under Dutch law on the record date and are recorded as such in one or more registers designated by the Management Board shall be considered to have those rights at the General Meeting, irrespective of any changes in the composition of the shareholder base between the record date and the date of the General Meeting. The Company's articles of association require shareholders and others with meeting rights under Dutch law to notify the Company of their identity and their intention to attend the General Meeting. This notice must be received by the Company ultimately on the seventh day prior to the General Meeting, unless indicated otherwise when such General Meeting is convened.

5.4.2 Powers of the General Meeting

All powers that do not vest in the Management Board or the Supervisory Board pursuant to applicable law, the Company's articles of association or otherwise, vest in the General Meeting. The main powers of the General Meeting include, subject in each case to the applicable provisions in the Company's articles of association:

a. the appointment, suspension and dismissal of Managing Directors and Supervisory Directors;

b. the approval of certain resolutions of the Management Board concerning a material change to the identity or the character of the Company or its business;

c. the reduction of the Company's issued share capital through a decrease of the nominal value, or cancellation, of shares in its capital;

d. the adoption of the Company's statutory annual accounts;

e. the appointment of the Dutch independent auditor to audit the Company's statutory annual accounts;

f. amendments to the Company's articles of association;

g. approving a merger or demerger by the Company, without prejudice to the authority of the Management Board to resolve on certain types of mergers and demergers if certain requirements are met; and

h. the dissolution of the Company.

In addition, the General Meeting has the right, and the Management Board and the Supervisory Board must provide, any information reasonably requested by the General Meeting, unless this would be contrary to an overriding interest of the Company.

5.4.3 Shareholder rights

Each share in the Company's capital carries one vote. Shareholders, irrespective of whether or not they have voting rights, have meeting rights under Dutch law (including the right to attend and address the General Meeting, subject to the concept of a record date as described in section 5.4.1). Furthermore, each share in the Company's capital carries an entitlement to dividends and other distributions as set forth in the Company's articles of association. Pursuant to the Company's articles of association, any such dividend or other distribution shall be payable on such date as determined by the Management Board and the Management Board may also set a record date for determining who are entitled to receive any such dividend or other distribution (irrespective of subsequent changes in the shareholder base). The record date for dividends and other distributions shall not be earlier than the date on which the dividend or other distribution is announced. In addition, shareholders have those rights awarded to them by Dutch law.

5.5 Management Board and Supervisory Board

5.5.1 Board Structure

We have a two-tier board structure consisting of a management board (*bestuur*) and a separate supervisory board (*raad van commissarissen*). There are no family relationships among any of our managing directors and supervisory directors.

5.5.2 Management Board

The Management Board is charged with managing the Company's affairs and the implementation of its strategy. In performing their duties, our managing directors shall be guided by the interests of the Company and of the business connected with it. Our senior management has an average of 21 years of experience in the biopharmaceutical industry. Many of the members of our management team have worked together as a team for many years.

Our Management Board has developed a view on sustainable long-term value creation by the Company and has formulated a strategy consistent with that view. The Supervisory Board has been actively engaged at an early stage in formulating the Company's strategy and supervises the manner in which the strategy is implemented.

As at December 31, 2022, the Management Board was composed as follows:

Name and age	**Gender**	**Nationality**	**Date of initial Appointment**	**Expiration of current term of office**	**Attendance rate at meetings of the board**
Franz-Werner Haas, LLD, LLM (53)	M	German	6/2012*	3/2023	50/50 (100%)
Mariola Fotin-Mleczek, Ph.D. (56)	F	Polish	9/2015**	1/2022	2/4 (50%)

Pierre Kemula, B.Sc. (49)	M	French	11/2016**	10/2024	47/50 (94%)
Antony Blanc, Ph.D. (55)	M	French	12/2020	11/2023	46/50 (92%)
Igor Splawski, Ph.D., MSc (55)	M	Polish	7/2020**	6/2023	49/50 (98%)
Dr. Klaus Edvardsen (60)	M	Danish	8/2021	6/2022	21/25 (84%)
Malte Greune, Ph.D. (58)	M	German	7/2021	6/2024	49/50 (98%)

* The date of initial appointment includes the term of office served as managing director of CureVac SE (at that time named: CureVac AG). Mr. Haas has been appointed as managing director of CureVac N.V. (at that time named: CureVac B.V.) on April 7, 2020.

** The date of initial appointment includes the term of office served as managing director of CureVac SE (at that time named: CureVac AG). Dr. Fotin-Mleczek, Mr. Kemula and Dr. Splawski have each been appointed as managing director of CureVac N.V. on August 14, 2020.The above table does not include Alexander Zehnder, MD, MBA, and Myriam Mendila, MD, who have each been appointed as managing director after December 31, 2022.

The following is a brief summary of the prior business experience and principal business activities performed outside of CureVac of our managing directors. Unless otherwise indicated, the current business addresses for each managing director is Friedrich-Miescher-Strasse 15, 72076 Tübingen, Germany.

Franz-Werner Haas, LLD, LLM has been our chief executive officer from August 2020 until March 2023. Mr. Haas was our chief corporate officer from 2012 until 2018 and our deputy chief executive officer from March 2020 until August 2020. Before joining CureVac, he was Vice President of Operations and Chief Compliance Officer of SYGNIS Pharma AG from May 2005 until March 2012, where he was responsible for the execution of M&A and capital market transactions. Mr. Haas started his professional career as an Assistant to the Executive Board of a privately held international commercial and service enterprise before assuming several management positions in the life science industry, including Vice President and General Counsel of LION bioscience from 2002 until December 2004. Mr. Haas also served as the General Counsel of Sirona Dental Systems from January 2005 to May 2005. He studied law at the University of Saarbruecken, K.U. Leuven and also holds an LLM from the University of Edinburgh.

Mariola Fotin-Mleczek, Ph.D. has been our chief technology officer from October 2018 until January 2022. She joined CureVac in May 2006 and was responsible for the development and preclinical testing of mRNA technology applied in different therapeutic areas such as: infectious diseases, oncology and protein delivery. Her scientific expertise includes immunology, cell biology, signal transduction, apoptosis and mechanism of cellular uptake. Dr. Fotin-Mleczek was trained in biology at the University of Stuttgart. She is the inventor of multiple mRNA technology-related key patents and she authored more than 30 scientific publications with a focus on mRNA technology.

Pierre Kemula, B.Sc. has been our chief financial officer since 2016. Previously, he was the chief financial officer of Pixium Vision from 2014 until 2016, where he successfully contributed to the listing of the company on Euronext in Paris, and Vice President of Corporate Finance, Treasury and Financial Markets, as well as Director of Investor Relations, Vice President of Investor Relations and Investor Relations Officer at Ipsen from 2008 until 2014. Earlier in his career, Mr. Kemula worked with major strategy consulting firms (Roland Berger, Bossard Consultants and Gemini Consulting). He holds a Bachelor of Science in Management Sciences from the London School of Economics, or LSE, in the United Kingdom.

Igor Splawski, Ph.D., MSc has been our chief scientific officer since July 2020. Prior to joining us, Dr. Splawski was an executive director at the Novartis Institutes for BioMedical Research (NIBR) Biologics Center since 2018, and director from 2016 until 2018. Previously, he was a director in the cardiovascular and metabolism disease area at NIBR from 2009 until 2016 and a senior investigator in ophthalmology at NIBR from 2005 to 2009. At NIBR, Dr. Splawski successfully led over 100 scientists in identifying and evaluating protein, mRNA and AAV targets, and discovered mRNA technology for antibody generation. His work at Novartis contributed to 12 clinical antibodies and proteins, which have achieved 11 positive proof-of-concept trials. Seven of these 12 compounds are currently in multiple phase 1 to phase 3 clinical trials. Earlier in his career, he served as an associate at both the Howard Hughes Medical Institute and the

Children's Hospital in Boston. Dr. Splawski acted as an assistant professor and instructor at Harvard Medical School, where he identified genes for inherited and drug-induced disorders, including arrhythmias, cardiac disease, deafness, nemaline myopathy, and autism. Dr. Splawski is the inventor on 28 patents and author of 23 research publications. Dr. Splawski holds a Ph.D. in human genetics from the University of Utah and a MSc in biotechnology from Sofia University.

Antony Blanc, Ph.D. has been our chief business officer and our chief commercial officer since December 2020. Previously, Dr. Blanc served biotech clients in Europe as consultant and as an Associate Partner with McKinsey & Company. Dr. Blanc has served as a managing director of Clarentis SRL since January 2018. Between 2009 and 2017, Dr. Blanc developed deep and broad cross-functional expertise in vaccines by serving in several senior roles at GSK Vaccines, including leading strategic marketing, strategic pricing, joint ventures and the integration of the Novartis Vaccines business unit. From 2000 to 2009, Dr. Blanc held leadership roles in several biotech companies as Chief Business Officer, such as Synosia, as the Head of Biopharma at Syngenta, where he built a business unit of over 100 people focusing on biologicals and plant-made antibodies, and as VP Business Development at Syntem. Dr. Blanc started his career at the strategy consulting firm McKinsey & Company in 1994, focusing on pharma and biotech. He holds a Ph.D. in Molecular Biology (control of mRNA translation) and a BS.c. in Biochemistry from McGill University in Montreal, Canada

Klaus Edvardsen, MD, Ph.D. has been our chief development officer from August 2021 until June 2022. Previously, Dr Edvardsen led early- and late-stage global oncology development as a Senior Vice President and Head of Global Oncology Development at Merck KGaA. He served at AstraZeneca prior to that, as Senior Vice President and Head of Global Medicines Development Oncology, where he was responsible for the overall development strategy for oncology and hematology programs. Dr. Edvardsen also held leadership roles at both GlaxoSmithKline PLC and at Genmab A/S in medicines development within various therapeutic areas. Dr. Edvardsen's previous research work includes several positions as adjunct member and professor in oncology at various institutes in Denmark, USA, Norway and Sweden. Dr. Edvardsen holds a MD degree as well as a PhD in cancer biology from University of Copenhagen.

Malte Greune, Ph.D. has been our chief operating officer since July 2021. Dr. Greune joins CureVac from Sanofi-Aventis Deutschland GmbH, where he held various management positions for almost ten years. As General Manager and Vice President Cartridges, Devices & Insulin Technology Group, he was responsible for several manufacturing sites in Frankfurt. Under his leadership, six isolator filling lines for insulins, oncology drugs and biologics were set up including one for a COVID-19 vaccine. Prior to his position as Head of Diabetes, Oncology and Devices at Sanofi, he worked as the Senior Vice President of Animal Health Manufacturing for the Merck Manufacturing Division, USA, where he led an international network of 28 sites, including 18 integrated vaccine sites. Furthermore, he held various leadership roles at the pharmaceutical companies Schering-Plough and Intervet International B.V. Dr. Greune started his career at Hoechst AG in Corporate Planning. Dr. Greune received his Ph.D. in Economics from the University of Cologne, Germany, graduated from the University of Trier, Germany, and completed a Master of Business Administration at Clark University in Worcester, USA.

5.6 Supervisory board

The Supervisory Board is charged with the supervision of the policy of the Management Board and the general course of affairs of the Company and of the business connected with it. The Supervisory Board provides the Management Board with advice. In performing their duties, our supervisory directors shall be guided by the interests of the Company and of the business connected with it. The Management Board provides the Supervisory Board with the information necessary for the performance of its tasks in a timely fashion. At least once a year, the Management Board also informs the Supervisory Board in writing of the main features of the strategic policy, the general and financial risks and the administration and control system of the Company.

As at December 31, 2022, the Supervisory Board was composed as follows:

Name and age	**Gender**	**Nationality**	**Date of initial appointment**	**Expiration of current term of office**	**Attendance rate at Supervisory Board meetings**
Baron Jean Stéphenne, MSc, MBA (73)	M	Belgian	8/2015*	2024	11/11 (100%)

Ralf Clemens, MD, Ph.D. (70)	M	German	8/2015*	2024	9/11 (82%)
Mathias Hothum, Ph.D. (56)	M	German	8/2015*	2024	9/11 (82%)
Hans Christoph Tanner, Ph.D. (71)	M	Swiss	8/2015*	2024	11/11 (100%)
Friedrich von Bohlen und Halbach, Ph.D. (59)	M	German	8/2015*	6/2022	2/6 (33%)
Craig A. Tooman, MBA (57)	M	USA	6/2019*	2025	10/11 (91%)
Viola Bronsema, Ph.D. (60)	F	German	8/2020	2024	11/11 (100%)
Debra Barker, MD (60)	F	Swiss	6/2022	2025	4/5 (80%)
Klaus Schollmeier, Ph.D. (66)	M	German	6/2022	2025	4/5 (80%)

* The date of initial appointment includes the term of office served as supervisory director of CureVac SE (at that time named: CureVac AG). Mr. Stéphenne, Dr. Clemens, Dr. Hothum, Dr. Tanner, Dr. von Bohlen und Halbach and Mr. Tooman have each been appointed as supervisory director of CureVac N.V. on August 14, 2020.

The following is a brief summary of the prior business experience and principal business activities performed outside of CureVac of our supervisory directors. Unless otherwise indicated, the current business addresses for each of our supervisory directors is Friedrich-Miescher-Strasse 15, 72076 Tübingen, Germany.

Baron Jean Stéphenne, MSc, MBA has served as a supervisory director since 2015. Since 2018 Mr. Stéphenne has served as the Chairman of the board at Bone Therapeutics. Mr. Stéphenne was the CEO of GSK Biologicals from 1989 until 2012 and the President of GSK Biologicals from 2002 until 2012, where he was instrumental in building one of the world's leading vaccine companies. In 1974, Mr. Stéphenne joined SmithKline-Rit, as engineer in biology in research and development. He also served as the President of UWE (Union Wallonne des Entreprises) from 1997 until 2000. Mr. Stéphenne was the chairman of BESIX Group S.A./N.V. and TiGenix N.V., IBA Wallonia Foreign Trade and Investment Agency, Henogen S.A., Aseptic Technologies. He was also a director of Fortis bank, GBL and Bone Therapeutics.

Ralf Clemens, MD, Ph.D. has served as a supervisory director since 2015. Dr. Clemens served as a director at Valneva from 2017 until 2019. Dr. Clemens is the principal and founder of Grid Europe Ltd. Consulting (Global Research in Infectious Diseases) since 2015. Dr. Clemens has been working in the pharmaceutical industry since 1988 in various senior scientific and business positions. He served as Senior Vice President and Head of Development for the Global Vaccine Business Unit at Takeda Pharmaceuticals International, Inc. from 2012 until 2014. Prior to this position, Dr. Clemens led the global vaccine development at Novartis from 2006 until 2012, and before that, he was the Head of GSK Biologicals' vaccine development and Latin American business strategy from 1992 until 2006. During these years, Mr. Clemens developed and brought to licensure more than 25 different vaccines globally. He currently serves as a Member of the Board of Trustees of the International Vaccine Institute IVI in Seoul, Korea and as external scientific advisor to the Bill & Melinda Gates Foundation. He is a member of the Selection Committee of GHIT Tokyo, Japan, and Chairman of the Scientific Advisory Board of Clover Biopharma. He graduated with an M.D. from the University of Mainz, Germany and holds an executive business degree from the Wharton Business School.

Mathias Hothum, Ph.D. has served as a supervisory director since 2015. Dr. Hothum is the managing director of dievini Hopp BioTech holding GmbH & Co. KG, or dievini. dievini manages the biotech investments of SAP co-founder Dietmar Hopp. For the past 25 years, Dr. Hothum has worked as a health economist in the healthcare, health services and life sciences sectors. Dr. Hothum specializes in financing, pricing, reimbursement and in the evaluation of mid-sized companies as well as of publicly owned/market-listed companies. He is the owner and founder of HMM-Consulting. Furthermore, Dr. Hothum serves as a supervisory director of a few biotech companies, including Heidelberg Pharma AG, Apogenix AG, Winheim 216 GmbH, Novaliq GmbH, Molecular Health GmbH and Joimax GmbH. He received his Ph.D. in economics from the University of Magdeburg and degree in economics from the University of Mannheim.

Hans Christoph Tanner, Ph.D. has served as a supervisory director since 2015. Dr. Tanner served as the chief financial officer and head of investor relations of Cassiopea S.p.A. from 2015 until December 31, 2020. Dr. Tanner served as director of Private Equity Holding AG from 2011 until 2018. He served as Cosmo Pharmaceuticals N.V.'s chief financial officer from 2006 until 2016, head of investor relations from 2006 until 2017 and head of transactions office from 2017 to 2020. Dr. Tanner also served as a board member of Cosmo Pharmaceuticals N.V. since 2006 up until May

2021. Dr. Tanner is also a member of the supervisory board or advisory board (Verwaltungsrat/Beirat) of DKSH AG, Paion AG since 2017, Qvanteq AG since 2011, and Joimax GmbH since 2003. From 1998 to 2001 he was a partner of Dr. Ernst Mueller-Moehl and co-founder of the 20 Minuten group of newspapers and founded A&A Active Investor, a SIX listed investment company. From 1992 to 1998 Dr. Tanner was the head of corporate finance & capital markets of UBS in Zurich and from 1976 to 1991 he had various functions in the Corporate Banking Department of UBS in Zurich, Madrid and Los Angeles. He received his Ph.D. in economics from the University of St. Gallen and degree in economics from the University of St. Gallen.

Friedrich von Bohlen und Halbach, Ph.D. has served as a supervisory director from 2015 until June 2022. Dr. von Bohlen und Halbach is the managing partner and co-founder of dievini. dievini manages the life science activities and investments of Dietmar Hopp, co-founder of SAP, and his family. Between 1992 to 1997 he held various positions at Fresenius AG, FAG Kugelfischer KGaA and WASAG Chemie AG. In 1997, Dr. von Bohlen und Halbach founded LION bioscience, AG and served as its CEO until 2003. He is chairman of the Board of Apogenix AG and Novaliq GmbH, and board member of CureVac NV, Heidelberg Pharma AG and Co-Chair of the Evaluation Board of the Wyss Translational Center Zurich. Friedrich is also co-founder and managing director of Molecular Health GmbH. Dr. von Bohlen und Halbach received his Ph.D. in neurobiology from the Swiss Federal Institute of Technology (ETH) in Zurich and a diploma in biochemistry from the University of Zurich.

Craig A. Tooman, MBA has served as a supervisory director since 2019. Mr. Tooman has experience in the biopharmaceutical industry spanning more than 30 years, including more than 15 years of such experience as the Chief Executive Officer and Chief Financial Officer at several public companies. Mr. Tooman currently serves as the President, Chief Executive Officer and as a member of the board of directors of Silence Therapeutics. He was previously the Chief Financial Officer of Silence. Prior to joining Silence, from September 2019 to January 2021, he served as CFO and COO at Vyome Therapeutics, Inc. and prior to his tenure at Vyome, from November 2013 to July 2019, Mr. Tooman served as CFO, and then subsequently as CEO and Board Director of Aratana Therapeutics, where he successfully negotiated a merger with Elanco. Before Aratana, from 2005 to 2010, Mr. Tooman served as the CFO of Enzon Pharmaceuticals until its acquisition by Sigma Tau, and prior to that led the $1.1 billion M&A initiative and integration of ILEX Oncology and Genzyme Corporation. Mr. Tooman has also held key positions at Pharmacia, and Upjohn. Mr. Tooman also serves on the Board of Directors of Ondine Biomedical Inc. Mr. Tooman earned his MBA in finance from the University of Chicago and a Bachelor of Arts degree in economics from Kalamazoo College.

Viola Bronsema, Ph.D. has served as a supervisory director since August 2020. Dr. Bronsema has been Secretary General and CEO of BIO Deutschland, Germany's Biotechnology Industry Association, since 2006. With its 350 corporate members, the sector association represents the interests of Germany's biotechnology industry nationally and internationally. Currently, she is member of the Advisory Boards of the German Federal Government (Bioeconomy Advisory Board), the German Life Sciences Association (VBIO e. V.) and one of the oldest German economic policy associations (WPCD e.V.). Previously, Dr. Bronsema was Head of Communications of Roche Diagnostics GmbH and of Roche Diagnostics Europe, Middle East, Africa, and before that, of Lilly Pharma Holding GmbH. She earned her Ph.D. at the Centre for Molecular Biology (ZMBH) at the University of Heidelberg, Germany.

Debra Barker, MD has served as a supervisory director since June 2022. Dr. Barker is a seasoned pharmaceutical executive with more than 25 years of experience in drug development and commercialization from Novartis, Roche, SmithKline Beecham and Knall in Europe, the Americas and Asia. She currently serves as a Non-Executive Director for two additional public companies including BergenBio ASA, a Norwegian Oncology company, and Destiny Pharma PLC, a late-stage British Anti-infective company. Previously, Dr. Barker led as Chief Medical and Development Officer at Polyphor LTD for two years. From 2006 to 2017 she held various leadership positions at Novartis, where she most recently served as Vice President, Medical Affairs Franchise Head for Ophthalmology as well as interim Franchise Head for Neuroscience. In addition, she held the role of Regional Medical Director, Asia Pacific for Novartis where she led teams to develop and execute medical communication, clinical trial and opinion leader development activities across the franchises. Dr. Barker holds a degree in pharmaceutical medicine and received a master's degree in immunology from King's College in London and a medical degree from Queens' College, Cambridge, UK.

Klaus Schollmeier, Ph.D has served as a supervisory director since June 2022. Dr. Schollmeier is an advisor to the Pharma/Biotech industry. He was Chief Executive Officer of SuppreMol in Munich from 2013 until 2015, when the company was sold to Baxalta. From 2004 to 2011, he served as CEO of Santhera in Basel, and as Chairman of the Board of Santhera until 2013. Dr. Schollmeier joined Graffinity Pharmaceuticals AG in Heidelberg, Germany as CEO in 2003 and merged the company with MyoContract AG, Basel in 2004 to form Santhera. Prior to joining the biotechnology industry in 2003, he was managing director of the healthcare/biotechnology group at ING-BHF Bank for ING Group Europe. Before that, he spent 16 years in the pharmaceutical industry at BASF, Knoll and Abbott. Dr. Schollmeier is

member of the board and chairman of several biotech companies including Tacalyx (Germany), Modra Pharmaceuticals (Netherlands), Affiris Pharma (Austria) and Eternygen (Germany).He holds a Ph.D. in biology from the University of Düsseldorf, Germany, and is currently an adjunct research associate professor at the Boston University Medical School, Massachusetts.

All of our supervisory directors, except for Baron Jean Stéphenne and Mathias Hothum, are independent within the meaning of the DCGC.

5.7 Evaluation

During the fiscal year to which this Annual Report relates, the Supervisory Board has evaluated its own functioning, the functioning of the committees of the Supervisory Board and that of the individual managing directors and supervisory directors on the basis of self-evaluation form distributed to, and completed by, the managing directors and supervisory directors. As part of these evaluations, the Supervisory Board has considered (i) substantive aspects, mutual interaction and the interaction between the Supervisory Board and the Management Board, (ii) events that occurred in practice from which lessons may be learned and (iii) the desired profile, composition, competencies and expertise of the Supervisory Board. In addition, the Management Board has evaluated its own functioning and that of the individual managing directors. These evaluations are intended to facilitate an examination and discussion by the Management Board and the Supervisory Board of their effectiveness and areas for improvement. On the basis of these evaluations, the Supervisory Board has concluded that the Management Board and Supervisory Board are functioning properly.[1]

5.8 Committees

5.8.1 General

The Supervisory Board has established an audit committee, a compensation committee, a nomination and corporate governance committee and a special committee. Each committee operates pursuant to its charter.

5.8.2 Audit Committee

The audit committee consists of Hans Christoph Tanner (as chairman), Craig A. Tooman and Klaus Schollmeier. The audit committee assists the supervisory board in overseeing our accounting and financial reporting processes and the audits of our financial statements. In addition, the audit committee is responsible for the appointment, compensation, retention and oversight of the work of our independent registered public accounting firm. Our supervisory board has determined that Hans Christoph Tanner, Craig A. Tooman and Klaus Schollmeier satisfy the "independence" requirements set forth in Rule 10A-3 under the Exchange Act and qualifies as an "audit committee financial expert", as such term is defined in the rules of the SEC. The composition of our audit committee is consistent with the best practice provisions of the DCGC.

The audit committee is governed by a charter, which charter has been posted on our website.

During the fiscal year to which this Annual Report pertains, the Audit Committee met seven times and discussed matters relating to the following topics, among others: Group, local and IFRS Financial Statements, Treasury and Treasury policy, budget, Insider Information, Whistle Blowing, Risk Management, Internal Audit and Controls esp. with regards of SOX compliance, Follow on and ATM Financing, Registration of Shares, old and new stock option plans including settlement; and the Audit Committee's self-assessment.

5.8.3 Compensation Committee

The compensation committee consists of Craig A. Tooman (as chairman), Hans Christoph Tanner, Mathias Hothum and Viola Bronsema. The compensation committee assists the supervisory board in determining compensation for our management and supervisory board members.

The composition of our compensation committee complys with best practice provisions of the DCGC.Under SEC and Nasdaq rules, there are heightened independence standards for members of the Committee, including a prohibition against the receipt of any compensation from us other than standard director fees. As permitted by the listing

[1] If there are other relevant conclusions that were drawn from the evaluations, those should be disclosed as well.

requirements of Nasdaq, we opted out of Nasdaq Listing Rule 5605(d), which requires that a compensation committee consist entirely of independent supervisory directors.

The compensation committee is governed by a charter, which has been posted on our website.

During the fiscal year to which this Annual Report pertains, the Compensation Committee met four times and exchanged on several occasions via mail and discussed matters relating to the following topics, among others: contract negotiations with potential CEO and CDO candidates, salary negotiations and contract extension and termination with management, incentive plans for Supervisory Board, Management and eligible employees; and the Compensation Committee's self-assessment.

5.8.4 Nomination and Corporate Governance Committee

The nomination and corporate governance committee consists of Craig Tooman (as chairman), Hans Christoph Tanner, Mathias Hothum and Viola Bronsema. The nomination and corporate governance committee assists our supervisory board in identifying individuals qualified to become our managing directors or supervisory directors consistent with criteria established by us and in developing our code of business conduct and ethics.

The nomination and corporate governance committee is governed by a charter, which has been posted on our website.

During the fiscal year to which this Annual Report pertains, the Nomination and Corporate Governance Committee met one time exchanged on several occasions via mail and discussed matters relating to the following topics, among others: appointment of Myriam Mendila as members of the Management Board and Klaus Schollmeier as member of the Supervisory Board and the Nomination and Corporate Governance Committee's self-assessment.

The Compensation as well as the Nomination and Corporate Governance Committee meetings were partially hold together and topics discussed.

5.8.5 Special Committee

Under the internal rules applicable to our supervisory board, resolutions of our supervisory board to approve a resolution of our management board to exclude or limit pre-emption rights (except in connection with the ordinary operation of our equity incentive plans) or to issue shares against non-cash contribution, shall require the approval of a special committee consisting of one supervisory director nominated by dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for dievini), the supervisory director nominated by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for KfW) and, if applicable, one supervisory director nominated by a nomination concert. In this special committee, the affirmative votes of one supervisory director nominated by dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for dievini) and the supervisory director nominated by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for KfW) shall be required. Similarly, the affirmative votes of at least one supervisory director nominated by dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for dievini) and the supervisory director nominated by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) (during the initial nomination period for KfW) shall be required for certain resolutions of the supervisory board specified by our articles of association and the internal rules applicable to our supervisory board.

5.9 Diversity policy

The Company has a diversity policy with respect to the composition of the Management Board and the Supervisory Board. The Company is committed to supporting, valuing and leveraging diversity and we recognize and welcome diversity with respect to gender, age, race, ethnicity, nationality, sexual orientation and other important cultural differences. In its evaluation of new candidates, the nomination and corporate governance committee may consider race or ethnicity, nationality, gender, sexual orientation, age, background, education skills and experience, as well as the restrictions, requirements and recommendations concerning those matters under applicable law, Nasdaq rules or best practice provisions of the DCGC in relation to our management board, supervisory board and/or individual directors

or director candidates. However, we also believe that there is a fine line between diversity and unintentional discrimination. For that reason, the importance of diversity, in and of itself, should not set aside the overriding principle that someone should be recommended, nominated and appointed for being "the right person for the job."

Although we have not yet set specific targets with respect to certain elements of diversity (other than with regard to gender as required by section 2:166(2) DCC, which targets are set out below), we believe that it is important for the management board, supervisory board and our senior management to represent a diverse composite mix of personal backgrounds, experiences, qualifications, knowledge, abilities and viewpoints, consistent with the principles outlined above. We also seek to combine the skills and experience of long-standing members of the management board, supervisory board and our senior management with the fresh perspectives, insights, skills and experiences of new candidates from time to time. To further increase the range of viewpoints, perspectives, talents and experience, we strive for a mix of experience among the management board, supervisory board and its senior management, but we have not set a specific target in this respect (other than as set out below with regard to gender as required by section 2:166(2) DCC).

At the date of this Annual Report, five of our managing directors are male and one is female. To the extent possible and practicable, we intend for the composition of the management board to remain balanced, provided that at least 66% of the members are male and at least 33% are female. Although our current management board composition does not yet comply with the aforementioned self-set targets, we believe that we are on a trajectory to achieve our diversity objectives with respect to the management board as we pay close attention to gender diversity in the process of recruiting and appointing new managing directors, but also take into account other elements of diversity such as personal backgrounds, experiences, qualifications, knowledge, abilities and viewpoints.

At the date of this Annual Report, six of our supervisory directors are male and two are female. To the extent possible and practicable, we intend for the composition of the supervisory board to remain balanced, provided that at least 75% of the members are male and at least 25% are female. We believe that we are on a trajectory to achieve our diversity objectives with respect to the supervisory board, as our current supervisory board composition complies with the aforementioned self-set target.

In connection with our diversity objectives, we have defined our senior management as employees at the vice president position and above. Six out of our 31 senior management members are female. We believe that we are on a trajectory to achieve our diversity objectives with respect to our senior management.

We have taken the following activities and measures for a more balanced gender ratio within the organization:

- establishing policies that support equal opportunities for employees, senior management and applicants for employment;
- encouraging and enforcing respectful communication and cooperation among all employees and senior management;
- fostering a corporate culture where employees and senior management are treated with dignity, respect and understanding;
- actively encouraging employees and officers who feel that they have been subjected to discrimination or harassment to report this to their supervisor or to our human resources department; and
- regularly review our corporate policies to ensure equal treatment.

Given the gender ratios both in the management board, supervisory board and as well as senior management, we are satisfied overall with our efforts towards improving gender diversity and we believe that our activities, training, mentoring and programs will continue to enhance our diversity objectives.

5.10 Corporate values and code of conduct and ethics

The Supervisory Board and Management Board have adopted a written Code of Conduct and Ethics that applies to our managing directors, supervisory directors, officers and employees, including our officers, permanent and temporary employees, leased and contract employees of CureVac or our subsidiaries. The Code of Conduct and Ethics is available on our website, https://www.curevac.com. Our management board is responsible for administering the Code of Conduct

and Ethics. The management board is allowed to amend, alter or terminate the Code of Business Conduct and Ethics. In addition, we intend to post on our website all disclosures that are required by law or the rules of Nasdaq, concerning any amendments to, or waivers from, any provision of the Code of Business Conduct and Ethics.

6. Compensation report

6.1 Compensation policy

Pursuant to Section 2:135(1) DCC, our General Meeting has adopted a compensation policy for our Management Board members (the "**Compensation Policy**").

The Compensation Policy is designed to:

- attract, retain and motivate Management Board members with the leadership qualities, skills and experience needed to support and promote the growth and sustainable success of the Company and its business;
- drive strong business performance, promote accountability, incentivize Management Board members to achieve short and long-term performance targets with the objective of substantially increasing the Company's equity value;
- assure that the interests of the Management Board members are closely aligned to those of the Company, its business and its stakeholders; and
- ensure the overall market competitiveness of the compensation packages which may be granted to the Management Board members, while providing the Supervisory Board sufficient flexibility to tailor the Company's compensation practices on a case-by-case basis, depending on the market conditions from time to time.

We believe that this approach and philosophy will benefit the realization of the Company's long-term objectives while keeping with the Company's risk profile.

The Supervisory Board is currently not contemplating to propose any change to the Compensation Policy or the implementation thereof in the upcoming fiscal years.

6.2 Compensation of managing directors

For the year ended December 31, 2022, the aggregate compensation accrued or paid to our managing directors for services in all capacities was EUR 3,067,113. The following table sets forth the compensation and benefits provided to our management board in the year ended December 31, 2022.

Name*	Salary (€)	Bonus(1) (€)	All Other Compensation(2) (€)	Total Compensation(3) (€)
Mariola Fotin-Mleczek (4)	26,666	64,896	3,487	95,049
Franz-Werner Haas (5)	417,500	79,040	89,172	585,712
Pierre Kemula	342,500	59,904	146,514	548,918
Antony Blanc	342,500	59,904	64,809	467,213
Igor Splawski	338,706	54,463	90,471	483,640
Klaus Edvardsen (6)	180,889	32,067	30,103	243,059
Malte Greune	342,500	29,952	54,448	426,900
Ulrike Gnad-Vogt(7)	133,875	44,297	38,450	216,662

(1) This amount represents the annual variable payment received based on a percentage of yearly gross remuneration for reaching certain targets agreed upon with the supervisory board, as described further below.

(2) All other compensation includes other monetary benefits and contributions to social security insurance, if any.

(3) This column does not include the virtual shares held by certain of the management board members. Information can be found in Note 10 (share-based payment) of our Consolidated Financial Statement (section 9).

(4) Mariola Fotin-Mleczek resigned as managing director with effect from January 31, 2022.

(5) Franz-Werner Haas resigned as managing director with effect from March 31, 2023.

(6) Klaus Edvardsen resigned as managing director with effect from June 30, 2022.

(7) Dr. Gnad-Vogt became the interim chief development officer in March 2021 and has not been formally appointed as a managing director of CureVac N.V. Dr. Gnad-Vogt resigned as interim chief development officer on January 31, 2023.

We did not provide pension, retirement or similar benefits to our managing directors and supervisory directors board in the year ended December 31, 2022.

Bonus Plan

We maintain and implement a management bonus plan for our managing directors. Under the management bonus plan, we provide a variable bonus payment as a component of management compensation that ranges from 50% to 55% of the individual's annual base salary, depending on management level. We agree upon the respective individual target bonus amount with each employee on an individual contractual basis. The annual performance review is used to measure the achievement of objectives. The Supervisory Board finally decides on the goal achievement of the Managing Directors. The bonus payment is calculated based on the individual's degree of target bonus achievement, which is then calculated as a percentage of annual base salary, and is generally paid out in March of the following year. The bonus is calculated on a pro rata basis if the individual joins or leaves CureVac during the year.

Equity Incentive Plans

We maintain a virtual share plan (the "Prior VSOP") for members of the management board and the supervisory board. As of December 31, 2022, there are 5,614,246 virtual shares outstanding and no awards are available for issuance under the Prior VSOP. Ten percent (10%) of each award under the Prior VSOP became exercisable upon expiration of the 180-day lock-up period following the closing of CureVac's IPO, which occurred on February 9, 2021. A second 10% portion of the (vested) virtual shares became exercisable on the first anniversary after the IPO on August 14, 2021, because certain minimum trading volumes of the CureVac N.V. shares and liquidity levels were reached (Exercise case "Liquidity after IPO), and a third 10% portion of the (vested) virtual shares became exercisable on the second anniversary of the IPO on August 14, 2022, as the exercise case "Liquidity upon IPO" was again reached. The remaining portion of each award may be exercised (in whole or in part) upon the occurrence of certain defined triggering events, including, but not limited to, drug approval or the sale by a majority shareholder of 5% of our outstanding shares, in each case subject to the terms and conditions of the Prior VSOP. All rights under the Prior VSOP will terminate following the ninth calendar year of our listing on Nasdaq. The Prior VSOP was restructured upon the completion of our Corporate Reorganization. Following this restructuring, upon vesting of virtual shares, the holder will be able to exchange his or her virtual shares (in whole or in part) for cash or common shares of CureVac N.V. (instead of shares of CureVac SE) on a 1 to 133.0778 basis.

Due to the increase in value of CureVac prior to our Corporate Reorganization, we modified our incentive program to allow members of the supervisory board, management board and other employees to participate in the value-increased business based on CureVac's valuation at the time of the Corporate Reorganization subject to the occurrence of certain enumerated exercise cases reflecting such value-increase (the "New VSOP"). Each virtual share awarded under the New VSOP tracked one underlying series A share of CureVac SE (formerly CureVac AG). The New VSOP provides a cash-claim against CureVac in the amount of the positive difference between the value of CureVac per virtual share at the grant date (as determined by CureVac when the New VSOP was established) and the value per virtual share at the time of exercise of such virtual share (such value to be derived from the valuation of CureVac in the relevant triggering event), subject to CureVac's discretion to provide tradable shares against payment of the value of CureVac per virtual share at the grant date. Such awards provided under the New VSOP have a term of ten years from the date of grant and vest over four years, where 25% vest after the first anniversary of the individual's hire date and the remainder vesting monthly. These virtual shares were assumed by CureVac N.V. upon the completion of our Corporate Reorganization, and were converted into options, exercisable for common shares of CureVac N.V. on a 1 to 133.0778 basis. Following this conversion, subject to the same vesting, exercise and expiration terms discussed above, these option awards are governed by the Plan (as defined below).

In connection with our initial public offering, we established the Long Term Incentive Plan "LTIP" (the "Plan") pursuant to which we may grant options, restricted stock, restricted stock units, share appreciation rights and other

equity and equity-based awards to our employees, managing directors and supervisory directors, consultants or other advisors. As of December 31, 2022, there are 6,831,772 awards outstanding and 22,417,792 shares remained available for issuance under the Plan. The maximum number of common shares underlying awards granted pursuant to the Plan, including the awards granted under the New VSOP and the common shares underlying outstanding awards under the Prior VSOP, will not exceed an equivalent of 15% of our issued share capital from time to time. The Plan is administered jointly by our management board, supervisory board and compensation committee. Awards under the Plan may be granted to our employees, managing directors and supervisory directors, consultants or other advisors. Awards under the Plan may be conditioned upon the achievement or satisfaction of certain performance criteria. The vesting conditions for awards under the Plan are determined by the Committee and will be set forth in the applicable award documentation. The Plan provides for special provisions for good leavers and bad leavers as well as for a change in control of CureVac NV.

6.3 Compensation of supervisory directors

For the year ended December 31, 2022, the aggregate compensation accrued or paid to our supervisory directors for services in all capacities was EUR 1,179,092. The following table sets forth the aggregate compensation and benefits provided to our supervisory board members in the year ended December 31, 2022.

Name	Fixed Compensation (€)	RSU Awards (€)	Total Compensation (€)
Baron Jean Stéphenne	123,750	89,834	213,584
Ralf Clemens	89,164	68,793	157,957
Mathias Hothum	96,118	69,871	165,989
Hans Christoph Tanner	96,250	69,871	166,121
Friedrich von Bohlen und Halbach (1)	45,620	79,346	124,966
Craig A. Tooman	79,392	51,936	131,328
Viola Bronsema	68,750	0	68,750
Debra Barker (2)	68,368	33,324	101,692
Klaus Schollmeier (3)	34,177	14,528	48,705

(1) Friedrich von Bohlen und Halbach resigned as supervisory director on June 22, 2022.

(2) Debra Barker joined the Supervisory Board on June 22, 2022.

(3) Klaus Schollmeier joined the Supervisory Board on June 22, 2022.

7. Related party transactions

For information on related party transactions, see note 15 of the Company Financial Statements (section 10 Company financial statement).

Where applicable, best practice provisions 2.7.3, 2.7.4 and 2.7.5 of the DCGC have been observed.

8. Protective measures

Established Dutch law allows Dutch companies to have certain protective measures in place, in order to safeguard the interests of a company, its business and its stakeholders. We adopted an anti-takeover measure pursuant to which our management board, subject to the approval by our supervisory board, may issue preferred shares without shareholder approval pursuant to a call option agreement with a special purpose foundation, or the protective foundation. Such call option agreement may be entered into between us and such protective foundation after the later of (a) dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) and its affiliates as defined by our articles of association and ultimate beneficiaries as defined by our articles of association (individually or collectively) no longer holding at least 25% of our issued share capital (or an earlier change of control over dievini, as defined in our articles of association), which we refer to as the initial period, or (b) the termination or expiry of the KfW dievini Shareholders' Agreement, which we refer to as the initial approval period. We may issue an amount of preferred shares up to the lesser of (i) the total number of shares (of whichever class) comprised in the Company's issued share capital when the call option is exercised pursuant to the call option agreement on the relevant

occasion, less the number of preferred shares already held by the protective foundation at that time (if any) and less one (1); or (ii) the maximum number of preferred shares that may be issued under the Company's authorized share capital as included in the Company's articles of association when the call option is exercised.

In addition, certain provisions of our articles of association may make it more difficult for a third party to acquire control of us or effect a change in our management board and supervisory board. These include:

- a provision that our managing directors and supervisory directors are appointed on the basis of a binding nomination, the binding nature of which can only be overruled by a simple majority of votes cast representing at least one-third of our issued share capital;

- a provision that our managing directors and supervisory directors may only be dismissed by the general meeting by a two-thirds majority of votes cast representing more than 50% of our issued share capital (unless the dismissal is proposed by the supervisory board or, with respect to supervisory directors nominated by dievini or KfW, by dievini (or its legal successor or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for dievini or by KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) during the nomination period for KfW, respectively, in which case a simple majority of the votes would be sufficient);

- a provision that certain provisions of our articles of association can only be amended with the affirmative vote of (i) during the nomination period for dievini, dievini (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement) and (ii) during the nomination period for KfW, KfW (or its legal successors or permitted assigns under the KfW dievini Shareholders' Agreement);

- a provision that if a supervisory director is no longer in office or is unable to act, he or she may be replaced temporarily by a person who the supervisory board has designated for that purpose and, where a supervisory director who has been appointed upon a nomination of dievini or KfW, as applicable, is no longer in office or unable to act, such supervisory director may only be temporarily replaced by a person designated for such purposes by dievini or KfW, as applicable. Such person shall become a full member of the supervisory board with the rights of the relevant supervisory director appointed upon a nomination of dievini or KfW, as applicable, as soon as a written designation to that effect has been received by the chairman or vice-chairman of our supervisory board, subject to limitations, under applicable law regarding dievini's rights under this provision;

- a provision allowing, among other matters, a former chairman of our supervisory board, a former nominee of dievini, and a former nominee of KfW to jointly take on the supervisory functions, which persons jointly may designate one or more other persons to be charged with the supervision of our company (instead of or together with the former chairman of our supervisory board), as applicable, to supervise our affairs if all of our supervisory directors are removed from office and to appoint others to be charged with the supervision of our affairs, until new supervisory directors are appointed by the general meeting on the basis of a binding nomination discussed above;

- a provision allowing the management board to temporarily replace a managing director who is no longer in office or unable to act, with another person or persons designated for this purpose by the management board and attributing the management of the company to the supervisory board in case all managing directors are no longer in office or unable to act; and

- a requirement that certain matters, including an amendment of our articles of association, may only be brought to our shareholders for a vote upon a proposal by our management board with the approval of our supervisory board.

In addition, Dutch law allows for staggered multi-year terms of our managing directors and supervisory directors, as a result of which only part of our managing directors and supervisory directors may be subject to appointment or re-appointment in any one year.

Furthermore, in accordance with the DCGC, shareholders who have the right to put an item on the agenda for our General Meeting or to request the convening of a General Meeting shall not exercise such rights until after they have consulted our management board. If exercising such rights may result in a change in our strategy (for example, through the dismissal of managing directors or supervisory directors), our management board must be given the opportunity to invoke a reasonable period of up to 180 days to respond to the shareholders' intentions. If invoked, our management board must use such response period for further deliberation and constructive consultation, in any event

with the shareholder(s) concerned and exploring alternatives. At the end of the response time, our management board shall report on this consultation and the exploration of alternatives to our General Meeting. The response period may be invoked only once for any given General Meeting and shall not apply (i) in respect of a matter for which a response period or a cooling-off period (as referred to below) has been previously invoked or (ii) if a shareholder holds at least 75% of our issued share capital as a consequence of a successful public bid.

In addition, our management board, with the approval of our supervisory board, can invoke a cooling-off period of up to 250 days when shareholders, using their right to have items added to the agenda for a general meeting or their right to request a general meeting, propose an agenda item for our general meeting to dismiss, suspend or appoint one or more managing directors or supervisory directors (or to amend any provision in our articles of association dealing with those matters) or when a public offer for our company is made or announced without our support, provided, in each case, that our management board believes that such proposal or offer materially conflicts with the interests of our company and its business. During a cooling-off period, our general meeting cannot dismiss, suspend or appoint managing directors and supervisory directors (or amend the provisions in our articles of association dealing with those matters) except at the proposal of our management board. During a cooling-off period, our management board must gather all relevant information necessary for a careful decision-making process and at least consult with shareholders representing 3% or more of our issued share capital at the time the cooling-off period was invoked, as well as with our Dutch works council (if we or, under certain circumstances, any of our subsidiaries would have one). Formal statements expressed by these stakeholders during such consultations must be published on our website to the extent these stakeholders have approved that publication. Ultimately one week following the last day of the cooling-off period, our management board must publish a report in respect of its policy and conduct of affairs during the cooling-off period on our website. This Annual Report must remain available for inspection by shareholders and others with meeting rights under Dutch law at our office and must be tabled for discussion at the next general meeting. Shareholders representing at least 3% of our issued share capital may request the Enterprise Chamber of the Amsterdam Court of Appeal, or the Enterprise Chamber (Ondernemingskamer), for early termination of the cooling-off period. The Enterprise Chamber must rule in favor of the request if the shareholders can demonstrate that:

- our management board, in light of the circumstances at hand when the cooling-off period was invoked, could not reasonably have concluded that the relevant proposal or hostile offer constituted a material conflict with the interests of our company and its business;
- our management board cannot reasonably believe that a continuation of the cooling-off period would contribute to careful policy-making; or
- other defensive measures, having the same purpose, nature and scope as the cooling-off period, have been activated during the cooling-off period and have not since been terminated or suspended within a reasonable period at the relevant shareholders' request (i.e., no 'stacking' of defensive measures).

CureVac N.V.

Consolidated Financial Statements

As of December 31, 2022 and 2021

CureVac N.V.

Consolidated Statements of Operations and Other Comprehensive Income (Loss)

(in thousands of EUR, except per share amounts)	Note	Year ended December 31, 2020	2021	2022
Revenue	3.1	48,871	102,990	67,420
Cost of sales	3.2	(14,173)	(238,195)	(183,993)
Selling and distribution expenses	3.3	(733)	(1,743)	(2,817)
Research and development expenses	3.1, 3.4	(113,808)	(815,907)	(62,550)
General and administrative expenses	3.5	(53,554)	(100,402)	(104,178)
Income from release of governmental contract liabilities	3.6	—	574,502	—
Other operating income	3.7	24,150	67,702	37,932
Other operating expenses		(568)	(1,210)	(1,271)
Operating loss		**(109,815)**	**(412,263)**	**(249,457)**
Finance income		2,070	10,103	4,009
Finance expenses		(22,103)	(10,338)	(3,707)
Loss before income tax		**(129,848)**	**(412,498)**	**(249,155)**
Income tax benefit/ (expense)	13	726	782	126
Net loss for the period		**(129,122)**	**(411,716)**	**(249,029)**
Other comprehensive income:				
Items that may be subsequently reclassified to profit or loss				
Foreign currency adjustments		35	(91)	(105)
Total comprehensive loss for the period		**(129,087)**	**(411,807)**	**(249,134)**
Net loss per share (basic and diluted)		**(0.98)**	**(2.21)**	**(1.32)**

The accompanying notes are an integral part of these consolidated financial statements.

CureVac N.V.

Consolidated Statements of Financial Position

(in thousands of EUR)	Note	December 31, 2021	December 31, 2022
Assets			
Non-current assets			
Intangible assets and goodwill	4.1	13,238	31,778
Property, plant and equipment	4.1	168,264	197,941
Right-of-use assets	4.2	32,129	43,761
Other assets	4.3	1,731	1,666
Deferred tax assets	14	2,861	1,297
Total non-current assets		**218,223**	**276,443**
Current assets			
Assets held for sale	5	—	10,467
Inventories	6	56,159	23,989
Trade receivables		18,504	6,295
Contract assets		—	2,707
Other financial assets	7	4,648	4,487
Prepaid expenses and other assets	8	49,244	40,287
Cash and cash equivalents		811,464	495,797
Total current assets		**940,019**	**584,029**
Total assets		**1,158,242**	**860,472**
Equity and liabilities			
Equity	9		
Issued capital		22,454	23,400
Capital reserve		1,728,658	1,817,287
Treasury Shares		(5,817)	(1,481)
Accumulated deficit		(1,056,785)	(1,305,814)
Other comprehensive income		(34)	(139)
Total equity		**688,476**	**533,253**
Non-current liabilities			
Lease liabilities	4.2	25,423	37,106
Contract liabilities	3.1	86,345	72,549
Provisions	12	—	61,320
Other liabilities	12	264	19
Total non-current liabilities		**112,032**	**170,994**
Current liabilities			
Lease liabilities	4.2	3,469	4,980
Trade and other payables	11	127,703	73,463
Provisions	12	122,042	1,922
Other liabilities	12	48,031	40,491
Income taxes payable	14	739	610
Contract liabilities	3.1	55,750	34,759
Total current liabilities		**357,734**	**156,225**
Total liabilities		**469,766**	**327,219**
Total equity and liabilities		**1,158,242**	**860,472**

The accompanying notes are an integral part of these consolidated financial statements.

CureVac N.V.

Consolidated Statements of Changes in Shareholders' Equity

(in thousands of EUR)	Issued capital	Capital reserve	Treasury Shares	Accumulated deficit	Currency translation reserve	Total equity
Balance as of January 1, 2020	**11,603**	**461,520**	**—**	**(515,947)**	**22**	**(42,802)**
Net loss	—	—	—	(129,122)	—	(129,122)
Other comprehensive income (loss)	—	—	—	—	35	35
Total comprehensive income (loss)	**—**	**—**	**—**	**(129,122)**	**35**	**(129,087)**
Equity component of convertible loans (net of tax)	—	87	—	—	—	87
Share-based payment expense (net of tax)	—	15,432	—	—	—	15,432
Exercise of options	383	(383)	—	—	—	—
Issuance of share capital (net of transaction costs)	9,669	858,048	—	—	—	867,717
Balance as of December 31, 2020	**21,655**	**1,334,704**	**—**	**(645,069)**	**57**	**711,347**

(in thousands of EUR)	Issued capital	Capital reserves	Treasury Shares	Accumulated deficit	Currency translation reserve	Total equity
Balance as of January 1, 2021	**21,655**	**1,334,704**	**—**	**(645,069)**	**57**	**711,347**
Net loss	—	—	—	(411,716)	—	(411,716)
Other comprehensive income (loss)	—	—	—	—	(91)	(91)
Total comprehensive income (loss)	**—**	**—**	**—**	**(411,716)**	**(91)**	**(411,807)**
Share-based payment expense (net of tax)	—	15,789	—	—	—	15,789
Exercise of options	109	3,077	—	—	—	3,186
Issuance of share capital (net of transaction costs)	690	403,372	—	—	—	404,062
Repurchase of common shares	—	(28,284)	(5,817)	—	—	(34,101)
Balance as of December 31, 2021	**22,454**	**1,728,658**	**(5,817)**	**(1,056,785)**	**(34)**	**688,476**

(in thousands of EUR)	Issued capital	Capital reserves	Treasury Shares	Accumulated deficit	Currency translation reserve	Total equity
Balance as of January 1, 2022	**22,454**	**1,728,658**	**(5,817)**	**(1,056,785)**	**(34)**	**688,476**
Net loss	—	—	—	(249,029)	—	(249,029)
Other comprehensive income (loss)	—	—	—	—	(105)	(105)
Total comprehensive income (loss)	**—**	**—**	**—**	**(249,029)**	**(105)**	**(249,134)**
Share-based payment expense (Net of Taxes)	—	7,539	—	—	—	7,539
Issuance of share capital (net of transaction costs)	829	65,552	—	—	—	66,381
Share issuances and contingent consideration from business combination	103	18,978	—	—	—	19,081
Exercise of options / Settlement of share-based payment awards	14	(3,440)	4,336	—	—	910
Balance as of December 31, 2022	**23,400**	**1,817,287**	**(1,481)**	**(1,305,814)**	**(139)**	**533,253**

The accompanying notes are an integral part of these consolidated financial statements.

CureVac N.V.

Consolidated Statements of Cash Flows

(in thousands of EUR)	Note	Year ended December 31, 2020	2021	2022
Loss before income tax		**(129,848)**	**(412,498)**	**(249,155)**
Adjustments to reconcile loss before tax to net cash flows				
Finance income		(2,070)	(10,103)	(4,009)
Finance expense		22,103	10,338	3,707
Depreciation and amortization	4.1	10,671	15,674	23,741
Impairment of property, plant and equipment	4.1	—	22,810	6,594
Loss on disposal of fixed assets	4.1	5,921	587	11,981
Impairment of assets held for sale	5	—	—	19,064
Impairment of inventory and prepayments	6	—	185,832	80,021
Share-based payment expense		14,240	14,956	9,185
Income from release of governmental contract liabilities	3.6	—	(574,502)	—
Releases in provision for onerous contracts	12	—	—	(58,799)
Working capital changes				
Decrease / (increase) in trade receivables and contract assets		15,332	(16,682)	9,502
Decrease / (increase) in inventory	6	(8,334)	(227,460)	(47,851)
Decrease / (increase) in prepaid expenses and other assets		(47,578)	(3,118)	8,968
Receipts from grants from government agencies and similar bodies		31,599	93,531	—
(Decrease) / increase in trade and other payables and contract liabilities		620,305	179,316	(96,186)
(Decrease) / increase in other current financial and other liabilities		(55)	(20)	—
Decrease / (increase) in deferred taxes		(1,096)	(1,583)	4
Income taxes paid		(93)	(502)	(128)
Interest received		—	81	1,790
Interest paid		(8,694)	(9,785)	(4,606)
Net cash flow provided by (used in) operating activities		**522,403**	**(733,128)**	**(286,177)**
Investing activities				
Purchase of property, plant and equipment		(36,329)	(124,222)	(88,023)
Purchase of intangible assets		(11,023)	(3,679)	(5,199)
Proceeds from asset-related grants		3,239	—	—
Purchases of financial assets		(1,161)	—	—
Acquisition of subsidiary, net of cash acquired	21	—	—	(277)
Net cash flow provided by (used in) investing activities		**(45,274)**	**(127,901)**	**(93,499)**
Financing activities				
Payments on lease obligations		(2,995)	(3,183)	(4,221)
Proceeds from the issuance of shares (net of transaction costs)		867,717	404,062	—
Payment on / proceeds from treasury shares/exercise of options		—	(30,915)	910
Proceeds from at-the-market offering program (net of transaction costs)		—	—	66,484
Proceeds from (repayment of) the EIB loan		25,000	(25,000)	—
Proceeds from the convertible loan		24,860	—	—
Repayments of convertible loan		(94,749)	—	—
Net cash flow provided by financing activities		**819,833**	**344,964**	**63,173**
Net increase (decrease) in cash and cash equivalents		1,296,962	(516,065)	(316,503)
Effect of currency translation gains on cash and cash equivalents		(5,053)	4,936	836
Cash and cash equivalents, beginning of period		30,684	1,322,593	811,464
Cash and cash equivalents, end of period		**1,322,593**	**811,464**	**495,797**

The accompanying notes are an integral part of these consolidated financial statements.

1. Corporate Information

CureVac N.V. ("CureVac" or "CV" or the "Company") is the parent company of CureVac Group ("Group") and, along with its subsidiaries, is a global biopharmaceutical company developing a new class of transformative medicines based on the messenger ribonucleic acid (mRNA) that has the potential to improve the lives of people.

We were incorporated pursuant to the laws of the Netherlands as CureVac B.V. on April 7, 2020 to become a holding company for CureVac AG prior to our initial public offering. Pursuant to the terms of a corporate reorganization (the "Corporate Reorganization"), all of the outstanding shares in CureVac AG were contributed and transferred to CureVac B.V. in a capital increase in exchange for common shares of CureVac B.V. and, as a result, CureVac AG became a wholly-owned subsidiary of CureVac B.V. and then current shareholders of CureVac AG became the shareholders of CureVac B.V. Immediately following such exchange, and prior to the listing of our common shares on Nasdaq, we converted into a public company (naamloze vennootschap) under Dutch law pursuant to a Dutch notarial deed of amendment and conversion, following which our legal name became CureVac N.V. As part of our Corporate Reorganization, outstanding shares of all series in CureVac AG were exchanged for common shares in CureVac N.V. On May 4, 2022, CureVac AG, as absorbing and parent entity, entered into a plan of merger with CureVac Beteiligungsverwaltungs AG, as transferring entity, which became effective on September 26, 2022. Upon effectiveness of the merger plan, CureVac Beteiligungsverwaltungs AG ceased to exist and CureVac AG adopted the legal form of SE (societas Europaea) preserving its identity and operating under the name CureVac SE.

We are registered in the commercial register at the Netherlands Chamber of Commerce under company number 77798031 (RSIN 861149336). Our principal executive offices are located at Friedrich-Miescher-Strasse 15, 72076 Tübingen, Germany.

During fiscal 2022, dievini Hopp BioTech holding GmbH & Co. KG (dievini), which is an investment company dedicated to the support of companies in health and life sciences, was the largest shareholder of CureVac. Together with its related parties, dievini held shares and voting rights in CureVac between appr. 43 – 46 % (prior year: 46 – 49 %) during that period. dievini is thus considered to be the de facto parent of the Group. Dietmar Hopp, Daniel Hopp and Oliver Hopp are the ultimate controlling persons (of the main shareholders) of dievini, and, therefore, control the voting and investment decisions of dievini.

2. Significant accounting policies, judgments, estimates, and assumptions

These consolidated financial statements are prepared on a historical cost basis under the going concern assumption. The significant accounting policies adopted in the preparation of these consolidated financial statements are described below. These accounting policies have been consistently applied to all years presented unless otherwise stated.

The preparation of financial statements requires the use of certain accounting estimates. It also requires management to exercise its judgment in applying the Group's accounting policies. The areas that require a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the financial statements, are disclosed below.

Basis of preparation

The consolidated financial statements of the Group have been prepared in accordance with International Financial Reporting Standards (IFRS) as as adopted by the European Union (EU-IFRSs) and part 9 of Book 2 of the DCC and were authorized by the Management Board for presentation to the Supervisory Board on April 21, 2023. The Group's consolidated financial statements are presented in Euros ("EUR"), which is also the parent company's functional currency. Unless otherwise stated, the numbers are rounded to thousands of Euros, except per share amounts. Liabilities for contract termination and onerous contracts are separately presented as 'Provisions' in the 2022 statement of financial position to make clear their provisional nature. The prior year contract termination provisions of EUR 81,587k and provisions for onerous contracts of EUR 40,555k have been reclassified from 'Other liabilities' to 'Provisions' to conform with the current year presentation.

Basis of consolidation

The consolidated financial statements include the Company's wholly-owned subsidiaries CureVac SE (prior years: CureVac AG, Tuebingen, Germany), CureVac Inc. (Boston, Massachusetts, USA), CureVac Manufacturing GmbH (prior years: CureVac Real Estate GmbH, Tuebingen, Germany), with CureVac Corporate Services GmbH (Tuebingen, Germany), CureVac RNA Printer GmbH (Tuebingen, Germany) and CureVac Swiss AG (Basel, Switzerland) being incorporated in 2021and CureVac Belgium SA being incorporated in 2022. Effective July 1, 2022, we acquired Frame Pharmaceuticals B.V., Amsterdam, Netherlands ('Frame Pharmaceuticals'), which was renamed to CureVac Netherlands B.V.; refer to Note 21 for additional information about this business combination.

Control is achieved when the Company is exposed, or has rights, to variable returns from its involvement with the investee and has the ability to affect those returns through its power over the investee.

All intra-group assets and liabilities, equity, income, expenses, and cash flows relating to transactions between members of the Group are eliminated upon consolidation.

The fiscal year of all Group entities corresponds to the calendar year ending December 31.

Summary of significant accounting policies

Business combinations and goodwill

Business combinations are accounted for using the acquisition method. The cost of an acquisition is measured as the aggregate of the consideration transferred, which is measured at acquisition date fair value acquisition-related costs are expensed as incurred and included in general and administrative expenses in the statement of operations.

The Group determines that it has acquired a business when the acquired set of activities and assets include an input and a substantive process that together significantly contribute to the ability to create outputs. The acquired process is considered substantive if it is critical to the ability to continue producing outputs, and the inputs acquired include an organized workforce with the necessary skills, knowledge, or experience to perform that process or it significantly contributes to the ability to continue producing outputs and is considered unique or scarce or cannot be replaced without significant cost, effort, or delay in the ability to continue producing outputs.

Any contingent consideration to be transferred by the acquirer is recognized at fair value at the acquisition date. Contingent consideration classified as equity is not remeasured and its subsequent settlement is accounted for within equity. Contingent consideration classified as an asset or liability that is a financial instrument and within the scope of IFRS 9 Financial Instruments, is measured at fair value with the changes in fair value recognized in the statement of operations in accordance with IFRS 9. Other contingent consideration that is not within the scope of IFRS 9 is measured at fair value at each reporting date with changes in fair value recognized in the statement of operations.

Goodwill is initially measured at cost (being the excess of the aggregate of the consideration transferred over the fair value of net identifiable assets acquired and liabilities assumed). If the fair value of the net assets acquired is in excess of the aggregate consideration transferred, the Group re-assesses whether it has correctly identified all of the assets acquired and all of the liabilities assumed and reviews the procedures used to measure the amounts to be recognized at the acquisition date. If the reassessment still results in an excess of the fair value of net assets acquired over the aggregate consideration transferred, then the gain is recognized in the statement of operations.

After initial recognition, goodwill is measured at cost less any accumulated impairment losses.

Current and non-current classification

The Group presents assets and liabilities in the statement of financial position based on current/non-current classification.

Current assets include assets that are sold, consumed, or realized as part of the normal operating cycle (the operating cycle is assumed to be 12 months), or cash and cash equivalent unless restricted from being exchanged or used to settle a liability for at least twelve months after the reporting period. All other assets are classified as non-current.

Current liabilities, such as trade payables, lease liabilities, or employee benefits with a term of up to 12 months, and payables for operating costs or social security charges, are part of the working capital used in the Group's normal operating cycle. Such operating items are classified as current liabilities even if they are due to be settled more than 12 months after the reporting period. All other liabilities are classified as non-current.

Foreign currency translation

For each entity, the Group determines the functional currency and items included in the financial statements of each entity are measured using that functional currency. Foreign currency transactions are initially translated at the spot rate applicable between the functional currency and the foreign currency on the date of the transaction. Monetary assets and liabilities in foreign currencies are translated to the functional currency using the prevailing rate at the reporting date. Foreign currency exchange differences are recorded in the statement of operations. Upon consolidation, the assets and liabilities of foreign operations are translated into Euro at the rate of exchange prevailing at the reporting date and their statements of operations are translated at the average exchange rate of the fiscal period. The exchange differences arising on translation for consolidation are recognized in other comprehensive income (loss).

Revenue recognition

Revenue from the sale of products and services is recognized when the Group transfers control to the customer. Control generally transfers when the customer gains the ability to direct the use of and obtain substantially all of the remaining benefits from the good or service. If the contract contains more than one performance obligation, the consideration which the Group expects to receive is allocated to each of the performance obligations, using the relative stand-along selling price method. Revenue is recognized at the amount of consideration that the Group is expected to receive in exchange for these goods or services. The Group has concluded that it acts as a principal in sales transactions as it has control over the goods or services before transferring control to the customer.

The Group primarily generates revenue from its licensing and development agreements with its customers, which include collaboration partners for the development of mRNA medicines against a variety of targets in diseases and conditions. These arrangements contain multiple contractual promises, including (i) licenses, or options to obtain licenses, to the Group's mRNA technology, (ii) delivery of products, and (iii) research and development services. Such arrangements provide for various types of payments to the Group, including upfront fees, funding of research and development services, payment for delivered products, development, regulatory and commercial milestone payments, license fees, and royalties on product sales, all of which may be satisfied at different points in time. Outlicensing agreements may be entered into with or without any further significant contractual obligations.

Goods or services promised in collaborative arrangements are accounted for as separate performance obligations if such promises are distinct (i.e., if the customer can benefit from the good or service on its own or together with other resources readily available to it and if the promise is separately identifiable from other promises in the contract).

In determining whether contractual promises are separately identifiable, the Group considers whether:

It provides a significant service of integrating the goods or services with other goods or services that represent the combined output or outputs for which the other party has contracted.

One or more of the goods or services significantly modifies or customizes one or more of the other goods or services promised in the agreement.

The goods or services the Group promised to transfer or to provide are highly interdependent or highly interrelated.

Based on these criteria, management evaluates whether the intellectual property (IP) licenses granted, and to which further research and development activities may apply under the terms of a collaboration agreement, are distinct from the unperformed obligations to the collaboration partner, considering the relevant facts and circumstances of each arrangement. Factors considered in this determination include the nature of the IP license, the stage of development of the IP license granted, the research capabilities of the partner, and the availability of mRNA technology research expertise in the general marketplace.

When an IP license is not considered to be distinct from research services, the Group generally recognizes revenue, including any upfront payment, attributable to the license on a straight-line basis, which reflects the performance of services by the Group towards satisfaction of the obligation, over the contractual or estimated performance period, which is typically from the effective date of the

related collaboration agreement through the estimated date of market entry of a product developed under the agreement. The determination of the estimated date of market entry requires a significant amount of judgment given the uncertainty inherent in developing innovative pharmaceutical products and is based upon development plans with the customer, which are subject to change, clinical trials, and approval of regulatory authorities. Changes in the estimated date of market entry could have a material impact on the amount and timing of revenue the Group records in future periods.

When an IP license is considered to be distinct, the Group determines whether it provides the customer with either (1) a right to access the IP throughout the license period (for which revenue is recognized over the license period) or (2) a right to use the IP as it exists at the point in time that the license is granted (for which revenue is recognized at a point in time where the customer can first use and benefit from the license).

If the transaction price in an agreement includes a variable amount, the Group estimates the amount of consideration to which the Group will be entitled in exchange for transferring the goods to the customer. At contract inception, the variable consideration is estimated based on the most likely amount of consideration expected from the transaction and constrained until it is highly probable that a significant revenue reversal in the amount of cumulative revenue recognized will not occur when the associated uncertainty with respect to the variable consideration is subsequently resolved. The estimated deferred contract liability is updated at each reporting date to reflect the current facts and circumstances.

Collaboration agreements may also provide a customer with the option to acquire additional goods or services. The accounting treatment for such options depends on the nature of these options. Options are considered to be substantive if, at the inception of an agreement, the Group is at risk as to whether the customer will choose to exercise the options to secure additional licenses. Factors that are considered in evaluating whether options are substantive include the overall objective of the arrangement, the benefit the customer might obtain from the agreement without exercising the options, the cost to exercise the options relative to the total upfront consideration, and the additional financial commitments or economic penalties imposed on the customer as a result of exercising the options.

Product sales related to collaboration agreements include RNA products and are recognized over time as goods are produced because such goods have no alternative use and the Group has an enforceable right to payment. Otherwise, revenue for product sales is recognized at a point in time. In 2022, 2021, and 2020, no revenue from product sales was recognized on a point-in-time basis. Revenue from certain research and development services, delivered as a distinct performance obligation under the collaboration agreements, are recognized over time as the services provided have no alternative use and the Group has an enforceable right to payment.

A receivable is recognized when the consideration is unconditional and only the passage of time is required before payment is due. The transaction price is quoted in the relevant contractually agreed pricing in force at the date of the customer placing the respective order for such goods or services. Amounts received prior to satisfying the above revenue recognition criteria are recorded as contract liability in the statements of financial position.

The Group may present the following contract balances:

- Contract assets — Represents the Group’s right to consideration in exchange for goods or services that the Group has transferred to the customer when that right is conditioned on something other than the passage of time

- Trade receivables — Represents the Group’s right to an amount of consideration that is unconditional (i.e., only the passage of time is required before payment of the consideration is due)

- Contract liabilities — Represents the Group’s obligations to transfer goods or services to a customer for which the Group has received consideration (or consideration is due) from the customer

The Group recognizes revenue from contracts with customers relating to its core business. All other operating proceeds are presented as other operating income in the statements of operations.

Grants from government agencies and similar bodies

The Group receives grants from government agencies and similar bodies for the active participation in specific research and development projects. Each grant agreement is assessed to determine whether there are elements of the supply of products that are

recognized separately from the grant. For the supply of products, the standalone selling price is determined by reference to observed prices with other customers. The grants are recognized when there is reasonable assurance that the grant will be received and all grant conditions will be met. If grant funds are received prior to qualifying expenses being incurred or assets purchased, they are recorded as a liability in other liabilities. If the funds reimburse expenses, the liability is amortized into other operating income on a systematic basis over the period in which the corresponding expenses are incurred. If the funds reimburse purchased assets, the liability is reduced with a corresponding amount deducted from the asset's carrying amount upon recording of the qualified asset. According to the terms of the grants, grantors generally have the right to audit qualifying expenses submitted by the Group.

Financial instruments

A financial instrument is any contract that gives rise to a financial asset of one entity and a financial liability or equity instrument of another entity.

i) Financial assets

Initial recognition and measurement

Financial assets are initially measured at fair value. After the initial measurement, the financial assets are subsequently classified as either amortized cost, fair value through other comprehensive income, or fair value through profit or loss.

The classification of financial assets at initial recognition depends on the financial asset's contractual cash flow characteristics and the Group's business model for managing them. The Group initially measures a financial asset at its fair value plus, in the case of a financial asset not at fair value through profit or loss, transaction costs. Trade receivables that do not contain a significant financing component are measured at the transaction price determined under IFRS 15.

For a financial asset to be classified and measured at amortized cost or fair value through other comprehensive income, it needs to give rise to cash flows that are "solely payments of principal and interest (SPPI)" on the principal amount outstanding. This assessment is referred to as the SPPI test and is performed at an instrument level.

Subsequent measurement

For purposes of subsequent measurement, financial assets are classified into four categories:

- financial assets at amortized cost (debt instruments);
- financial assets at fair value through other comprehensive income with recycling of cumulative gains and losses (debt instruments);
- financial assets designated at fair value through other comprehensive income with no recycling of cumulative gains and losses upon derecognition (equity instruments); or
- financial assets at fair value through profit or loss.

In fiscal 2020, 2021, and 2022, the Group only had the following financial assets to be measured at amortized cost:

- Cash and cash equivalents
- Other financial assets
- Trade receivables and contract assets

Financial assets at amortized cost are subsequently measured using the effective interest (EIR) method and are subject to impairment. Gains and losses are recognized in the statement of operations when the asset is derecognized, modified, or impaired.

Derecognition

A financial asset (or, where applicable, a part of a financial asset or part of a group of similar financial assets) is primarily derecognized when the Group no longer has the contractual rights to the asset or the right to receive cash flows from the asset have expired.

Impairment of financial assets

An allowance for expected credit losses (ECLs) is recognized for all debt instruments not held at fair value through profit or loss. ECLs are based on the difference between the contractual cash flows due in accordance with the contract and all of the cash flows that the Group expects to receive, discounted at an approximation of the original effective interest rate. The expected cash flows will include cash flows from the sale of collateral held or other credit enhancements that are integral to the contractual terms.

For credit exposures for which there has not been a significant increase in credit risk since initial recognition, ECLs are provided for credit losses that result from default events that are possible within the next 12- months (a 12- month ECL). For those credit exposures for which there has been a significant increase in credit risk since initial recognition, a loss allowance is required for credit losses expected over the remaining life of the exposure, irrespective of the timing of the default (a lifetime ECL).

For cash and cash equivalents, trade receivables, and contract assets, the Group applies a simplified approach in calculating ECLs. Therefore, the Group does not track changes in credit risk but instead recognizes a loss allowance based on lifetime ECLs at each reporting date.

The Group considers a financial asset in default when contractual payments are 180 days past due. However, in certain cases, the Group may also consider a financial asset to be in default when internal or external information indicates that the Group is unlikely to receive the outstanding contractual amounts in full before taking into account any credit enhancements held by the Group. A financial asset is written off when there is no reasonable expectation of recovering the contractual cash flows.

ii) Financial liabilities

Initial recognition and measurement

Financial liabilities are classified, at initial recognition, as financial liabilities at fair value through profit or loss, loans and borrowings or as payables.

All financial liabilities are recognized initially at fair value and, in the case of loans and borrowings and payables, net of directly attributable transaction costs.

The Group’s financial liabilities include lease liabilities, trade payables, the EIB-loan, which was repaid in 2021 (see note 13), and the convertible loans (see note 13), which were repaid immediately before the IPO in fiscal 2020.

Subsequent measurement

After initial recognition, interest-bearing loans and borrowings, trade payables, and other financial liabilities are subsequently measured at amortized cost using the EIR method. Gains and losses are recognized in the statement of operations when the liabilities are derecognized as well as through the EIR amortization process.

Amortized cost is calculated by taking into account any discount or premium on acquisition and fees or costs that are an integral part of the EIR. The EIR amortization is included as finance costs in the statement of operations.

This category generally applies to interest-bearing loans and borrowings, including convertible loans.

Derecognition

A financial liability is derecognized when the obligation under the liability is discharged or canceled or expires.

Accounting for EIB loan

In 2020, the Group received from the European Investment Bank, or EIB, a line of credit which was available in three tranches, each of which can be drawn separately.

The Group accounted for the first tranche of EUR 25 million drawn in 2020 as a financial liability at amortized cost, using the effective interest method based on expected cashflows including any amount of variable remuneration. In doing so, the Group assessed what is the most probable scenario for the exercise of its rights as the borrower. In addition, the Group determined an effective interest rate that is consistent with the accounting for other financing arrangements. In December 2021, the loan was terminated early and as of December 31, 2021, the EIB loan was fully repaid. For further information on the EIB loan, see Note 13.

Accounting for convertible loans

IFRS requires that a convertible loan be bifurcated into a debt component and a conversion right if the latter is an equity instrument.

The Group assessed that the conversion right of the convertible loan is not an equity instrument, but a liability with an insignificant value.

The debt component of the convertible loan was measured using the market interest rate obtainable on similar debt instruments. The debt component was measured as a liability at amortized cost until it is converted into equity or becomes due for repayment. The carrying amount of the debt component was based on an expected repayment in 2021, which was the earliest possible date at which repayment could be required by the lender unless specified events occurred.

The component of the loan proceeds allocated to equity represents the residual value between the consideration received for each single tranche and the fair value of the corresponding financial liabilities at initial recognition.

For further information on the convertible loan, see Note 13.

Acquired intangible assets

Acquired intangible assets are initially measured at cost. The cost of intangible assets acquired in a business combination is the fair value at the date of acquisition. Following initial recognition, intangible assets are carried at cost less any accumulated amortization and any accumulated impairment losses.

The useful lives of intangible assets are assessed to be either finite or indefinite. Intangible assets with finite useful lives are amortized over their useful life, generally using the straight-line method. The amortization period and the amortization method for an intangible asset with a finite useful life are reviewed at least annually at each fiscal year-end. Changes in the expected useful life or the expected pattern of consumption of future economic benefits are accounted for prospectively. Amortization of an intangible asset is reported in the consolidated statement of operations in accordance with the function of the intangible asset.

Gains or losses arising from the derecognition of an intangible asset are measured as the difference between the net disposal proceeds and the carrying amount of the asset and are recognized in the consolidated statement of operations in the period in which the asset is derecognized.

Acquired intangible assets are mainly comprised of software and licenses. Regarding the acquired intangible assets (i.e., technology and goodwill) in the business combination with Frame Pharmaceuticals, refer to Note 21.

The Group has entered into non-exclusive license agreements for patent rights and/or know-how with reputable universities, cancer research institutes, and other research partners. The cost of these licenses includes fixed as well as contingent consideration mainly linked to specified events in the collaborations for which the licenses are used. The licenses are measured initially at cost which comprises the fixed purchase price components. The Group records a liability for contingent consideration and capitalizes such amounts as part of the cost of the acquired intangible asset when the future event, upon which the contingent consideration depends, occurs or a present obligation exists.

The estimated useful lives for each intangible asset class are as follows:

Software	3 to 5 years
Licenses	8 to 20 years
Frame Technology	8 years

With the exception of goodwill, the Group does not have any intangible assets with indefinite useful lives.

Research and development costs

Research costs are expensed as incurred. Development expenditures on an individual project are recognized as an intangible asset when the Group can demonstrate:

- The technical feasibility of completing the intangible asset so that the asset will be available for use or sale
- Its intention to complete and its ability and intention to use or sell the asset
- How the asset will generate future economic benefits
- The availability of resources to complete the asset
- The ability to measure reliably the expenditure during development

Since our own development projects are mostly subject to regulatory approval and other uncertainties, the conditions for the capitalization of expenditures incurred prior to approval are generally not met.

Property, plant and equipment

Property, plant and equipment are stated at cost less accumulated depreciation and accumulated impairments. These costs also comprise the costs for replacement parts, which are recognized at the time they are incurred, providing they meet the recognition criteria. All other repair and maintenance costs are expensed as incurred. Depreciation is recognized on a straight-line basis over the estimated useful lives as follows:

Leasehold improvements	1 to 10 years
Technical equipment and machines:	3 to 14 years
Other equipment, furniture and fixtures:	3 to 14 years

Property, plant and equipment are derecognized upon disposal or when no further economic benefits are expected from their continued use or sale. The gain or loss on derecognition is determined as the difference between the net disposal proceeds and the carrying amount and recognized in profit or loss in the period in which the item is derecognized.

The residual values of the assets, useful lives, and depreciation methods are reviewed at the end of each year and any changes are accounted for prospectively.

The estimated useful lives and depreciation methods remained unchanged from 2020 through 2022. The residual values of the assets are generally considered to be zero.

Impairment of non-financial non-current assets

At each reporting date, the Group assesses whether there is an indication that a non-financial asset may be impaired. If there is any indication of impairment or if an annual impairment test is required, the Group estimates the recoverable amount of the asset. The recoverable amount of an asset is the higher of the asset's or CGU´s fair value less costs of disposal and its value-in-use. It is determined for an individual asset unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets, in which case it is determined at the level of the cash-generating unit (CGU). If the carrying amount of an asset or CGU exceeds its recoverable amount, the asset is impaired and written down to its recoverable amount. In assessing value in

use, the estimated future cash flows are discounted to their present value using a pre -tax discount rate that reflects current market assessments of the time value of money and the risks specific to the asset. In determining fair value less costs of disposal, recent market transactions are taken into account. If no such transactions can be identified, an appropriate valuation model is used. These calculations are corroborated by valuation multiples, quoted share prices for publicly traded companies or other available fair value indicators.

As the Group operates as one cash-generating unit, for the purpose of impairment testing in 2022, goodwill was allocated at Group level.

Impairment losses of continuing operations are recognized in the statement of operations in expense categories consistent with the function of the impaired asset.

For assets excluding goodwill, an assessment is made at each reporting date to determine whether there is an indication that previously recognized impairment losses no longer exist or have decreased. If such indication exists, the Group estimates the asset's or CGU's recoverable amount. When there has been a change in the estimates used to determine the asset's recoverable amount since the last impairment loss was recognized, any impairment loss previously recognized is reversed. The reversal may not exceed the carrying amount that would have been determined after amortization or depreciation had no impairment loss been recognized for the asset in prior periods. The amount of the reversal is recognized in the statement of operations for the period.

There were no impairments or reversals of impairments in 2020. However, in fiscal year 2021, impairments of EUR 22,810k were recognized. These pertained largely to machinery and technical equipment recorded as assets under construction and resulted from the partial impairment of production lines which were obsolete due to the withdrawal of the EMA regulatory approval application for CVnCoV, see Note 4.1.

Beginning in year 2022, goodwill is tested for impairment annually as at December 31 and when circumstances indicate that the carrying value may be impaired.

For 2022, impairment was evaluated for goodwill by assessing the recoverable amount on Group level. When the recoverable amount is less than its carrying amount, an impairment loss is recognized. Impairment losses relating to goodwill cannot be reversed in future periods.

There was no impairment of goodwill in 2022. However, there were impairments of technical equipment amounting to EUR 5,884k; refer to Note 4.1 for additional information.

Further disclosures relating to impairment of non-financial assets are also provided in the following notes:

- Disclosures for significant assumptions
- Goodwill and other intangible assets
- Property, plant and equipment
- Right-of-Use Assets

Non-current other assets — costs to obtain a contract

Amortization of assets recognized from the costs to obtain a contract with a customer within the scope of IFRS 15 is recognized on a straight-line basis over their associated estimated useful lives.

Assets held for sale

The Group classifies non-current assets as held for sale if their carrying amount will be recovered principally through a sale transaction rather than through continiuing use. Non-current assets classified as held for sale are measured at the lower of their carrying amount and fair value less costs to sell. Costs to sell are the incremental costs directly attributable to the disposal of an asset, excluding finance costs and income tax expenses. The criteria for held for sale classification is regarded as met only when the sale is highly probable, and the asset is available for immediate sale in its present condition. Actions required to complete the sale indicate

that it is unlikely that significant changes to the sale will be made or that the decision to sell will be withdrawn. Management is committed to the plan to sell the asset and the sale is expected to be completed within one year from the date of classification. Property, plant and equipment are not depreciated or amortized once classified as held for sale.

Borrowing costs

Borrowing costs directly attributable to the acquisition, construction, or production of an asset that necessarily takes a substantial period of time to get ready for its intended use or sale are capitalized as part of the cost of the asset. All other borrowing costs are expensed in the period in which they occur. Borrowing costs consist of interest and other costs that an entity incurs in connection with the borrowing of funds.

The Group capitalizes borrowing costs when it meets all the following conditions: (a) it incurs expenditures for the asset; (b) it incurs borrowing costs, and (c) it undertakes activities that are necessary to prepare the asset for its intended use or sale.

The Group capitalized EUR 2,291k borrowing costs during fiscal 2022 (2021: 2,932k, 2020: 1,989k). The capitalization rate used to determine the amount of the borrowing costs eligible for capitalization during fiscal 2022 was a weighted average of 5,78% (2021: 7.17%, 2020: 8.90%).

Right-of-use assets

The Group recognizes right-of-use assets at the commencement date of the lease (i.e., the date the underlying asset is available for use). Right-of-use assets are measured at cost, less any accumulated depreciation and impairment losses, and adjusted for any remeasurement of lease liabilities. The cost of right-of-use assets includes the amount of lease liabilities recognized, initial direct costs incurred, and lease payments made at or before the commencement date less any lease incentives received as well as any estimated costs to be incurred by the lessee for dismantling and removing the underlying asset. Unless the Group is reasonably certain to obtain ownership of the leased asset at the end of the lease term, the recognized right-of-use assets are depreciated on a straight-line basis over the shorter of its estimated useful life, indicated below, and the lease term. Right-of-use assets are subject to impairment. Refer to the section above “Impairment of non-financial assets”.

Land and Buildings	1 to 15 years
Vehicles	3 to 4 years
Other equipment	2 to 5 years

Lease liabilities

At the commencement date of the lease, the Group recognizes lease liabilities measured at the present value of lease payments to be made over the lease term. The lease payments include fixed payments (including in- substance fixed payments) less any lease incentives receivable, variable lease payments that depend on an index or a rate, and amounts expected to be paid under residual value guarantees. The lease payments also include the exercise price of a purchase option reasonably certain to be exercised by the Group and payments of penalties for terminating a lease, if the lease term reflects the Group exercising the option to terminate.

Variable lease payments that do not depend on an index or a rate are recognized as expenses in the period in which the event or condition that triggers the payment occurs. In calculating the present value of lease payments, the Group uses the incremental borrowing rate at the lease commencement date if the interest rate implicit in the lease is not readily determinable. After the commencement date, the amount of lease liabilities is increased to reflect the accretion of interest and reduced for the lease payments made. In addition, the carrying amount of lease liabilities is remeasured if there is a modification, a change in the lease term, a change in the in-substance fixed lease payments, or a change in the assessment to purchase the underlying asset. When the lease liability is remeasured, a corresponding adjustment is made to the carrying amount for the right-of-use asset or is recorded in profit or loss if the carrying amount of the right-of-use asset has been reduced to zero.

Short-term leases and leases of low-value assets

The Group applies the short-term lease recognition exemption to its short-term leases of machinery and equipment (i.e., leases that have a lease term of 12 months or less from the commencement date and do not contain a purchase option). It also applies the lease of low-value assets recognition exemption to leases of office equipment that are considered of low value. Lease payments on short-term leases and leases of low-value assets are recognized as expenses on a straight-line basis over the lease term.

Separation of lease and non-lease components

As a practical expedient, the Group elected not to separate the fixed (but not variable) portion of non-lease components in respect of leases of building and instead accounts for them as a single lease component.

Inventories

Inventories are valued at the lower of cost and net realizable value. Net realizable value is the estimated selling price in the ordinary course of business, less estimated costs of completion and the estimated costs necessary to make the sale. Inventories are comprised of raw materials, work in progress, and finished goods.

Costs incurred in bringing each product to its present location and condition are accounted for, as follows:

- Raw materials: purchase cost on a first-in/first-out basis
- Finished goods and work in progress: cost of direct materials and labor and a proportion of manufacturing overhead based on normal operating capacity, but excluding borrowing costs

The costs of inventories may not be recoverable if those inventories are damaged, if they become wholly or partially obsolete, or if the selling prices have declined. The practice of writing inventories down below cost to net realizable value is consistent with the view that assets should not be carried in excess of amounts expected to be realized from the sale or use.

Pre-launch products

Prior to initial regulatory approval, costs relating to the production of products are expensed as research and development expenses in the period incurred unless recoverable through means other than sale. If pre-launch products are sold, the respective product gross margin may be higher compared to the expected recurring margin as the underlying costs will not be included in cost of sales. For the year ended December 31, 2022, 2021, and, 2020, no revenues have been recorded related to pre-launch products. However, the Company recognizes in cost of sales costs from set-up and quality assurance activities for the Company's production processes, including those relating to pharmaceutical products which are under development in the Company's collaboration agreements and for which revenues have not yet been generated.

Cash and cash equivalents

Cash and cash equivalents include cash on hand, bank balances on-demand, and short-term deposits with an original maturity of three months or less.

Onerous contracts

An onerous contract is a contract under which the unavoidable costs (i.e., the costs that the Group cannot avoid because it has the contract) of meeting the obligations under the contract exceed the economic benefits expected to be received under it. The unavoidable costs under a contract reflect the least net cost of exiting from the contract, which is the lower of the cost of fulfilling it and any compensation or penalties arising from failure to fulfil it. The cost of fulfilling a contract comprises the costs that relate directly to the contract (i.e., both incremental costs and an allocation of costs directly related to contract activities).

If the Group has a contract that is onerous, the present obligation under the contract is recognized and measured as a provision. However, before a separate provision for an onerous contract is established, the Group recognizes any impairment loss that has occurred on assets dedicated to that contract.

Share-based payment awards

The Group operates several share-based payment programs.

An equity-settled share-based payment award is accounted for by recognizing the related expense over the vesting period of the award, with a corresponding increase recorded in equity. The expense is based on the fair value determined at the grant date of the

award and the number of awards expected to vest. The fair value remains unchanged after grant date. Once the award has vested, there is no reversal of expense related to the award.

When a share-based payment award provides for different ways of settlement (i.e. cash versus shares) depending on the occurrence of contingent events, the award is accounted for based on the manner of settlement that is most probable. A change in the expected manner of settlement is accounted for as a modification.

Expenses for employer taxes arising upon the exercise of equity-settled share-based payments are recognized in profit or loss.

The related share-based payment expense is recorded in the functional cost category to which the award recipient's costs are classified.

Taxes

Current income tax

Current income tax assets and liabilities are measured at the amount expected to be recovered from or paid to the taxation authorities based on the tax rates and tax laws that are enacted or substantively enacted at the end of the reporting period in the countries where the Group operates and generates taxable income.

Current income tax relating to items recognized directly in equity is recognized in equity and not in the statement of operations. Management periodically evaluates positions taken in the tax returns with respect to situations in which applicable tax regulations are subject to interpretation and establishes provisions where appropriate.

Deferred tax

Deferred tax is recognized using the liability method on all temporary differences as of the end of the reporting period between the carrying amounts of assets and liabilities and their tax bases.

Deferred tax liabilities are recognized for all taxable temporary differences, except:

- When the deferred tax liability arises from the initial recognition of goodwill or an asset or liability in a transaction that is not a business combination and, at the time of the transaction, affects neither the accounting profit nor taxable profit or loss.

- In respect of taxable temporary differences associated with investments in subsidiaries when the timing of the reversal of the temporary differences can be controlled and it is probable that the temporary differences will not reverse in the foreseeable future.

Deferred tax assets are recognized for deductible temporary differences, the carry forward of unused tax credits and any unused tax losses, and to the extent that it is probable that future taxable income will allow the deferred tax asset to be realized.

The carrying amount of deferred tax assets is reviewed at each reporting date and reduced to the extent that it is no longer probable that sufficient taxable profit will be available to allow all or part of the deferred tax asset to be utilized. Unrecognized deferred tax assets are re-assessed at each reporting date and are recognized to the extent that it has become probable that future taxable profits will allow the deferred tax asset to be recovered.

Deferred tax assets and deferred tax liabilities are measured at the tax rates that are expected to apply in the year when the asset is realized or the liability is settled based on tax rates (and tax laws) that have been enacted or substantively enacted by the end of the reporting period.

If transactions and other events are recognized directly in equity, any related taxes on income are also recognized directly in equity.

Tax benefits acquired as part of a business combination, but not satisfying the criteria for separate recognition at that date, are recognized subsequently if new information about facts and circumstances change. The adjustment is either treated as a reduction in goodwill (as long as it does not exceed goodwill) if it was incurred during the measurement period or recognized in profit or loss.

Deferred tax assets and deferred tax liabilities are offset if there is a legally enforceable right to offset current tax assets and current tax liabilities and these relate to income taxes levied by the same tax jurisdiction.

Segments

An operating segment is defined as a component of an entity for which discrete financial information is available and whose operating results are regularly reviewed by our Management Board as the Chief Operating Decision Maker (CODM). The Group operates as a single segment dedicated to the discovery and development of biotechnological applications and the CODM makes decisions about allocating resources and assessing performance based on the Group as a whole. Accordingly, the Group has determined it operates in one operating and reportable segment.

Significant accounting judgments, estimates and assumptions

The preparation of financial statements in conformity with IFRS requires management to make judgments, estimates, and assumptions that affect the reported amounts in the financial statements. Management continually evaluates its judgments and estimates in relation to assets, liabilities, contingent liabilities, revenues, and expenses. Management bases its judgments and estimates on historical experience and other various factors, which it believes to be reasonable under the circumstances, the result of which forms the basis of the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions and conditions and may materially affect the financial results or the financial position reported in future periods.

Significant judgments

In the process of applying the accounting policies, management has made the following judgments, which have the most significant effect on the amounts recognized in the consolidated financial statements.

Accounting for share-based payments

The Group has multiple share-based payment programs. Significant judgments include the determination of the grant date fair value of the awards.

The awards granted in 2022 as well as in prior years are accounted for as equity-settled share-based payments and described under Note 10.

Revenue recognition and collaboration agreements

The Group applied the following judgments in determining the amount and timing of revenue from collaboration agreements:

- Identification and determination of the nature of performance obligations in collaboration and license agreements.

The Group generates revenues from collaboration and license agreements under which the Group grants licenses to use, research, develop, manufacture, and commercialize candidates and products. As these agreements comprise several promises, it must be assessed whether these promises are capable of being distinct within the context of the contract. If these promises are not distinct, they are combined until the bundle of promised goods and services is distinct. For some agreements, this results in the Group accounting for all goods and services promised in a collaboration and license agreement as a single performance obligation with a single measure of progress.

For these combined performance obligations, it must be assessed which of these promises is the predominant promise to determine the nature of the performance obligation. The Group determined that the grant of the license is the predominant promise within the (combined) performance obligation to grant a license to the customers. It was assessed that the Group grants its customers a right to access or a right to use the Group’s IP due to the collaboration and license agreements.

As a result, the promise to grant a license is accounted for as a performance obligation satisfied over time as the Group's customer simultaneously receives and consumes the benefits from the Group's performance.

- Estimation of variable consideration and assessment of the constraint when determining the amount of revenue of which to defer recognition

The Group's collaboration and license agreements comprise variable considerations which are contingent on the occurrence or non-occurrence of a future event (i.e., reaching a certain milestone). When determining the deferral of revenue in a collaboration and license agreement, the Group is required to estimate the amount of consideration to which it will be entitled in exchange for transferring the promised goods or services to the customer.

As there are usually only two possible outcomes (i.e., a milestone is reached or not), the Group has assessed that the method of the most likely amount is the best method to predict the amount of consideration to which the Group will be entitled.

The most likely amount of these milestone payments (i.e., the full milestone payment) is only included in the transaction price if the occurrence of reaching a future milestone is highly probable. The Group has assessed that the likelihood of achieving the respective milestone decreases depending on how far the expected date of achieving the milestone lies in the future.

The Group has concluded that future milestone payments are fully constrained at each of the fiscal years. Future milestone payments would become unconstrained at the satisfaction of the milestone event, specifically a development event, regulatory approval, or achievement of a sales milestone.

Clinical trial accruals and related research and development costs

The value of goods and services received from contract research organizations (CROs) and contract manufacturing organizations (CMOs) in the reporting period is estimated based on the level of services performed and progress made in the respective period, unless the respective arrangements require recognition of, and thus have been accounted for with, an onerous contract provision or contract termination provision. Amounts are recorded as accrued expenses in cases where the Company has not received an invoice from the service provider. Advance payments for goods or services that will be used or rendered for future research and development activities are recognized as (current) prepaid expenses and other assets or in (non-current) other assets if the benefit is expected to be received more than a year from the statement of financial position date. These amounts are recognized as an expense as the related goods are delivered or the services performed. Management's estimates are based on the best information available at the time. However, additional information may become available in the future and management may adjust the estimate in such future periods. In this event, the Company may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. The Company considers resulting increases or decreases in cost as changes in estimates and reflects such changes in research and development expenses in the period identified.

Accounting for assets held for sale

Non-current assets are classified as asset held for sale if their carrying amount will be recovered through a sale transaction rather than through continued use; the carrying value of such assets is measured at the lower of their previous carrying value and their fair value less costs to sell. In evaluating whether the criterion, for classification as assets held for sale, of a sale being highly probable, the Group considered that a plan to sell the assets was committed to and an active program to locate a buyer was initiated with an equipment reseller. The Group applied judgment in determining the assets' fair value less costs to sell and considered various indicative prices of expected auction proceeds quoted by the equipment reseller. Additionally, judgment was applied in determining whether the plan to sell the assets could be completed within one year from the date of classification and whether actions required to complete the plan indicate that it is unlikely that significant changes to the plan will be made or that the plan will be withdrawn.

Accounting for onerous contract provisions

The Group has entered into binding legal agreements for the supply of services by CROs to the Group for CVnCoV clinical trials. Such services are generally associated with the ongoing monitoring and care for enrolled participants in the clinical trials. Due to the discontinuation of the CVnCoV program, the remaining services, which the Group is obligated to procure, do not have a value for the Group anymore. Judgment is required in estimating the cost of the remaining services, particularly in estimating the number of participants completing the clinical trials, when measuring provisions for such contracts with clinical research organizations.

Accounting for contract termination provisions

Contract termination provisions are established under certain conditions in the case of legal risks. Settlement and legal proceedings often raise complex issues and are subject to many uncertainties and complexities including, but not limited to, the facts and circumstances of each particular case. The outcome of any current or future proceedings cannot normally be predicted. The Group considers the need for accounting measures in respect of pending or future settlements for terminated contracts on the basis of the information available to its legal department and in close consultation with legal counsel acting for the Group. Where it is more likely than not that such settlement will result in an outflow of resources that is already reasonably estimable, a provision for settling terminated contracts is recorded in the amount of the present value of the expected cash outflows.

Estimating the incremental borrowing rate

In most cases, the Group cannot readily determine the interest rate implicit in the lease. Therefore, it uses its incremental borrowing rate (IBR) to measure lease liabilities. The IBR is the rate of interest that the Group would have to pay to borrow over a similar term, and with a similar security, the funds necessary to obtain an asset of a similar value to the right-of-use asset in a similar economic environment. The IBR, therefore, reflects what the Group "would have to pay," which requires estimation when no observable rates are available (such as for subsidiaries that do not enter into financing transactions) or when they need to be adjusted to reflect the terms and conditions of the lease. The Group estimates the IBR using observable inputs (such as market interest rates, country risk premiums, and credit spreads) when available and is required to make certain entity-specific adjustments.

Changes in accounting policies and disclosures

Summary of significant accounting policies

This section describes significant accounting policies adopted in the preparation of these consolidated financial statements. These policies have been consistently applied to all the years presented unless otherwise stated.

The below-listed amendments and interpretations apply for the first time in 2022, but do not have any impact on the consolidated financial statements of the Group:

- Reference to the Conceptual Framework – Amendments to IFRS 3
- Property, Plant and Equipment: Proceeds before Intended Use – Amendments to IAS 16
- Onerous Contracts – Costs of Fulfilling a Contract – Amendments to IAS 37
- IFRS 9 Financial Instruments – Fees in the '10 per cent' test for derecognition of financial liabilities

The Group has not early adopted any standards, interpretations, or amendments that have been issued but are not yet effective.

Standards issued but not yet effective

The following amendments will be adopted effective January 1, 2023, or at a later effective date:

- IFRS 17 Insurance Contracts
- Amendments to IAS 1: Classification of Liabilities as Current or Non-current and Non-current Liabilities with Covenants

- Amendments to IAS 8: Definition of Accounting Estimates
- Amendments to IAS 1 and IFRS Practice Statement 2: Disclosure of material Accounting policies
- Amendments to IAS 12: Deferred Tax related to Assets and Liabilities arising from a Single Transaction

Impact of COVID-19 and the Russia-Ukraine Conflict

As the Group is currently devoting significant resources to the development of COVID vaccines, such development may impair the ability to timely progress other product candidates in clinical trials or into clinical trials from their current preclinical stage. In addition, enrollment in other programs have been delayed as a result of the COVID-19 pandemic and our focus on developing a COVID vaccine; however, thus far, this has had a minimal negative impact on our progress on and associated revenue recognition from our non-COVID-19 collaborations. The partial disruption, even if temporary, may, ultimately, negatively impact the Company's operations and overall business by delaying the progress of its clinical trials and preclinical studies. The Group's operations, including research and manufacturing, could also be disrupted due to the potential of the impact of staff absences as a result of self-isolation procedures or extended illness. However, the Group has taken a series of actions aimed at safeguarding its employees and business associates, including implementing a work-from-home policy for employees except for those related to its laboratory and production operations. The Group was running COVID antigen tests on a weekly basis for employees on the premises.

The ongoing military conflict between Russia and Ukraine has not and is not expected to have a material direct or indirect effect on the Group's operations or financial condition; however, the Group is currently operating in a period of economic uncertainty and capital markets disruption, which has been significantly impacted by geopolitical instability due to the ongoing military conflict between Russia and Ukraine. As a result of this instability and responding actions taken by the United States, Russia, EU, and other foreign governments, this may limit or prevent filing, prosecuting, and maintaining of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications in Russia, resulting in partial or complete loss of patent rights in Russia. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit, without consent or compensation, inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in countries that Russia has deemed unfriendly. Consequently, we would not be able to prevent third parties from using our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be materially adversely affected.

3. Notes to the consolidated financial statements

3.1 Revenue from contract with customers

The Group recognized the following revenues in 2020, 2021 and 2022:

	December 31		
	2020	2021	2022
	EUR k	EUR k	EUR k
Belgium			
GSK	8,809	74,298	62,263
Germany			
Boehringer Ingelheim	1,885	26,003	—
Netherlands			
Genmab	2,628	1,770	1,787
Switzerland			
CRISPR	695	919	3,370
United States			
Eli Lilly	34,854	—	—
Total	**48,871**	**102,990**	**67,420**

Of these revenues, all of which were recognized over time as part of collaboration agreements, in 2022, EUR 44,787k (2021: EUR 79,827k, 2020: EUR 46,597k) related to delivery of research and development services combined with an IP license (recognized from the upfront payments as further illustrated in the table below), EUR 3,062k (2020: EUR 457k, 2019: EUR 556k) related to delivery of products and EUR 19,571k (2021: EUR 22,706k, 2019: EUR 1,718k) were recognized from those research and development services considered distinct within the agreements.

GlaxoSmithKline

In July 2020, the Group entered a collaboration with GlaxoSmithKline (GSK) for the research, development, manufacture and commercialization of mRNA-based vaccines and monoclonal antibodies targeting infectious disease pathogens. In addition to an equity investment of EUR 150,000k as part of the 2020 Private Investment, GSK made a non-refundable upfront cash payment of EUR 120,000k which was deferred upon receipt and recognized as a contract liability. Additionally, the Group is eligible to receive a one-time reimbursable payment of EUR 30,000k for manufacturing capacity reservation, upon certification of CureVac's commercial scale manufacturing facility currently under construction in Germany as well as to receive development and regulatory milestone payments of up to EUR 320,000k, commercial milestone payments of up to EUR 380,000k and tiered royalties on product sales. GSK will fund R&D activities incurred by CureVac related to the development projects covered by the collaboration. CureVac will be responsible for the preclinical- and clinical-development through the Phase 1 trials of these projects, after which GSK will be responsible for further development and commercialization. CureVac will be responsible for the manufacturing of the product candidates, including for commercialization, and will retain commercialization rights for selected countries for all product candidates. Revenue is being recognized in accordance with the Company's accounting policy for collaboration arrangements with the exception that the upfront payment, attributable to the IP license, is being recognized straight-line from the effective date of the collaboration agreement through the estimated completion date of Phase 1 clinical trials, at which time GSK will be responsible for further development and commercialization. In the year ended December 31, 2022, EUR 41,379k (2021: EUR 47,148k) in revenue was recognized under the collaboration agreement with GSK, entered into in July 2020, for the research, development, manufacturing and commercialization of mRNA-based vaccines and monoclonal antibodies targeting infectious disease pathogens.

Additionally, in April 2021, the Group entered into a new collaboration agreement with GSK, which we refer to as the GSK COVID Agreement, pursuant to which we are collaborating with GSK to research, develop and manufacture next-generation mRNA vaccines targeting the original SARS-CoV-2 strain as well as emerging variants, including multivalent and monovalent approaches ("GSK COVID Products"), such as the CureVac's second-generation COVID-19 vaccine candidate, CV2CoV. These vaccine candidates may either be used to protect unvaccinated individuals or to serve as boosters in the event that SARS-CoV-2 immunity gained from an initial vaccination reduces over time. The GSK COVID Agreement was amended and restated in September 2021. Pursuant to the amendment in September 2021, CureVac and GSK are required to complete certain development activities with respect to the GSK COVID Products set forth in updated development plans. CureVac and GSK agree to decide whether the GSK COVID Products required for clinical studies will be manufactured by CureVac, GSK or jointly.

Under the GSK COVID Agreement, GSK has paid CureVac an upfront payment of EUR 75,000k in 2021. Under the terms of the 2020 GSK Agreement, CureVac granted GSK a worldwide exclusive, sublicensable (subject to certain conditions) license under certain of our intellectual property relating to vaccines and antibodies encoded by our proprietary mRNA targeting certain selected pathogens, or GSK Program Products, and a non-exclusive license under certain LNP technology to develop, manufacture and commercialize a certain number of such GSK Program Products for use in connection with the infectious diseases targeted under the 2020 GSK Agreement. CureVac also granted GSK an exclusive option, after a certain date, to obtain exclusive licenses to develop, manufacture and commercialize CVnCoV and boosters for such vaccine. CureVac and GSK agreed to equally share all development costs for GSK COVID Products, subject to certain exceptions. CureVac and GSK will share all net profits generated from sales of GSK COVID Products, other than certain products defined in the agreement as "Combination Products", under profit sharing arrangements that in certain cases vary depending upon the GSK COVID Product in question, the time of sale, the number of doses sold and the party to whom the sale is made. CureVac is eligible to receive tiered royalty payments ranging from a low-teen percentage to a mid-teens percentage on net sales of Combination Products, subject to certain customary reductions. Under the GSK COVID Agreement, CureVac has the right to commercialize GSK COVID Products in Austria, Germany and Switzerland and if CureVac exercises such right, CureVac's sales of GSK COVID Products, other than Combination Products will be subject to the profit share and CureVac will be required to pay GSK a high-teen percentage royalty on net sales of all Combination Products in such countries. In the year ended December 31, 2022, EUR 20,884k (2021: EUR 27,150k) in revenue was recognized under the GSK COVID Agreement.

Boehringer Ingelheim

In August 2014, the Group entered into an Exclusive Collaboration and License Agreement, which it refers to as the Boehringer Agreement, with Boehringer Ingelheim, whereby it granted Boehringer Ingelheim exclusive global rights for development and commercialization of its investigational therapeutic mRNA vaccine BI 1361849 (formerly CV9202) formulated with a legacy protamine technology. The Group received, in 2014, an upfront payment of EUR 30,000K, as well as, an option fee payment of EUR 5,000K and in 2018 an additional EUR 7,000K in development milestone payments, all of which are non-refundable and non-creditable in the event of expiry or termination of the agreement. In June 2021, Boehringer Ingelheim provided notice of its intention to terminate the Boehringer Agreement, with such termination to become effective on November 17, 2021. Upon termination of the Boehringer Agreement, the rights and licenses granted by the Group to Boehringer Ingelheim reverted back to the Group, provided that Boehringer Ingelheim has the right to sell off existing inventory of BI 1361849 for a certain period. In addition, Boehringer Ingelheim assigned to us all regulatory approvals or applications and grant us a non-exclusive, cost-free, perpetual and worldwide license to intellectual property held by Boehringer Ingelheim that has been used in the development, manufacture or commercialization of BI 1361849 or any other product developed under the Boehringer Agreement. As a result of the termination in 2021, the remaining contract liability, related to the upfront payment, EUR 14,003k was recognized over a shorter period through the termination date. In addition, the option fee payment of EUR 5,000k and the additional EUR 7,000k development milestone were recognized in 2021. Therefore, for the year ended December 31, 2022, no revenue was recognized related to this agreement (2021: EUR 26,003k, 2020: 1,885k).

CRISPR Therapeutics Development and License Agreement

In November 2017, we entered into a Development and License Agreement with CRISPR Therapeutics, which, as amended by an amendment entered into in June 2020, we refer to as the CRISPR Therapeutics Agreement, pursuant to which we will develop novel Cas9 mRNA constructs for use in gene editing therapeutics. CRISPR Therapeutics has paid us an upfront one-time technology access fee of USD 3 million, which is being recognized through the date of market entry of a product developed under the agreement. In the year ended December 31, 2022, EUR 3,370k (2021: EUR 919k, 2020: EUR 695k) in revenue was recognized under this agreement.

Genmab Collaboration and License Agreement

In December 2019, the Group entered into a Collaboration and License Agreement with Genmab, which we refer to as the Genmab Agreement, to research and develop up to four potential differentiated mRNA-based antibody products, to be selected by Genmab, based on the combination of our proprietary RNAntibody technology with Genmab's proprietary antibody technology for the treatment of human diseases. In partial consideration for entering into the Genmab Agreement, in 2019 Genmab made a USD 20 million equity investment and paid us an upfront fee of USD 10 million, which is being recognized through the date of market entry of a product developed under the agreement. In the year ended December 31, 2022, EUR 1,787k (2021: EUR 1,770k, 2020: 2,628k) in revenue was recognized under this agreement.

Eli Lilly

In June 2020, the Group and Eli Lilly terminated their collaboration and the following agreements: License and Collaboration Agreement dated November 29, 2017, Early Clinical Supply Agreement dated July 5, 2018 and related Quality Agreement dated June 29, 2018. As a result, on the termination date, EUR 33,100k in contract liabilities from an upfront payment was recognized as no further associated performance obligations remained.

The Group has received upfront payments which were initially deferred and are subsequently recognized as revenue as the Group renders services over the performance period or upon termination of the agreement, when no services are provided anymore. Below is a summary of such payments and the related revenues recognized:

Customer	Upfront payments	Upfront payments included in contract liabilities at		Revenue recognized from upfront payments		
		December 31, 2021	December 31, 2022	2020	2021	2022
	(in k)	EUR k	EUR k		EUR k	
GSK	EUR 195,000	135,494	102,804	7,778	51,728	42,690
Boehringer Ingelheim	EUR 30,000	—	—	1,867	14,003	—
Genmab	USD 10,000 (EUR 8,937) *	5,362	3,575	1,787	1,787	1,787
CRISPR	USD 3,000 (EUR 2,524)*	1,239	929	310	310	310
Eli Lilly	USD 50,000 (EUR 42,200)*	—	—	34,855	—	—
Total		**142,095**	**107,308**	**46,597**	**67,828**	**44,787**

*Translated at the currency exchange rate prevailing on the transaction date

Contract balances:

	December 31, 2021 EUR k	December 31, 2022 EUR k
Trade receivables	18,504	6,295
Contract assets	—	2,707
Contract liabilities	142,095	107,308

Contract liabilities include advances received from the Group's major license and collaboration agreements.

Contract liabilities allocated to the remaining performance obligations (unsatisfied or partially unsatisfied) as at year-end are as follows:

	Year ended December 31,	
	2021	2022
	EUR k	EUR k
Within one year	55,750	34,759
More than one year	86,345	72,549
Total	**142,095**	**107,308**

Trade receivables are non-interest bearing and are generally settled within 30 to 45 days.

As of December 31, 2022, the Group had two collaboration partners (2021: three) that owed 100% (2021: 100)% of all the receivables and contract assets outstanding. There was one collaboration partner (2021: one) with balances greater than 10% of the total amounts of receivable and contract assets.

The nature of expenses recognized in the functional categories of the statement of operations are as follows:

3.2 Cost of sales

The cost of sales consists of the following:

	2020	2021	2022
	EUR k	EUR k	EUR k
Personnel	(2,896)	(22,159)	(27,185)
Materials	(1,598)	(46,250)	(88,891)
Third-party services	(2,652)	(139,975)	(32,331)
Maintenance and lease	(1,016)	(2,874)	(2,425)
Amortization and depreciation	(5,913)	(3,992)	(6,295)
Impairment of equipment	—	(22,810)	(24,948)
Other	(98)	(135)	(1,918)
Total	**(14,173)**	**(238,195)**	**(183,993)**

During the year ended December 31, 2022, cost of sales mainly decreased compared to the same period of 2021 due to Third-Party Services having been higher last year for set-up activities for the CVnCoV production process. This decrease was partially offset by increased write-offs and scrap of raw materials amounting to EUR 80,021k in 2022, which were procured for manufacturing of products to sell to GSK that are no longer expected to be sold to them or were determined to be excess materials on hand. Additionally, the Company recognized an impairment of assets held for sale amounting to EUR 19,064k in 2022 (refer to Note 5 for further information).

3.3 Selling and distribution expenses

Selling and distribution expenses consist of the following:

	2020	2021	2022
	EUR k	EUR k	EUR k
Personnel	(631)	(1,369)	(2,029)
Maintenance and lease	(1)	(1)	(35)
Amortization and depreciation	(98)	(86)	(336)
Other	(3)	(287)	(417)
Total	**(733)**	**(1,743)**	**(2,817)**

Personnel expenses mainly include salary and salary-related expenses of EUR 1,791k (2021: EUR 1,076k, 2020: EUR 370k) and expenses from share-based payments of EUR 238k (2021: EUR 293k, 2020: 261k). Refer to Note 10 for further information.

3.4 Research and development (R&D) expenses

R&D expenses consist of the following:

	2020	2021	2022
	EUR k	EUR k	EUR k
Materials	(29,834)	(232,292)	(32,982)
Personnel	(21,313)	(33,733)	(33,944)
Amortization and depreciation	(2,578)	(4,259)	(8,650)
Patents and fees to register a legal right	(3,073)	(3,199)	(3,813)
Third-party services	(55,571)	(539,786)	20,499
Maintenance and lease	(717)	(347)	(1,069)
Other	(723)	(2,291)	(2,591)
Total	**(113,808)**	**(815,907)**	**(62,550)**

During the year ended December 31, 2022, research and development expenses decreased significantly in comparison to the same period of 2021, as the prior period was largely impacted by the Group´s CVnCoV program. In the prior year, these expenses consist primarily of cost incurred to CROs involved in the CVnCoV development as well as materials used in the administration of clinical trials. As a result of more participants leaving the clinical trials prior to completion, than originally estimated and of renegotiations of

contracts with CROs during the year ended December 31, 2022, the estimated outstanding costs for the CVnCoV studies decreased, which resulted in the reversal of provision for onerous contracts in the amount of EUR 38,533k. Additionally in 2022, GSK took over the Group's committed capacity at Novartis (see Note 3.7 for additional information) which resulted in a reduction in the estimated contract termination provisions in the amount of EUR 25,059k. The net effect of these two events resulted in an overall gain within the Third-party services category.

Since inception through December 31, 2022, the Group had no development expenditures which met the requirements for capitalization. In 2021, according to the terms and conditions of the grant from BMBF, the Group earned income (recognized in other operating income) for certain eligible expenses incurred for the COVID-19 vaccine development; refer to Note 3.6 for more information on amounts recognized from this grant in the year ended December 31, 2021.

Personnel expenses mainly include salary and salary-related expenses of EUR 33,068k (2021: EUR 32,779k 2020: EUR 16,543k) and expenses from share-based payments of EUR 876k (2021: EUR 954k, 2020: 4,770k); refer to Note 10 for further information.

3.5 General and administrative expenses

General and administrative expenses include the following:

	2020	2021	2022
	EUR k	EUR k	EUR k
Personnel	(29,884)	(37,393)	(36,765)
Maintenance and lease	(2,505)	(4,306)	(5,853)
Third-party services	(6,914)	(28,875)	(27,669)
Legal and other professional services	(3,531)	(9,230)	(10,394)
Amortization and depreciation	(6,020)	(8,895)	(11,360)
Other	(4,700)	(11,703)	(12,137)
Total	**(53,554)**	**(100,402)**	**(104,178)**

Personnel expenses mainly include salary and salary-related expenses of EUR 28,704k (2021: EUR 24,274k, 2020: EUR 20,442k) and expenses from share-based payments of EUR 8,061k (2021: EUR 13,119k, 2020: EUR 9,442k). During the fiscal year ended December 31, 2022, amortization and depreciation expenses increased, compared to the same period of 2021, mainly due to increased depreciation expense of right-of-use assets EUR 1,152k (refer to Note 4.2 for further information). Expenses in the 'Other' category mainly result from insurance costs related to D&O insurance EUR 5,533k (2021: EUR 5,457k, 2020: EUR 1,288k).

3.6. Income from release of governmental contract liabilities

Due to the withdrawal of the EMA regulatory approval application for CVnCoV, in October 2021, CureVac recorded in 2021 "Income from release of governmental contract liabilities" amounting to EUR 574,502k, which is explained further below. There was no such event in 2022.

Advance Purchase Agreement with European Commission

On November 30, 2020, CureVac entered into an Advance Purchase Agreement (APA) with the European Commission (EC), acting on behalf and in the name of all Member States of the European Union. The APA provided for the advance purchase by the Member States of 225 million doses of our SARS-CoV-2 vaccine. In order to support our accelerated efforts to develop a safe and effective vaccine, the APA provided support to our operations in the form of up-front payments. The first up-front payment of EUR 450 million was paid by the EC on behalf of the Member States and was included in contract liabilities as of December 31, 2020.

The second up-front payment would have had been due after the submission of the interim data package to the EMA in view of obtaining EC marketing authorization for CVnCoV. The up-front payments were designed to support the development and prepare the commercial supply of the vaccine.

In October 2021, we notified the EC of the withdrawal of our regulatory approval application for CVnCoV, which notification automatically terminated the APA. According to the APA, in such case of termination, CureVac would return the unspent amount of the up-front payment. In the context of the APA, "spent" means either costs occurred, or commitments made in relation to the purpose

as set out in the APA. CureVac demonstrated that the up-front payment was used in accordance with the contract and no repayment was required.

As described above, CureVac recognized the consideration related to its delivery obligations, existing at the outset of the arrangement, as contract liabilities. Upon the automatic termination of the APA, the ability for CureVac to satisfy the contractual performance obligations of the arrangement ceased and the EC ceased to have the ability to exercise its rights for performance by the CureVac. As such, the substance of the arrangement changed from a revenue contract to that of a government grant. Due to the material magnitude of the amount, its non-recurring nature and to better enable comparability to past performance and predictability of future performance, CureVac recognized the €450 million into income in an additional line item "Income from release of governmental contract liabilities" in the 2021 statement of operations. The "spent" amounts incurred by CureVac, and which demonstrate use of the up-front payment, have been included in "Research and development expenses" (refer to Note 3.4).

Additionally, CureVac was required transfer, upon EC's request any raw material and primary components paid for with the up-front payment and not used as of the termination date. Should the EC request any raw material and primary components or should CureVac successfully sell some of these, an applicable portion of raw material, primary components or proceeds would be remitted to the EC. This agreement expired at the end of 2022 and an amount of EUR 4,114k is accrued as 'other liabilities' as of December 31, 2022 for the related amount due to be remitted to the EC.

German Federal Ministry of Education and Research

In 2020, the Company announced with the German Federal Ministry of Education and Research (Bundesministerium für Bildung und Forschung), or BMBF, a German government-related entity, established a grant to support the development and production of its COVID-19 vaccine candidates. In July 2020, CureVac applied for this grant as part of a special program to accelerate the research and development of urgently needed vaccines against SARS-CoV-2. The grant amounted up to EUR 252 million and the payments were contingent to reaching predefined milestones. Based on the terms and conditions of the arrangement, the Company assessed the arrangement as having two components: a grant component and a supply component which were separated. The amount attributed to the supply of future deliveries was determined based on the relative stand-alone selling price of the vaccine observed in similar arrangements and is presented in contract liabilities.

The Company reached all the predefined milestones for 2020. Due to the withdrawal of the EMA regulatory approval application for CVnCoV in October 2021, CureVac was not able to reach all predefined milestones in 2021. From 2020 to December 2021, CureVac received a total of € 196.3 million. In November 2021, CureVac notified BMG of the inability to supply CVnCoV, triggering the automatic termination of the supply agreement.

Consistent with the rationale and treatment described above under the APA with the EC, the substance of the supply component of the BMBF arrangement changed from a revenue contract to that of a government grant and thus, consistent with the presentation of the contract liabilities under the APA, CureVac recognized the EUR 124 million in 2021 from the BMBF agreement as income in the line item "Income from release of governmental contract liabilities" and the corresponding expenses have been included in research and development expenses. The remaining amount of EUR 65 million, not related to the supply component, was reflected as grant income in "other operating income" in 2021. (Refer to Note 3.7).

3.7 Other operating income

Other operating income relates to:

	2020	2021	2022
	EUR k	EUR k	EUR k
Compensation for CMO/Materials transfer	—	—	35,393
Reimbursement claim	—	—	610
Sale of equipment	—	—	785
Grants and other reimbursements from government agencies and similar bodies	23,736	66,394	440
Other	414	1,308	704
Total	**24,150**	**67,702**	**37,932**

In March 2022, CureVac AG and GlaxoSmithKline Biologicals SA amended and restated the 2020 GSK agreement and the GSK COVID Agreement in connection with GSK entering into a direct agreement with Novartis for use of Novartis as a CMO at the same

time as CureVac exited its CMO agreement with Novartis. Additionally, under the restated agreement, CureVac is entitled to further compensation by GSK. The compensation mainly consist of consideration for set-up activities undertaken by CureVac (EUR 20,500k) and for reimbursement of prepayments (EUR 12,000k), which were recognized in 'Compensation for CMO/Materials transfer' in other operating income during the year ended December 31, 2022.

In 2022, 2021 and 2020 income from grants with government agencies and similar bodies resulted from the following:

German Federal Ministry of Education and Research

As discussed in Note 3.6, in 2020 the Company received a grant from BMBF to support the development of its COVID-19 vaccine candidate for which it was determined the arrangement contained two components: a grant component (in the scope of IAS 20) and a supply component (in the scope of IFRS 15). The Group recognized grant income of EUR 65,218k from this grant. As the grant ended in 2021, no such income was recognized in 2022..

Coalition for Epidemic Preparedness Innovations

The Coalition for Epidemic Preparedness Innovations (CEPI) is an innovative partnership between public, private, philanthropic, and civil organizations, launched at the World Economic Forum in Davos in 2017, to develop vaccines to stop future epidemics. CEPI's priority diseases include Ebola virus, Lassa virus, Middle East Respiratory Syndrome coronavirus, Nipah virus, Rift Valley Fever and Chikungunya virus. CEPI also invests in platform technologies that can be used for rapid vaccine and immunoprophylactic development against unknown pathogens (i.e., Disease X).

In February 2019, CureVac entered into a partnership agreement worth up to USD 34,000k with CEPI to further develop CureVac's The RNA Printer™ prototype. Under the three-year partnership agreement, CureVac used its mRNA platform for the preclinical development of a Lassa virus vaccine (a high-priority disease on the World Health Organization R&D list), a yellow fever vaccine and CureVac's rabies virus vaccine. Funds are received semi-annually in advance, to cover costs for the next six months. These payments are allocated to the agreed and signed statements of work. Management concluded that the arrangement should be accounted for by analogy to IAS 20.

CureVac is required to use reasonable efforts to achieve certain development milestones and is responsible for conducting certain clinical trials. In the event of an infectious disease outbreak, where such outbreak can be addressed by a Lassa virus, SARS-CoV-2 or future vaccine developed under the agreement, CureVac must manufacture such vaccine for use in the area affected by the outbreak on economic terms that satisfy CEPI's equitable access guidelines or otherwise allow CEPI or a third party to supply such vaccine in the affected area.

CureVac is required to grant certain approved manufacturers all necessary rights to use certain of CureVac's pre-existing IP and IP developed under the CEPI Agreement to further develop CureVac's automation solution and manufacture products for the treatment of certain diseases in geographic areas where there is an outbreak on economic terms that satisfy CEPI's equitable access guidelines. CureVac must provide all necessary commercially reasonable support to such approved manufacturers to facilitate such efforts.

CureVac solely owns all IP developed under the CEPI Agreement but is required to obtain CEPI's consent prior to exploiting any IP developed under the CEPI Agreement if such exploitation is in conflict with or goes against CEPI´s mission or policies.

In the event that CEPI terminates the agreement, CureVac will grant CEPI a license under CureVac's background IP and IP developed under the agreement to, among other things, develop and use CureVac's RNA Printer for use in treating certain infectious diseases and to manufacture products developed under the agreement.

In January 2020, CureVac and CEPI entered a collaboration to develop a vaccine against the new coronavirus SARS-CoV-2. The aim of the cooperation is to safely advance vaccine candidates into clinical testing as quickly as possible. The agreement builds upon the existing partnership between CureVac and CEPI to develop a rapid-response vaccine platform and included additional initial funding of up to USD 8,300k. In May 2020, CEPI increased its grant award to the Group for SARS-CoV-2 vaccine development to up to USD 15,300k.

During the year ended December 31, 2022, CureVac recognized the reimbursement of approved expenses of EUR 42k (2021: EUR 688k; 2020: EUR 15,953k) as “other operating income” and EUR 0k (2021: EUR 0k; 2020: EUR 3,239k) were deducted from the carrying amount of qualifying assets recorded in property, plant and equipment.

As of December 31, 2022, EUR 309k in grant funds received have been deferred and are presented within other liabilities (2021: EUR 1,289k). Following the completion of the partnership agreement of February 2019 between CureVac and CEPI in May 2022, CEPI requested a partial reimbursement of the unspent funds up to USD 1,000k. Those were reclassified from other liabilities to trade and other payables as of December 31, 2022.

Bill & Melinda Gates Foundation (BMGF)

BMGF finances, in the form of grants, various programs that CureVac operates for the development of vaccines, hence promoting and accelerating the development of CureVac’s technology platform. Through its equity investment, BMGF supports mainly the development of CureVac’s technology platform including the construction of a production plant in accordance with the GMP (Good Manufacturing Practice) standard on an industrial scale.

In 2015, CureVac entered into a Global Access Commitments Agreement with the Bill & Melinda Gates Foundation pursuant to which the Company is required to take certain actions to support the Bill & Melinda Gates Foundation’s mission.

In November 2016, in connection with the Global Access Agreement, CureVac received a grant of USD 653k (EUR 614k) in funding for the development of a vaccine for picornaviruses. In November 2017, also in connection with the Global Access Agreement, the company received two additional grants: an amount of USD 1,000k (EUR 852k) was received for the development of a universal influenza vaccine and an amount of USD 800k (EUR 673k) was received for a malaria vaccine. In August 2019, the Company received a second payment for the universal influenza program amounting to USD 540k (EUR 486k). In November 2020, the Company received a third payment for the universal influenza program amounting to USD 322k (EUR 280k). In November and December 2020, the Company received further payment for the malaria program amounting to USD 1,449k (EUR 1,208k).

During the year ended December 31, 2022 CureVac recognized EUR 167k (2021: EUR 488k, 2020: EUR 1,183k) from the amortization of the grants on a straight-line basis and for services as other operating income.

As of December 31, 2022, EUR 1,712k in grant funds received have been deferred and presented within other liabilities (2021: EUR 1,879k).

4. Fixed Assets

4.1 Development of intangible assets and property, plant and equipment

The development of intangible assets and property, plant and equipment for the years ended December 31, 2022 and 2021 were as follows:

Intangible assets

(in thousands of EUR)	Software	Licenses	Technology	Goodwil	Advance payments	Total
Acquisition costs						
As of January 1, 2021	10,172	9,887	—	—	688	20,747
Additions	2,454	234	—	—	991	3,679
Disposals	—	—	—	—	(576)	(576)
Reclassifications	—	138	—	—	(138)	—
As of December 31, 2021	**12,626**	**10,259**	**—**	**—**	**965**	**23,850**
Cumulative amortization and impairment charges						
As of January 1, 2021	4,499	2,102	—	—	—	6,601
Amortization	1,466	2,545	—	—	—	4,011
As of December 31, 2021	**5,965**	**4,647**	**—**	**—**	**—**	**10,612**
Acquisition costs						
As of January 1, 2022	12,626	10,259	—	—	965	23,850
Additions	1,433	4,208	6,350	12,463	—	24,454
Disposals	(2,331)	(1,537)	—	—	(298)	(4,166)
Reclassifications	656	—	—	—	(656)	—
Currency translation	1	—	—	—	—	1
As of December 31, 2022	**12,385**	**12,930**	**6,350**	**12,463**	**11**	**44,139**
Cumulative amortization and impairment charges						
As of January 1, 2022	5,965	4,647	—	—	—	10,612
Amortization	1,730	2,865	484	—	—	5,079
Disposals	(2,217)	(1,114)	—	—	—	(3,331)
Currency translation	1	—	—	—	—	1
As of December 31, 2022	**5,479**	**6,398**	**484**	**—**	**—**	**12,361**
Carrying amount						
As of January 1, 2021	5,673	7,785	—	—	688	14,146
As of December 31, 2021	6,661	5,612	—	—	965	13,238
As of December 31, 2022	**6,906**	**6,532**	**5,866**	**12,463**	**11**	**31,778**

Property, plant and equipment

(in thousands of EUR)	Buildings	Technical equipment and machines	Other equipment, furniture and fixtures	Assets under construction	Total
Acquisition costs					
As of January 1, 2021	19,950	22,384	9,243	39,121	90,698
Additions	3,353	28,047	2,228	98,071	131,699
Disposals	(4)	(10)	(15)	(7,123)	(7,152)
Reclassifications	3,973	1,553	—	(5,526)	—
Currency translation	—	—	38	—	38
As of December 31, 2021	**27,272**	**51,974**	**11,494**	**124,543**	**215,283**
Cumulative depreciation and impairment charges					
As of January 1, 2021	3,415	8,308	5,250	7,120	24,093
Depreciation	1,934	3,420	1,883	—	7,237
Impairment	—	—	—	22,810	22,810
Disposals	(1)	(2)	(15)	(7,120)	(7,138)
Currency translation	—	—	17	—	17
As of December 31, 2021	**5,348**	**11,726**	**7,135**	**22,810**	**47,019**
Acquisition costs					
As of January 1, 2022	27,272	51,974	11,494	124,543	215,283
Additions	377	9,710	2,760	76,773	89,620
Assets held for sale	—	(6,719)	—	(50,851)	(57,570)
Disposals	(1,182)	(12,584)	(1,732)	(4,356)	(19,854)
Reclassifications	—	7,652	—	(7,652)	—
Currency translation	—	—	30	—	30
As of December 31, 2022	**26,467**	**50,033**	**12,552**	**138,457**	**227,509**
Cumulative depreciation and impairment charges					
As of January 1, 2022	5,348	11,726	7,135	22,810	47,019
Depreciation	4,445	6,999	1,950	—	13,394
Impairment	—	3,830	—	2,054	5,884
Disposals	(1,083)	(9,938)	(1,688)	(24,038)	(36,747)
Currency translation	—	—	18	—	18
As of December 31, 2022	**8,710**	**12,617**	**7,415**	**826**	**29,568**
Carrying amount					
As of January 1, 2021	16,535	14,076	3,995	31,998	66,604
As of December 31, 2021	21,924	40,248	4,359	101,733	168,264
As of December 31, 2022	**17,757**	**37,416**	**5,137**	**137,631**	**197,941**

In fiscal 2022, impairments of EUR 5,884k were recognized (2021: EUR 22,810k). These were recognized in cost of sales as they pertained largely to machinery and technical equipment recorded under technical equipment and machines and assets under construction and resulted from the partial impairment of production lines which are obsolete due to the withdrawal of the EMA regulatory approval application for CVnCoV. Refer to Note 5 for additional information on assets reclassified as ‘assets held for sale’.

4.2 Right-of-use assets and lease liabilities

Set out below, are the carrying amounts of the Group's right-of-use assets and the movements during the period:

	Right-of-use assets			
	Land and Buildings	Vehicles	Other equipment	Total
	EURk	EURk	EURk	EURk
As of January 1, 2022	31,547	142	440	32,129
Additions	14,834	231	2,179	17,244
Disposals	—	—	—	—
Depreciation expense	(4,639)	(98)	(316)	(5,053)
Impairment	(710)	—	—	(710)
Foreign currency translation	151	—	—	151
As of December 31, 2022	**41,183**	**275**	**2,303**	**43,761**

The main leasing contracts that have commenced relate to several buildings in Tübingen, a building in Frankfurt am Main and a building in Boston/USA. The right of use asset for the building in Frankfurt was 100% impaired. The additions mainly relate to a lease agreement for a building in Tübingen (EUR 10,287k) with a start date of March 1, 2022, four lease agreements for office space in Amsterdam (EUR 1,453k) and a lease agreement for a building in Wiesbaden (EUR 825k) with a start date of December 1, 2022. Furthermore, the acquisition costs increased by EUR 1,832k in 2022 due to lease increases for three rented buildings in Germany.

Below are the carrying amounts of lease liabilities and the movements during the period:

	EUR k
As of January 1, 2022	**28,892**
Additions	17,241
Disposals	—
Accretion of interest	2,218
Payments	(6,439)
Foreign currency translation	174
As of December 31, 2022	**42,086**
Current	4,980
Non-current	37,106

A maturity analysis of lease liabilities is disclosed in Note 16.

The following are the amounts recognized in the statement of operations:

	EUR k
Depreciation expense of right-of-use assets	(5,053)
Impairment expense	(710)
Interest expense on lease liabilities	(2,218)
Expense relating to short-term leases (included in cost of sales)	(76)
Expense relating to leases of low-value assets (included in administrative expenses)	(66)
Total amount recognized in profit or loss	**(8,123)**

Set out below, are the carrying amounts of the Group's right-of-use assets and the movements of prior period:

	Right-of-use assets			
	Land and Buildings	Vehicles	Other equipment	Total
	EURk	EURk	EURk	EURk
As of January 1, 2021	33,296	113	575	33,984
Additions	2,666	97	—	2,763
Disposals	(943)	—	—	(943)
Depreciation expense	(3,698)	(68)	(135)	(3,901)
Foreign currency translation	226	—	—	226
As of December 31, 2021	**31,547**	**142**	**440**	**32,129**

Below are the carrying amounts of lease liabilities and the movements during the period 2021:

	EUR k
As of January 1, 2021	30,087
Additions	2,763
Disposals	(943)
Accretion of interest	1,729
Payments	(4,913)
Foreign currency translation	169
As of December 31, 2021	**28,892**
Current	3,469
Non-current	25,423

A maturity analysis of lease liabilities is disclosed in Note 16.

The following are the amounts recognized in the statement of operations in 2020:

	EUR k
Depreciation expense of right-of-use assets	(3,901)
Interest expense on lease liabilities	(1,729)
Expense relating to short-term leases (included in cost of sales)	(119)
Expense relating to leases of low-value assets (included in administrative expenses)	(39)
Total amount recognized in profit or loss	**(5,788)**

Commitments for leases not yet commenced as of December 31, 2022, relate to two lease agreements of buildings in Tuebingen, Germany that have been signed in 2021 and one lease agreement of a building in Wiesbaden, Germany that was signed in 2022. One building has a fixed lease term of 10 years having two 5 years extension options. The starting date of this lease will be May 1, 2023 and the fixed gross lease-payments are EUR 1,292k and the optional payments EUR 1,292k. The second lease agreement is starting on January 1, 2024 over fixed lease term of 15 years, having two five years extension options. The fixed gross lease-payments are EUR 28,975k and the optional payments EUR 26,556k. The third lease agreement is starting on August 1, 2023 until December 31, 2027, having one five years extension option. The fixed gross lease-payments are EUR 502k and the optional payments EUR 569k.

4.3 Non-current other assets

Non-current other assets of EUR 1,666k (2021: EUR 1,731k) consist of costs to obtain a contract of EUR 302k (2021: EUR 515k) and deposit payments for leases of EUR 1,364k (2021: EUR 1,215k).

The amortization of capitalized costs to obtain a contract in 2022 was EUR 213k (2021: EUR 694k, 2020: EUR 215k).

5. Assets held for sale

In 2022, Management decided to dispose of certain equipment which had been procured for CMO activities (CMO Equipment) but that was no longer planned to be used by the Company. An external service-provider was appointed on June 14, 2022 to organize

the sale of the CMO Equipment. As of December 31, 2022, the CMO-Equipment identified for sale had a gross book value of EUR 29,531k and was written down by EUR 19,064k (with the corresponding expense recognized in cost of sales) to EUR 10,467k, the fair value less anticipated costs to sell. Criteria for the determination of the fair value were defined based on certain sales scenarios considering different sales campaigns. All sales activities are scheduled for 2023.

6. Inventories

The inventories include only raw materials amounting to EUR 23,989k (December 31, 2021: EUR 56,159k), which are recoverable under the Company's agreements with its collaboration partners. During the year ended December 31, 2022, the decrease in inventory of EUR 32,170k is primarily due to further write-offs and scrap of EUR 80,021k (refer to Note 3.2 for additional information regarding these write-offs), including the transfer of inventory EUR 9,800k (net value) to GSK in connection with an agreement into which it entered with Novartis (see Note 3.6 for additional information).

7. Other financial assets

Other financial assets as of December 31, 2022 amounted to EUR 4,487k (2021: EUR 4,647k) mainly include deposits held by third parties in amount of EUR 1,936k (2021: EUR 1,936k) and other receivables in the amount of EUR 2,551k (2021: EUR 2,711k).

8. Prepaid expenses and other current assets

Prepaid expenses and other current assets of EUR 40,287k (2021: EUR 49,244k) include prepayments for future service agreements and material in the amount of EUR 4,507k (2021: EUR 5,724k) and receivables for the GSK compensation/material transfer of EUR 5,595k (2021: EUR 0k). For more details, refer to Note 3.7. As of December 31, 2022 we had tax receivables of EUR 24,840k in other current assets (2021: EUR 35,234k). This consists mainly of outstanding VAT refund claims of EUR 24,555k and other tax receivables of EUR 285k.

9. Equity

Overview

According to the Company's articles of association, the Company's authorized shares are divided into 386,250,000 common shares and 386,250,000 preferred shares, each having a nominal value of EUR 0.12. As of December 31, 2022, no preferred shares had been issued and all issued common shares issued and outstanding were fully paid. However, in certain events, BMGF has the right to require the Company to redeem or facilitate the purchase by a third-party of all common shares it holds and Genmab had the right to subscribe once for common shares at a certain price under an anti-dilution and down round-protection clause which expired in February 2022.

All payments received from shareholders in excess of the nominal value of the shares issued and net of transaction costs are recognized in capital reserves. Capital reserves also consists of recognition of share-based payments and the equity components of convertible loans. The Company may only make distributions, whether a distribution of profits or of freely distributable reserves, to shareholders to the extent shareholders' equity exceeds the sum of the paid-in and called-up share capital plus any reserves required by Dutch law or by the Company's articles of association.

Due to the effect of the corporate reorganization described in Note 1, the number of shares issued and outstanding has been retrospectively adjusted to reflect the impact of the resulting 1:133.0778 share split and developed as follows in fiscal 2022:

Common shares issued and outstanding at December 31, 2019	**96,693,265**
Genmab Investment	2,175,157
2020 Private Investment	55,688,535
Initial Public Offering and Private Placement	22,708,332
Share option exercises	3,195,276
Common shares issued and outstanding at December 31, 2020	**180,460,565**
Follow-on public offering, incl. Greenshoe	5,750,000
Share option exercises	910,163
Common shares issued and outstanding at December 31, 2021	**187,120,728**
Shares issued as part of the at-the-market offering program	6,908,493
Shares issued to former shareholders of Frame Pharmaceuticals	858,496
Shares issued for LTIP option exercises and RSU deliveries	109,374 *
Common shares issued and outstanding at December 31, 2022	**194,997,091**

*56,113 shares were issued on December 30, 2022 to fulfill the RSU deliveries beginning of January 2023

Refer to Note 22 for additional information on share transactions occurring after December 31, 2022. The share transactions which occurred in 2020, 2021 and 2022 are as described below.

Genmab Investment

Pursant to an Investment and Shareholders` Agreement (“ISA”), effective December 19, 2019, Genmab, agreed to purchase 2,175,157 Series B shares in the Company in exchange for EUR 20,000k in cash. As of December 31, 2019, the Group had received a total amount of EUR 16,345, corresponding to the par value of EUR 1 per share agreed to be purchased under the ISA. However, as the shares were not yet registered in the commercial register as of December 31, 2019, according to German law, the shares were not considered issued as of this date. The remaining amount of EUR 19,983,655 was paid at the beginning of 2020 and the shares were finally issued on February 18, 2020.

2020 Private Investment

In July 2020, the Group issued to Kreditanstalt für Wiederaufbau (or “KfW”, a German government-related entity), GSK and various other investors a total of 55,688,534 common shares in exchange for an aggregate investment of EUR 559,280k (2020 Private Investment).

Initial Public Offering and Private Placement

In August 2020, the Group completed its IPO whereby it sold 13,333,333 common shares at USD 16.00 per share. In addition, the underwriters exercised their option to purchase an additional 1,999,999 common shares at the public offering price less the underwriting discount. The aggregate proceeds, net of underwriting discounts, received by the Group from these transactions were USD 228,200k (EUR 192,946k). Additional offering costs for legal, accounting, printing and registration fees of USD 5,200k (EUR 4,397k) were recognized as a reduction to capital reserve against the proceeds from the IPO.

Additionally, in August 2020, DH-LT Investments GmbH, a company beneficially owned by Dietmar Hopp, managing director of dievini, the Group’s largest shareholder, purchased EUR 100,000k of the Group’s common shares at a price of USD 16.00 per share.

Follow-on public offering

In February 2021, the Group completed a follow-on public offering whereby it sold 5,000,000 common shares at a price of USD 90.00 per share. In addition, the underwriters exercised their option to purchase an additional 750,000 common shares at this same price less the underwriting discount. The aggregate proceeds, net of underwriting discounts, received by the Group from these transactions were EUR 426,652k. Additional offering costs for legal, accounting, printing and registration fees of EUR 22,590k were recognized as reduction to capital reserve against the proceeds from the offering.

At-the-market offering

On September 17, 2021, CureVac filed a prospectus for an "at-the-market" offering program to raise additional cash of up to USD 600,000k. The program was activated in June 2022. Through December 31, 2022, CureVac has issued 6,908,493 shares and raised gross proceeds of USD 69,139k. Offering costs for legal, accounting, printing and registration fees of EUR 1,058k were recognized as reduction to capital reserve against the proceeds from the offering.

Frame Pharmaceuticals acquisition

On June 8, 2022, CureVac entered into a Share Purchase Agreement (SPA) to acquire all of the issued and outstanding shares of Frame Pharmaceuticals B.V., a research company focused on advanced genomics and bioinformatics, based in Amsterdam, Netherlands. Under the SPA, the total consideration for the the purchase was up to EUR 34 million, conditioned on the meeting of certain development milestone payments. On the date of acquisition, July 1, 2022, CureVac issued 858,496 shares to the former shareholders of Frame Pharmaceuticals. Refer to Note 21 for additional information.

Exercises of share options under the prior VSOP plan

The IPO in August 2020 triggered an exercise event under the set terms of the prior VSOP plan (see Note 10). In March 2021, CureVac received 759,677 shares from the old shareholders and transferred 390,023 shares to the participants of the old VSOP plan. CureVac withheld 369,654 shares equaling the amount to be paid for income tax and social security tax. A second triggering event, "liquidity after IPO" was met one year after IPO. In October 2021, CureVac received 765,223 shares from the old shareholders and transferred 523,897 shares to the participants of the VSOP plan. CureVac withheld 241,326 shares equaling the amount to be paid for income tax and social security tax.

A third triggering event, again "liquidity after IPO, was met on the second anniversary of the IPO. In December 2022, CureVac received 777,260 shares from the old shareholders. All shares were transferred to to the participants of the prior VSOP plan and the portion of shares equaling the amount to be paid for income tax and social security tax were sold to pay for these taxes and social security amounts. CureVac has recorded a receivable for income tax and social security tax for former employees.

Exercises of share options under the new VSOP plan

Participants of the new VSOP plan (see Note 10) were able to continue to exercise their options throughout the year of 2022. In 2022 147,620 shares (2021: 557,171 shares) were issued upon exercise of options and 96,785 options were forfeited (2021: 0).

Exercises of share options under the Legacy program

Three of the original founders used their 5,282 options granted from the legacy program (see Note 10) and exercised their options throughout June until October 2021. The 5,282 options were restructured upon the completion of our Corporate Reorganization. Following this restructuring, the option holder was able to exchange his options for common shares of CureVac N.V. (instead of shares of CureVac AG) on a 1 to 133.0778 basis. Therefore, the exercise resulted in issuance of 702,915 shares.

Shareholders' Agreement Among KfW, dievini, DH-LT Investments GmbH and Dietmar Hopp

In connection with the KfW's investment in 2020, KfW, dievini and Dietmar Hopp entered into a shareholders' agreement on June 16, 2020, or the KfW dievini Shareholders' Agreement, agreeing to certain transfer restrictions and rights of first refusal relating to their interests in CureVac, nomination rights, and a voting agreement relating to certain specified actions. In particular, dievini and Mr. Hopp agree to vote a specified number of their shares as directed by KfW on certain specified actions, subject to certain exceptions. These specified actions include, inter alia: (1) transferring the tax domicile of CureVac N.V. and/or the approval of the transfer of the corporate or administrative seat of CureVac; (2) relocating or ceasing activities in specified areas to a state outside the European Union to the extent (in particular in the area of the development of vaccines) they are material for the protection of the health of the population of the European Union; (3) entering into material mergers and acquisitions; and (4) amendments to the articles of association of CureVac which would affect the foregoing matters. The KfW dievini Shareholders' Agreement has an initial fixed term that expires on December 31, 2023, subject to a right to extend for one year for the benefit of KfW and dievini, and may be terminated after the initial fixed term, or the extended term, if applicable, by either party subject to six months' notice prior the end of the applicable calendar year. In addition, the agreement shall automatically terminate if KfW sells all or a part of its interest in the Company to a third party, subject to certain exceptions. On August 14, 2020, DH-LT Investments GmbH joined the KfW dievini Shareholders' Agreement via a First Supplement Agreement to the KfW dievini Shareholders' Agreement and on January 13, 2022, the parties to the KfW dievini Shareholders' Agreement entered into a Second Supplement to the KfW dievini Shareholders' Agreement which revised certain of the parties' restrictions and rights with respect to transfer of the shares held by them. Moreover, triggered by transfer of certain shares from dievini to so-called "dievini Shareholders", on dievini's side certain additional parties entered into the KfW dievini Shareholders' Agreement.

10. Share-based payments

Amounts in this Note reflect the retrospective effect of the share split resulting from the corporate reorganization described in Note 1.

During the years ended December 31, 2022, 2021, and 2020, the Group operated the following share-based plans for members of management and other key employees of the Group, as well as members of the supervisory board:

Prior VSOP
New VSOP — for US employees (from 2019 onwards)
LTIP Stock Options
LTIP RSUs (from 2021 onwards)
Former Chief Executive Officer Grant (fully exercised in 2021)
Legacy Plan (expired in 2021)

All programs were accounted for as equity-settled.

Measurement of the grant date fair value is based on valuation techniques appropriate in the circumstances, such a Black Scholes option pricing models or a Monte Carlo simulation. Expected volatility, a key input to such models, was based on an evaluation of the historical volatilities of comparable listed biotech-companies over the historical period commensurate with the expected option life. Regarding the expected option life of the stock option programs, this was based on the assumptions that the beneficiary would exercise his option in equal installments from the date of the first time possible (taking into account lock-up and potential trading windows restrictions) until maturity. The risk-free interest was derived from German or US-Government bonds, as appropriate.

The expense recognized for share-based payments during the years ended December 31 is as follows:

	2020	2021	2022
	EUR k	EUR k	EUR k
Prior VSOP	(5,188)	(624)	(131)
New VSOP	(1,764)	(572)	95
LTIP Stock Options	(4,736)	(12,472)	(5,562)
LTIP RSUs	—	(705)	(3,108)
RSU Supervisory board	—	(566)	(478)
Total	**(11,688)**	**(14,939)**	**(9,184)**

Prior VSOP

Exercise and/or vesting of the Prior VSOP is dependent on the occurrence of specified exit events, such as IPO or trade sale, and/or additional contingent events, such as financing rounds, product approvals or minimum trading volumes and liquidity levels of the CureVac N.V. shares. Further exit events relating to the program can be settled in cash or shares.

As CureVac considered an IPO-scenario most probable at the end of fiscal 2019 and had the discretion and the stated intent to settle in shares instead of cash in the case of an IPO, CureVac accounted for this program as equity-settled as of December 31, 2019. In August 2020, the IPO materialized and confirmed the Group's settlement choice. The Prior VSOP has a term of nine years after the day of the Group's initial listing in the case of an IPO.

The development of the virtual shares in this program granted to management and key employees was as follows:

	2020	2021	2022
Outstanding at the beginning of the period	7,305,838	7,951,265	6,426,365
Granted during the period	658,735	—	—
Forfeiteded during the period	(13,308)	—	(34,859)
Exercised during the period	—	(1,524,900)	(777,260)
Outstanding at the end of the period	7,951,265	6,426,365	5,614,246
Thereof vested	7,582,906	6,365,422	5,509,886
Thereof exercisable	none	none	none

658,735 virtual shares were awarded in May and June 2020 to18 key employees.

As of January 1, 2020, none of the virtual shares of the Prior VSOP were exercisable because an exit event or capital market transaction had not occurred. The IPO on August 14, 2020, triggered the right to exercise 10 % of the vested virtual shares at the end of the lock-up period, which ended on February 10, 2021. By March 10, 2021, the beneficiaries declared the exercise of all their exercisable 759,677 virtual shares and CureVac received 759,677 shares from their former majority shareholders as of 2015, on that day. On March 11, 2021, CureVac transferred 390,023 shares to the exercising beneficiaries and withheld 369,654 (treasury) shares equal to the monetary value (approximately EUR 26 million) of the beneficiaries (wage) tax and social security obligations, which CureVac transferred to the relevant authorities on the exercising employee´s behalf in cash. The share price of CureVac on March 11, 2021, was EUR 69.69.

A second 10 % portion of the (vested) virtual shares became exercisable on the first anniversary after IPO i. e., on August 14, 2021, because certain minimum trading volumes of the CureVac N.V. shares and liquidity levels were reached. The beneficiaries declared the exercise of their exercisable 765,223 virtual shares by October 18, 2021 and CureVac received 765,223 shares from the old shareholders on that day. On October 19, 2021, CureVac transferred 523,897 shares to the exercising beneficiaries and withheld 241,326 (treasury) shares equal to the monetary value (approximately EUR 8 million) of the beneficiaries (wage) tax and social security obligations, which CureVac transferred to the relevant authorities on the exercising employee´s behalf in cash. The share price of CureVac on October 19, 2021, was EUR 34.56.

A third 10 % portion of the (vested) virtual shares became exercisable on the second anniversary after IPO i. e., on August 14, 2022, because certain minimum trading volumes of the CureVac N.V. shares and liquidity levels were again reached. The beneficiaries declared the exercise of their then exercisable 777,260 virtual shares by Dec 12, 2022 and CureVac received 777,260 shares from the old shareholders on that day. On Dec 14, 2022, CureVac transferred 777,260 shares to the exercising beneficiaries. The portion of shares equaling the amount to be paid for (wage) tax and social security obligations were sold to pay for these amounts. For former employee's CureVac shows a receivable position equaling the amount to be paid for (wage) tax and social security obligations. The share price of CureVac on December 14, 2022, was EUR 6.96.

Expense recognized in the statement of operations and other comprehensive income (loss)

The expense recognized for this share-based payment plan during the years ended December 31 is as follows:

	2020	2021	2022
	EUR k	EUR k	EUR k
Selling and distribution expenses	(213)	(25)	(8)
Research and development expenses	(1,840)	(369)	(45)
General and administrative expenses	(3,135)	(230)	(78)
Total	**(5,188)**	**(624)**	**(131)**

Measurement of Fair Values

The grant date fair value of the 658,735 virtual shares granted in May and June 2020 was derived from the estimated equity value of CureVac on these dates, which lead to a fair value of one virtual share of EUR 10.04 at that time.

New VSOP

Effective November 25, 2019, the Group granted 745,236 share options to key employees of CureVac Inc. under the New VSOP program. Furthermore, in the first quarter of fiscal 2020, the Group granted another 267,822 share options. All these share options have an exercise price of USD 6.21.

The awards vest over a period of four years, which starts on the date the awardee was hired by the Group, with 25% vesting after 12 months and the rest in monthly installments. The awards have a term of 10 years.

In addition, the Group set up a provision for employer taxes arising according to US regulations for future exercises of EUR 51k as of December 31, 2022 (2021: EUR 147k).

Measurement of Fair Values

An advanced Black-Scholes Model (Enhanced American Stock Option Model) has been used to measure the fair value at the grant date of November 25, 2019.

The inputs used in the measurement of the fair value at grant dates in the first quarter of 2020 and 2019 were as follows:

	Grant Date	
	Q4 2019	Q1 2020
Weighted average fair value	EUR 3.80	EUR 4.05
Weighted average share price	EUR 9.19	EUR 8.91
Exercise price (USD 6.21)	EUR 5.64	EUR 5.60
Expected volatility (%)	50.0 %	55.0 %
Expected life (years)	1.16	1.11
Risk-free interest rate (%)	1.77 %	1.79 %

The remaining life of the option awards as of December 31, 2022 is between 5.5 and 6.9 years (2021: range between 3.7 and 8.5 years).

Reconciliation of outstanding awards

The number of awards in this program granted to key employees developed as follows:

	2020	2021	2022
Outstanding at the beginning of the period	745,236	906,595	349,424
Granted during the period	267,822	—	—
Forfeited during the period	(106,462)		(99,696)
Exercised during the period	—	(557,171)	(147,620)
Outstanding at the end of the period	906,595	349,424	102,108
Thereof vested	420,595	88,464	59,942
Thereof exercisable	none	88,464	59,942

As of December 31, 2019, none of the awards were exercisable because an exit event or capital market transaction had not occurred. With the defined exit event “financing round” before the IPO the awards became exercisable, but none of them were exercised. As the IPO had taken place on August 14, 2020, shortly after the “financing event” before the IPO, the awards became subject to the lock-up period, which is 180 days after the initial listing, i. e. on February 10, 2021. Hence, as of December 31, 2020, none of the awards were exercisable. In 2021 multiple exercises happened throughout the year. In total 557,171 options were exercised with an average share price of 61.28 USD. These exercises led to CureVac having to pay an amount of USD 493k employer taxes and to use USD 981k of the provision recorded in 2020.

In 2022, a number of exercises were carried out throughout the year. In total, 147,620 options were exercised with an average share price of 16.81 USD. These exercises led to CureVac having to pay an amount of USD 45k employer taxes and to use USD 51k of the provision recorded in 2021.

Expense recognized in the statement of operations and other comprehensive income (loss)

The expense recognized for employee services received during the years ended December 31, 2022, 2021, and 2020 is shown in the following table:

	2020 EUR k	2021 EUR k	2022 EUR k
Research and development expenses	(1,421)	(349)	69
Selling and distribution expenses	(296)	(188)	23
General and administrative expenses	(47)	(35)	3
Total	(1,764)	(572)	95

Long-Term Incentive Plan (LTIP) - Options

On November 16, 2020, CureVac granted 266,155 options to the Chief Scientific Officer (CSO). Furthermore, on December 1, 2020, CureVac granted 266,156 options (in 3 tranches) to the company`s Chief Business Officer (CBO) and Chief Commercial Officer (CCO). All grants were made at no cost under the terms of a new long-term incentive plan put in place by Curevac N.V. Options will be settled in shares of Curevac N.V.

Options granted to the CSO have an exercise price of EUR 10.04 per share option and an expiration date of July 14, 2030. The exercise price was based on value of the shares at entry date of the CSO. The award vests over a period of four years, with 25% vesting after 12 months and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of 20%, based on the 10 day VWAP at time of exercise.

For the grant to the CSO, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 57.40
Weighted average share price (10-days VWAP before grant date)	EUR 50.01
Exercise price (USD 11.90)	EUR 10.04
Expected volatility (%)	62.06 %
Expected life (years)	1.82
Risk-free interest rate (%)	0.07 - 1.48 %

At December 31, 2022, 6,303 options granted to the CSO had been exercised.

Options granted to the CBO / CCO have been granted in 3 tranches vesting over 1 to 3 years, with exercise prices applicable to future tranches being estimated. The exercise price of the first tranche is EUR 43.87 (USD 52.96), The exercise prices for future installments, 2021 and 2022, were estimated to be EUR 81.48 (USD 98.36) and EUR 81.65 (USD 98.57). For the second tranche the actual exercise price in fiscal year 2021 was determined to be EUR 33.07 (USD 39.92) and of the third tranche the actual exercise price in fiscal year 2022 was determined to be EUR 7.35 (USD 7.68). The tranches each have a term of 10 years. Exercise of all three tranches is contingent on a share price increase of 10 %, based on a 10 day VWAP at the time of each exercise.

For the grant to the CBO/CCO, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

First tranche:

Weighted average fair value per option	EUR 48.27
Weighted average share price (actual 10-days VWAP before grant date, USD 81.03)	EUR 67.12
Exercise price (USD 52.96)	EUR 43.87
Expected volatility (%)	62.27 %
Expected life (years)	1.78
Risk-free interest rate (%)	0.07 - 1.50 %

Second tranche:

Weighted average fair value per option	EUR 24.36
Weighted average share price (estimated by Monte Carlo simulation to be USD 98.36)	EUR 81.48
Exercise price (estimated by Monte Carlo simulation to be USD 98.36)	EUR 81.48
Expected volatility (%)	62.27 %
Expected life (years)	2.23
Risk-free interest rate (%)	0.07 - 1.50 %

Third tranche:

Weighted average fair value per option	EUR 20.01
Weighted average share price (estimated by Monte Carlo simulation to be USD 98.57)	EUR 81.65
Exercise price (estimated by Monte Carlo simulation to be USD 98.57)	EUR 81.65
Expected volatility (%)	62.27 %
Expected life (years)	2.66
Risk-free interest rate (%)	0.07 - 1.50 %

On March 1, 2021, CureVac granted 2,000 options to a key employee. Options granted to this key employee have an exercise price of EUR 77.73 (USD 88.16) per share option and an expiration date of February 28, 2031. The exercise price was based on the 30 day VWAP of March 1 – March 31, 2021 of the shares. The award vests over a period of four years, with 25% vesting after 12 months

and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of +10%, based on the 10 day VWAP at time of exercise.

For the grant to the key employee, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 0.65
Weighted average share price (30-days VWAP after grant date)	EUR 77.73
Exercise price (USD 88.16)	EUR 77.73
Expected volatility (%)	73.00 %
Expected life (years)	2.15
Risk-free interest rate (%)	0.08 - 0.49 %

On July 1, 2021, CureVac granted 20,000 options to the Chief Operations Officer (COO). Furthermore, on August 1, 2021, CureVac granted 30,000 options to the Chief Development Officer (CDO). Both grants were made at no cost under the terms of the new long-term incentive plan (LTIP) put in place by Curevac N.V. Options will be settled in shares of Curevac N.V.

The CDO has since left the company and, under the terms of his LTIP agreement, his options had expired as of December 31, 2022.

Options granted to the COO have an exercise price of EUR 70.92 (USD 84.03) per share option and an expiration date of July 2, 2026. The exercise price was based on the 20 day VWAP of the shares at entry date of the COO. The award vests over a period of four years, with 25% vesting after 12 months and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of +20%, based on the 10 day VWAP at time of exercise.

For the grant to the COO, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 17.56
Weighted average share price (20-days VWAP before grant date)	EUR 56.51
Exercise price (USD 84.03)	EUR 70.92
Expected volatility (%)	70.95 %
Expected life (years)	4.5
Risk-free interest rate (%)	0.099 – 0.903 %

Options granted to the CDO have, an exercise Price: EUR 46.16 (USD 54.79) per share option and an Expiration Date: August 2,2026. The exercise price was based on the 20 day VWAP of the shares at entry date of the COO. The award vests over a period of four years, with 25% vesting after 12 months and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of +20%, based on the 10 day VWAP at time of exercise.

For the grant to the COO, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 17.56
Weighted average share price (20-days VWAP before grant date)	EUR 41.81
Exercise price (USD 84.03)	EUR 46.16
Expected volatility (%)	75.13 %
Expected life (years)	4.6
Risk-free interest rate (%)	0.075 – 0.704 %

On January 1, 2022, CureVac granted 9,500 options to a key employee. Options granted to this key employee have an exercise price of EUR 30.67 (USD 33.87) per share option and an expiration date of December 31, 2031. The exercise price was based on the 30 day VWAP of January 1 – January 31, 2022 of the shares. The award vests over a period of four years, with 25% vesting after 12 months and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of +20%, based on the 10 day VWAP at time of exercise.

For the grant to the key employee, a Monte Carlo simulation has been used to measure the fair value at the relevant grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 14.31
Weighted average share price (30-days VWAP after grant date)	EUR 30.67
Exercise price (USD 34.87)	EUR 30.67
Expected volatility (%)	72.17 %
Expected life (years)	2.16
Risk-free interest rate (%)	0.40 - 1.15 %

On March 1, 2022, CureVac granted 130,000 supplemental options to the Company's management board. 30,000 options were granted to the CEO, and 25,000 options were granted to each of the CFO, CSO, COO and CBO/CCO. All grants were made at no cost under the terms of a new long-term incentive plan put in place by CureVac.

The options granted to the management board have an exercise price of USD 19.35 per share option and an expiration date of March 1, 2032. The exercise price was based on the 10day VWAP as of March 1, 2022 + a performance criteria of 15%. The award has a vesting of 25% on each of Dec 31, 2022, Dec 31, 2023, Dec 31, 2024, Dec 31, 2025.

For the grants to the management board, a Monte Carlo simulation has been used to measure the fair value at the grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 4.86
Weighted average share price (10 days VWAP before grant date)	EUR 15.07
Exercise price (USD 19.35)	EUR 18.37
Expected volatility (%)	73.87 - 86.09 %
Expected life (years)	2.33
Risk-free interest rate (%)	2.34 - 3.21 %

On April 1, 2022, CureVac granted 700 options to a key employee. Options granted to this key employee have an exercise price of EUR 17.45 (USD 19.28) per share option and an expiration date of March 31, 2032. The exercise price was based on the 10 day VWAP of March 21 – March 31, 2022 of the shares. The award vests over a period of four years, with 25% vesting after 12 months and the rest in 1/36 monthly installments thereafter. Exercise is contingent to a share price increase of +20%, based on the 10 day VWAP at time of exercise.

For the grant to the key employee, a Monte Carlo simulation has been used to measure the fair value at the grant date. The inputs used in the measurement of the fair value at grant date were as follows:

Weighted average fair value per option	EUR 6.81
Weighted average share price (10-days VWAP before grant date)	EUR 17.45
Exercise price (USD 19.28)	EUR 17.45
Expected volatility (%)	50.91 %
Expected life (years)	2.16
Risk-free interest rate (%)	2.67 %

The expense recognized for employee services received under the LTIP – options during the years ended December 31, 2022, is in an amount of EUR 5,564k (2021:EUR 12,472k) is included in general and administration expenses.

Long-Term Incentive Plan (LTIP) - Restricted Stock Units (RSUs)

Restricted Stock Units (RSUs)

In 2021, as part of the LTIP program, the group awarded RSUs (restricted stock units) to senior executives as well as supervisory board members.

On June 24, 2021, the group awarded 10,956 RSUs to supervisory board members and on December 23, 2021, the group awarded 63,095 RSUs to the executive board and various key employees. These RSU awards vest over 3 years with one third vesting taking

place each year on December 31. One third of these RSU awards had vested as of December 31, 2021, one further third as of December 31, 2022.

In addition, on July 1, 2021, the group also awarded 4,691 special RSU awards. These special RSU awards vest over 12 months and are fully vested as of December 31, 2021.

In 2022, as part of the LTIP program, the group awarded RSUs (RSU Award 2022) to senior executives as well as supervisory board members.

On June 22, 2022 the group awarded 225,888 RSU awards as part of the "LTIP - RSU Award 2022" to members of the supervisory board, executive board and various key employees. On November 30, 2022, the group awarded a further 7,633 RSU awards to key employees who joined the company during fiscal 2022. These RSU awards vest with one third vesting taking place each year on December 31, 2022, December 31, 2023 and December 31, 2024. One third of these RSU awards had vested as of December 31, 2022.

In addition, on January 1, 2022, the group awarded 36,000 supplemental RSU awards to the CEO. This RSU award vests over 12 months and is fully vested as of December 31, 2022.

On January 31, 2022, the group also awarded 5,000 supplemental RSU awards to the COO and 30,000 supplemental RSU awards to the CBO/CCO. These RSU awards vest in 2 tranches (50% on December 31 2022 and 50% on December 31, 2023). In order for the RSUs to settle and be delivered, the share price must reach 19.16 USD on or after vesting. As of December 31, 2022, 50% of these RSUs had vested but had not been settled or delivered.

On July 1, 2022, the group awarded 89,655 RSU awards to former Frame employees to replace existing share-based payment awards of Frame Pharmaceuticals. These RSU awards vest with one third vesting taking place each year on June 30, 2023, June 30, 2024 and June 30, 2025. The RSU program is accounted for by recognizing the related expense over the vesting period of the award, with corresponding increases recorded in equity. The expense is based on the fair value determined at the grant date of the award and the number of awards expected to vest. The fair value remains unchanged after grant date. Once the award has vested, there is no reversal of expense related to the award.

Expenses for employer taxes arising upon the delivery of RSUs are recognized in profit or loss.

The related RSU expense is recorded in the functional cost category to which the award recipient's costs are classified.

	2020	2021	2022
	EUR k	EUR k	EUR k
Research and development expenses	—	(240)	(909)
Selling and distribution expenses	—	(82)	(199)
General and administrative expenses	—	(383)	(2,000)
Total	—	(705)	(3,108)

Grant to Former Chief Executive Officer

In 2019, CureVac granted 3,866,309 options to Dan Menichella, then Chief Executive Officer (CEO) of CureVac from June 20, 2018, to March 10, 2020, with an exercise price of USD 8.28 per share option.

2,819,120 of these options vested in 2019 and the remainder in 2020. Except for 100,000 options, all options were exercised in 2020 against the issuance of 3,195,276 common shares of CureVac NV for no cash consideration. The weighted average share price at the date of exercises was USD 114.0345 (EUR 93.765) in fiscal 2021 and USD 55.22 (EUR 46.72) in 2020. The outstanding 100,000 options were all exercised as of June 30, 2021.

In FY 2020, EUR 2,551k (2019: EUR 12,409k) were recognized as expense in general and administrative expenses. Employer taxes were expensed and paid upon exercise under US regulations amounting to USD 139k in 2021 (2020: EUR: 2,033k expensed and paid or payable). These exercises led to CureVac having to pay an amount of USD 139K employer taxes and the use USD 146K of the provision booked in 2020.

Legacy plan

Under the terms of a legacy plan, at January 1, 2019, three members of (former) management held 702,917 of share options outstanding and exercisable. These share options grant the holder the right to acquire shares of CureVac AG at nominal value and are classified as equity-settled share-based payments.

All options were exercised in 2021.

No expenses have been recognized during the years ended December 31, 2022, 2021 and 2020 under this program.

11. Trade and other payables

Trade payables and other payables are all due within one year and include the following:

	2021 EUR k	2022 EUR k
Trade payables	122,263	68,246
License fees payable	38	—
Miscellaneous liabilities	5,402	5,218
Total	**127,703**	**73,463**

Trade Payables decreased by EUR 54,017k and refers to invoices received before fiscal year-end mainly for raw materials. There is no concentration of risk.

Miscellaneous liabilities consist mainly of payroll-related taxes and social security liabilities of EUR 5,027k (2021: EUR 4,802k).

12. Other liabilities and provisions

Provisions include the following:

	2021 EUR k	2022 EUR k
Contract termination provisions	—	61,320
Provisions (non-current)	**—**	**61,320**
Provision for onerous contracts	40,455	1,922
Contract termination provisions	81,587	—
Provisions (current)	**122,042**	**1,922**
Total Provisions (current & non-current)	**122,042**	**63,242**

Below are movements during the period:

	EUR k
As of January 1, 2022	**122,042**
additions	16,460
used (amounts charged against the provision)	(31,606)
unused amounts reversed	(71,694)
reclassified from accounts payable	28,040
As of December 31, 2022	**63,242**
Current	1,922
Non-current	61,320

Other liabilities include the following:

	2021 EUR k	2022 EUR k
Other (e.g. license liabilities, Deferred Tax Liability)	264	19
Other liabilities (non-current)	**264**	**19**
Personnel accrued liabilities (e.g. bonus, vacation)	7,210	7,778
Grants from government agencies and similar bodies	3,167	2,021
Outstanding invoices	35,242	28,146
Professional fees	1,183	1,344
VAT and other taxes (real estate transfer taxes)	924	924
Other	305	278
Other liabilities (current)	**48,031**	**40,491**
Total other liabilities (current & non-current)	**48,295**	**40,510**

In 2022, EUR 440k (2021:EUR 66,394k) of the grants from government agencies and similar bodies were recognized as other operating income.

The provision for onerous contracts relates to the CRO agreements and are expected to be used within one year from December 31, 2022. All amounts recognized as of December 31, 2022 arose during 2021, no additional provisions were made or utilized in 2022 and EUR 38,533k were reversed during the year (as described in Note 3.4). As described in Note 2, when initially measuring onerous contract provisions relating to CRO agreements, judgment was required in estimating the cost of the remaining services, particularly in estimating the number of participants completing the clinical trials. Due to the passage of time and thus additional visibility into how events actually transpired in 2022, little uncertainty in the amount and timing of remaining cash outflows remains as of December 31, 2022.

Contract termination provisions relate to amounts which the Company expects to pay out to settle its obligations under certain CMO contracts which it has terminated. All amounts recognized as of December 31, 2022 arose during 2021 except for EUR 16,460k in additional provisions made in 2022. EUR 31,605k provisions were utilized, EUR 28,040k were reclassified as a provision from accounts payable and EUR 33,162k were reversed during the year. As described in Note 2, judgment is required in estimating these amounts. The amount of the outflow of resources to settle the obligations to which these provisions relates may vary from the provision amount recognized as of December 31, 2022 due to potential variability in the amount required to be paid to ultimately release the company from its remaining obligations under the CMO contracts, including as a result of arbitration decisions. Contract terminations provisions have an expected maturity between one to five years from December 31, 2022 and are thus classified in Provisions (non-current).

The accrued liability for other taxes consists of real estate transfer taxes in the amount of EUR 924k (2021: EUR 924k).

As described in Note 3.7, CEPI requested a partial reimbursement of unspent funds up to USD 1,000k.

13. Loans

As of December 31, 2019, CureVac had been granted two convertible loan facilities (i.e., First Loan and Second Loan) by Dietmar Hopp. On June 26, 2020, CureVac drew down the second tranche of the Second Loan in the amount of USD 26,800k (EUR 24,860k). On July 24, 2020, the First Loan and Second Loan were terminated and on August 7, 2020, the total principal of EUR 94,749k and total accrued interest of EUR 5,641k were repaid in full. During the year ended December 31, 2020, EUR 11,008k of interest expense, inclusive of EUR 5,194k which resulted from the early termination of the First Loan and Second Loan (December 31, 2019: EUR 11,960k), was recognized.

On June 27, 2020, CureVac signed a financing arrangement with the European Investment Bank, or EIB, under which EIB agreed to provide the Company with a line of credit in an amount of up to EUR 75 million for the partial financing of CureVac´s clinical developments and large-scale production of the infectious disease vaccine candidates including a vaccine against SARS-CoV-2, or the Investment, provided that the amount of financing does not exceed 50% of the cost of the Investment. The EIB financing is available in three tranches of at least EUR 15 million and up to EUR 25 million upon completion of pre-defined milestones. These pre-defined milestones are tied to evidence of successful progress in the development and large-scale production of CureVac´s vaccine candidate against SARS-CoV-2. In addition, the disbursements of the second and third tranches are contingent upon the occurrence of the disbursement of the first and second tranches, respectively. Each tranche is due 7 years from the disbursement date. The EIB loan requires fixed remuneration at an interest at a rate of 0.5% per annum. Additionally, the loan agreement requires CureVac to pay variable remuneration depending on the output produced in the Company's GMP IV manufacturing facilities, which is EUR 200k per batch, up to an aggregate remuneration cap of EUR 75 million, on batches produced during the "Remuneration Period" beginning the earlier of the first financial year when CureVac AG has a positive EBITDA or in 2025 and extending for a period of 12 years thereafter. Payment of the variable remuneration is due on the first March 31st of the Remuneration Period and then each following March 31st, thereafter, in the Remuneration Period. The loan agreement provides CureVac an option to buy-out the variable remuneration by paying an amount equal to the higher of €5 million and 150-190% of the outstanding principal of the loan, depending on the number of years following the initial disbursement under the loan, but in any case, limited to an aggregate remuneration cap of EUR 75 million.

CureVac was subject to several restrictive covenants on its business activities as described in the financing agreement, including limitations on certain merger and acquisition transactions, disposition of certain assets, and mandatory maintenance of assets related to the Investment. In November 2020, a land charge (lien) amounting to EUR 75 million was registered in favor of the EIB to secure the loan. The EIB may demand, without prior notice, the immediate repayment of outstanding principal together with any accrued interest upon certain events including, among others, the Company's failure to continue the development of its Investment following a grace period.

During the year ended December 31, 2021, CureVac decided to early terminate the EIB loan for a total cash consideration of EUR 26,633k, which comprises of EUR 25,000k repayment of the loan and 1,633k interest and fees. As of December 31, 2021 the EIB loan was fully repaid.

14. Income tax

CureVac has tax losses in Germany that are available indefinitely for offsetting against future taxable profits of the companies in which the losses arose. Under German tax law, tax profits in a given year can be offset against tax loss carryforwards up to an amount of EUR 1,000k. 60% of tax profit in excess of this amount can be offset against any remaining tax loss carryforwards. As a result, 40% of the profits in excess of EUR 1,000k are subject to taxation.

The CureVac Group has four foreign entities:

- CureVac Inc. is an U.S.-based company
- CureVac Swiss AG is a Switzerland-based company
- CureVac Belgium SA is a Belgium-based company
- CureVac Netherlands B.V. is a Netherlands-based company

The CureVac Beteiligungsverwaltungs AG was an Austria-based company and in August 2022 merged with the CureVac AG to CureVac SE.

With the exception of those companies, all other CureVac' Group entities are considered Germany entities for tax purposes.

Tax loss carryforwards are examined by the German taxation authorities and may be adjusted. Furthermore, significant changes in the shareholder and company structure can lead to a reduction in the loss carryforwards under the current provisions of German tax law, which can be used to calculate the annual amount for offsetting against the future taxable income.

In fiscal 2022, 2021 and 2020, the Group recorded a consolidated income tax benefit and expense of EUR 126k, EUR 782k and EUR 726k, respectively. The income tax benefit in fiscal 2022 results from current income tax benefit (2021 and 2020 expenses) of EUR 106k (2021: EUR 1033k and 2020: EUR 403k) and deferred tax income on taxable temporary differences of EUR 26k (2021: EUR 1,815k and 2020: EUR 2,843k),. In fiscal 2022, the Group further recorded deferred tax liabilities of EUR 20k (2021: EUR 0k and 2020: EUR 39k). In fiscal 2022 the Group released (2021: recognized) deferred tax assets related taxable temporary differences arising from share-based-payments of EUR 1,590k (2021: EUR 581k) through equity. For outside basis differences of EUR 2.167k (2021: EUR 2,089k and 2020: EUR 972k) which are indefinitely reinvested and associated with investments in subsidiaries, deferred tax liabilities have not been recognized.

The significant components of income tax for the years ending December 31, 2022, 2021 and 2020 were as follows:

Tax reconciliation:

	2020	2021	2022
	EUR k	EUR k	EUR k
Loss before tax	(129,848)	(412,498)	(249,155)
Expected tax benefit (based on statutory tax rate of 29.48% in 2022 and 29.48% in 2021 and 29.13% for 2020)	37,818	121,584	73,426
Adjustments in respect of current income tax of previous years	18	—	—
Adjustments in respect of deferred income tax of previous years	160	—	—
Effects from Recognition or Non-Recognition of DTA through Equity	(1,012)	(581)	(1,590)
Effects of (Non-) Recognition of tax loss carryforwards recognized in prior years	(1,716)	—	327
Effects from differences between Group and local tax rates	8	(8)	(2)
Effects resulting from non-recognition of tax loss carryforwards	(30,168)	(114,999)	(69,724)
Effects resulting from non-recognition of DTA	(179)	(7,363)	(626)
Non-recognition of DTA for deductible temporary differences from SBP	(2,946)	—	—
Non-deductible expences for tax purposes	—	—	(119)
- Effects from (additions / deductions) for local trade taxes	(63)	(176)	(330)
- Other non-deductible expenses / including "Zinsschranke"	(1,154)	(101)	—
Other effects	(39)	2,426	(1,236)
Effective tax benefit / (expense)	**726**	**782**	**126**

Deferred taxes

Deferred taxes relate to the following:

	December 31, 2021 EUR k	December 31, 2022 EUR k
Intangible assets	(5)	19,081
Property, plant and equipment	(2,136)	(2,774)
Right of use-assets	(9,420)	(12,740)
Other assets	(153)	(90)
Inventories	—	—
Trade Receivables	151	134
Contract assets	—	15
Other current assets	1,215	1,660
Cash and cash equivalents	(308)	(224)
Assets	(10,656)	5,062
Lease liabilities (non-current portion)	7,445	10,810
Financial liabilities / Convertible Loan	—	—
Other Non-current financial liabilities	—	—
Other non-current liabilities	(130)	(77)
Trade and other payables and provision	(229)	(194)
Lease liabilities (current portion)	1,011	1,414
Other liabilities and provision	22,237	641
Liabilities	30,334	12,594
Deferred Taxes on temporary differences	19,678	17,656
Non-Recognition of Deferred Tax Assets (DTA) on temporary differences	(19,881)	(21,765)
DTA on deductible temporary differences Share-based Payment	2,769	3,995
Deferred Taxes on loss carryforwards	294	1,392
Deferred Taxes Total	2,861	1,278

The Balance Sheet as of December 31, 2022 shows a deferred tax asset of EUR 1,297k and deferred tax liability of EUR 19k. The deferred taxes as of this date were in total EUR 1,278k.

The following unused tax losses for which no deferred tax asset is recognized in the statement of financial position had been carried forward as of the end of the reporting periods:

Tax loss carryforwards	2020 EUR k	2021 EUR k	2022 EUR k
Unused tax losses for corporate income tax	775,956	1,181,225	1,427,735
Unused tax losses for trade tax	773,165	1,176,844	1,419,217
Unused interest carryforward (“Zinsschranke”)	3,627	2,879	—

DTA´s for temporary differences in the amount of EUR 21.8 million are valuated to zero at the year end 2022 because they are not recoverable. Most of those DTA results from differences in accruals between IFRS and German Tax GAAP.

The following deductible temporary differences for which no deferred tax asset is recognized in the statement of financial position had been carried forward as of the end of the reporting periods:

Deductible temporary differences	2020 EUR k	2021 EUR k	2022 EUR k
Not recognized over P&L	109,272	163,607	31,794
Not recognized over equity	415,018	110,749	—

The amounts disclosed above (in respect of the development of deductible temporary differences not recognized) also result mainly from share-based payments as described in Note 10 share-based payments. These programs will become tax-deductible according to German income tax regulations upon exercise. The reported amount "Not recognized over P&L" is the amount that has been cumulatively expensed in CureVac`s consolidated financial statements according to IFRS until December 31, 2022, for these programs (less the amounts for which deferred tax assets have been recognized) with appr. EUR 0,44 million relating to fiscal 2022 (2021: EUR 14.3 million) and the remainder to prior periods. The reported amount "Not recognized over equity" represents the amount that would be credited against equity according to IAS 12.68A-C (less the amounts for which deferred tax assets have been recognized).

An amount of EUR 1,200 k is shown as a DTA for anticipated losses of the SBP which will reduce the current tax in the next year when the options will be exercised.

The reported amount of "Not recognized over equity" may significantly fluctuate depending on the share price of CureVac which itself would lead to another allocation of the deferred tax asset recognized through profit or loss or equity. The same considerations apply to the deferred tax asset recognized for unused tax loss carryforwards. Hence, there might be significant changes in the allocation of deferred tax assets to be recognized through profit or loss or equity in the future which might lead to significant volatilities in the P&L line item income taxes solely due to the changes in the share price of CureVac.

Deferred tax assets on tax loss carryforwards and deductible temporary differences in excess of taxable temporary differences have not been capitalized as management concluded that there is not sufficient probability as per IAS 12 that there will be future taxable profits available in the foreseeable future against which the unused tax losses can be utilized. The accumulated unused tax losses relate entirely to Germany.

15. Earnings per share

Amounts in this Note reflect the retrospective effect of the share split resulting from the corporate reorganization described in Note 1.

Earnings per share is calculated by dividing the consolidated net loss of CureVac by the weighted average number of shares outstanding in the fiscal period.

The weighted average number of shares outstanding in fiscal 2020, 2021 and 2022 was 132,195,792, 186,012,586 and 189,074,911, respectively. This has led to basic loss per share of EUR 0.98, EUR 2.21 and EUR 1.32 for fiscal 2020, 2021 and 2022, respectively.

CureVac has several instruments, including contingently issuable shares, that could potentially dilute basic earnings per share in the future, but are not included in the calculation of diluted earnings per share because they are antidilutive for the period presented.

16. Disclosure of financial instruments and management of financial risks

General information

CureVac is exposed to certain financial risks with respect to its assets and liabilities and the transactions associated with its business model. These risks generally relate to credit risks, liquidity risks and market risks (including currency risk, interest rate risk and price risk).

The aim of risk management is to limit the potential negative impact on expected cash flows and take advantage of any opportunities that arise. As a result, the management of CureVac assesses at least once a year whether risks have changed and whether the measures in place to limit risk are still sufficient.

Credit risk

Credit risk is managed by CureVac's finance department. Credit risk arises from cash and cash equivalents and other financial assets, including deposits with banks and financial institutions, as well as credit exposures to customers, including outstanding receivables and contract assets.

CureVac is exposed to bank default and concentration risk as its cash is concentrated at few financial institutions. The Managememnt distributed the cash to decrease concentration risk at December 31, 2022, deciding to pool 16% of the cash at Germany's largest private bank and 79% at a major German Landesbank; the remaining cash balance is maintained at other banks. The focused cash management structure with few banks allows enhanced bank risk supervision. The market capitalization of all listed banks is regularly reviewed. Credit risk is further limited by investing only in liquid instruments.

CureVac is also exposed to a credit risk for all receivables and contract assets. Counterparty credit limits are reviewed by CureVac's Management Board on an annual basis and may be updated throughout the year. The limits are set to minimize the concentration of risks and therefore mitigate financial loss through a counterparty's potential failure to make payments. The Group manages its credit risk with customers by closely monitoring its receivables. The risk of default is considered to be low because the structure of customers consists of reputable collaborating parties and government grantors. Receivables management and financial accounting incorporates monitoring of payments received and any overdue receivables.

The carrying amount of other financial assets recognized determines the maximum theoretical credit risk. As of the end of fiscal 2022, available funds are deposited at two reputable financial institutions.

In connection with cash and cash equivalents, (other) financial assets, trade receivables and contract assets, CureVac uses the simplified approach under IFRS 9 in determining the loss allowance at an amount equal to the lifetime expected credit losses. As of December 31, 2022, the loss allowance for the "expected credit losses" totaled to EUR 99k (2021: EUR 105k, 2020: EUR 182k), resulting in an effect recognized in profit and loss in the consolidated statement of operations and other comprehensive expense in fiscal 2022 of EUR 6k (2021: EUR 77k, 2020: EUR 106k).

Liquidity risk / Capital management

For the purpose of CureVac's capital management, capital includes share capital and all other equity reserves attributable to the equity holders. The primary objective of CureVac's capital management is to maximize the shareholder value through investment in the development activities of the Group.

Based on its business as an active research group, CureVac has historically relied almost exclusively on equity funding by its shareholders and lenders as a means of financing itself prior to successful development and sales of a marketable product.

The Group's finance department reviews the total amount of cash of the Group on a weekly basis. As part of this review, the committee considers the total cash and cash equivalents, the cash outflow, currency translation differences and refinancing activities. The Group monitors cash using a burn rate. The cash burn rate is defined as the average monthly net cash flow from operating and investing activities during a financial year.

In meeting its financing objectives, the Group negotiates and enters into research cooperation agreements. In general, the aim is to maximize the financial resources available for further research and development projects.

CureVac is not subject to externally imposed capital requirements. However, certain grant funds received may be required to be returned if qualifying costs are not incurred or are not incurred in accordance with the grant terms (see also Note 3.2. and Note 3.7.).

As described in Note 9, the Group has an active at-the-market offering program through which, from time to time, it may be able to raise additional capital through the issuance of common shares.

No changes were made in the objectives, policies or processes for managing cash during the years ended December 31, 2022 and 2021.

In order to safeguard liquidity, the Group invests funds not required immediately for operating purposes in short-term investments at banks with high standing and call-deposit accounts with maturity up to three months. Liquidity risks are therefore expected to be low. The Group does not enter into trading of financial instruments and monitors its risk of a shortage of funds using a liquidity planning tool.

Historically, CureVac has relied on financing from shareholders, grant income and collaborators in order to ensure sufficient liquidity. Lack of external financial support could pose a risk of going concern. The liquidity management of CureVac ensures the availability of cash and cash equivalents for operational activities and further investments through appropriate budget planning.

Ultimately, the responsibility for liquidity risk management lies with management, who has established an appropriate approach to managing short-, medium- and long-term financing and liquidity requirements. CureVac manages liquidity risks by holding appropriate reserves, as well as by monitoring forecasted and actual cash flows and reconciling the maturity profiles of financial assets and liabilities.

The table below summarizes the maturity profile of the Group`s financial liabilities based on contractual undiscounted payments:

2022	less than 3 months EUR k	3 to 12 months EUR k	1 to 5 years EUR k	> 5 years EUR k	Total EUR k
Contractual commitments	—	(49,923)	(24,377)	—	**(74,300)**
Lease liabilities (Note 4.2)	(1,834)	(5,413)	(25,693)	(21,783)	**(54,723)**
Other liabilities (Note 12)	(21,603)	(19,844)	(62,286)	(20)	**(103,753)**
Trade and other payables (Note 11)	(68,786)	(4,677)	—	—	**(73,463)**
Total	**(92,223)**	**(79,857)**	**(112,356)**	**(21,803)**	**(306,239)**

2021	less than 3 months EUR k	3 to 12 months EUR k	1 to 5years EUR k	> 5 years EUR k	Total EUR k
Contractual commitments	—	(163,557)	—	—	(163,557)
Lease liabilities (Note 4.2)	(850)	(4,183)	(21,649)	(10,331)	(37,013)
Other liabilities (Note 12)	(79,927)	(80,116)	(10,018)	(12)	(170,073)
Trade and other payables (Note 11)	(99,035)	(638)	(28,030)	—	(127,703)
Total	**(179,812)**	**(248,494)**	**(59,697)**	**(10,343)**	**(498,346)**

Foreign currency risk

Foreign currency risk is the risk that the fair value or future cash flows of an exposure will fluctuate because of changes in foreign exchange rates. CureVac's exposure to the risk of changes in foreign exchange rates relates primarily to the Group's operating activities (when revenue or expense is denominated in a foreign currency) and the amounts held as cash and cash equivalents.

CureVac N.V.'s, CureVac SE's, CureVac Manufacturing GmbH's, CureVac Corporate Services GmbH'S, CureVac RNA Printer Gmbh's, CureVac Belgium SA's and CureVac Netherlands BV'S functional currency is the Euro. The functional currency of CureVac Inc. is the USD and of CureVac Swiss AG the CHF. CureVac AG's exposure in foreign currency at the end of 2022 and 2021 is as follows:

	2022 (in thousands)	
Cash and cash equivalents	106,566 EUR	113,664 USD
Trade and other receivables	— EUR	— USD
Total monetary assets in foreign currency	**106,566 EUR**	**113,664 USD**
Trade and other payables	26,232 EUR	27,979 USD
	87 EUR	77 GBP
	13 EUR	13 CHF
Total monetary liabilities in foreign currency	**26,332 EUR**	

	2021 (in thousands)	
Cash and cash equivalents	51,363 EUR	58,174 USD
Trade and other receivables	182 EUR	206 USD
Total monetary assets in foreign currency	**51,545 EUR**	**58,380 USD**
Trade and other payables	52,594 EUR	59,568 USD
	19 EUR	20 CHF
Total monetary liabilities in foreign currency	**52,613 EUR**	

As shown in the tables above, CureVac N.V. is exposed to a currency risk only in relation to the USD. Therefore, a foreign currency sensitivity analysis is only presented in respect to the net exposure in USD at fiscal year ends. CureVac's net exposure in USD is the difference between monetary assets in USD and monetary liabilities in USD and developed as follows:

Net exposure in USD

2021 (1 EUR= 1.1326 USD)	2022 (1 EUR = 1.0666 USD)
EUR -3,964k from USD -4,490k	**EUR 77,649k from USD 82,822k**

At December 31, 2022, if the EUR had weakened 10 per cent against the US dollar with all other variables held constant, pre-tax loss for the year would have been EUR 8,628k (2021: EUR -440k) lower and post-tax loss would have been EUR 6,085k (2021: EUR -310k). Conversely, if the EUR had strengthened 10 per cent against the US dollar with all other variables held constant, pre-tax loss would have been EUR 7,059k (2021: EUR -360k) higher and post-tax loss would have been EUR 4,978k (2021: EUR -254k) higher. The effects on pre- and post-tax loss and (accumulated) other comprehensive income due to fact that CureVac Inc's functional currency is the USD would still have been immaterial as of December 31, 2022.

CureVac did not have derivatives in 2022 and 2021.

Interest rate risk

Interest rate risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in market interest rates. CureVac's exposure to the risk of changes in market interest rates relates primarily to the CureVac`s cash and cash equivalents with floating interest rates.

If interest rates as of December 31, 2022 had been 1% higher while all other variables had remained the same, the net loss for the year (before and after tax) would have been EUR 4,959k (2021: EUR 8,116k) lower because the higher interest income would have been generated from floating rates on invested cash and cash equivalents.

Fair value measurement

All assets and liabilities for which fair value is measured or disclosed in the financial statements are categorized with the fair value hierarchy, described as follows, based on the lowest level input that is significant to the fair value measurement as a whole:

- Level 1 — Inputs use quoted prices in active markets for identical assets or liabilities
- Level 2 — Inputs are inputs, other than quoted prices included in Level 1, which are directly or indirectly observable
- Level 3 — Inputs are unobservable and have values estimated by management based on market participant assumptions which are reasonably available

All financial instruments are measured at amortized cost at December 31, 2022 and December 31, 2021. Apart from this, liabilities from licenses agreements (i.e., acquired intangible assets) of EUR 0k (2021: EUR 932k), are classified as financial liabilities at fair value through profit or loss under the Level 2 input factors. Management assessed that the fair values of cash and cash equivalents, short-term investments, trade receivables and other financial assets, trade payables and other current liabilities as well as liabilities from licensing agreement approximate their carrying amounts. Moreover, management assessed that the potential differences between carrying amounts and fair value of liabilities to banks, (finance) lease liabilities and the liabilities for licensing agreements should be immaterial.

17. Notes to the consolidated statements of cash flows

Changes in liabilities arising from financing activities

in thousands of EUR	January 1, 2022	Cash flows	Reclassification	Disposals	New Leases	Accrued interest	Paid Interest	Foreign Exchange Movements	December 31, 2022
Lease Liabilities (Note 4.2)	28,892	(6,439)	—	—	17,241	—	2,218	174	**42,086**
Total liabilities from financing activities	**28,892**	**(6,439)**	**—**	**—**	**17,241**	**—**	**2,218**	**174**	**42,086**

in thousands of EUR	January 1, 2021	Cash flows	Reclassification	Disposals	New Leases	Accrued interest	Paid Interest	Foreign Exchange Movements	December 31, 2021
EIB loan (Note 13)	25,189	(25,000)	—	—	—	1,444	(1,633)	—	—
Lease Liabilities (Note 4. 2)	30,087	(4,913)	—	(943)	2,763	—	1,729	169	28,892
Total liabilities from financing activities	**55,276**	**(29,913)**	**—**	**(943)**	**2,763**	**1,444**	**96**	**169**	**28,892**

The cash flow includes an interest component which is presented separately.

18. Commitments and contingencies

No material contingent liabilities resulting from claims and legal proceedings exist as of December 31, 2022. Refer to Note 12 for provisions recognized for contract terminations. For contractual commitments, refer to Note 16.

19. Remuneration of the Company's key management personnel

Total remuneration of key management personnel

Remuneration of the Company's key management personnel was as follows in 2022:

Remuneration of key management in 2022	Management Board	Supervisory Board
	EUR k	EUR k
Short-term benefits	3,067	669
Share-based payments	6,689	478
Total	9,756	1,147

Remuneration of the Company's key management personnel was as follows in 2021:

Remuneration of key management in 2021	Management Board	Supervisory Board
	EUR k	EUR k
Short-term benefits	3,098	646
Share-based payments	12,673	566
Total	15,771	1,212

The amounts disclosed in the table are the amounts recognized as an expense during the reporting period related to key management personnel.

20. Other related party disclosures

dievini Hopp BioTech holding GmbH & Co. KG

As disclosed in Note 1, during fiscal 2022, dievini Hopp BioTech holding GmbH & Co. KG (dievini), which is an investment company dedicated to the support of companies in health and life sciences, was the largest shareholder of CureVac. Together with its related parties, dievini has held shares and voting rights in CureVac between approximately 43–46 % during that period. dievini is thus the de facto parent of the Group. Dietmar Hopp, Daniel Hopp and Oliver Hopp are the ultimate controlling persons (of the main shareholders) of dievini, and, therefore, control the voting and investment decisions of dievini.

Other related party transactions

Transfer of shares from the Funding Shareholders

As discussed in Note 10, due to certain virtual share exercises under the Prior VSOP during the year 2022: 777,260 (2021:1,524,900) common shares were transferred to the Company by the Funding Shareholders, with no consideration paid in exchange, and all of these shares were subsequently transferred to fulfill obligations from option exercises.

Rittershaus Rechtsanwaelte

Since December 15, 2005, a consultant agreement is in place for an indefinite term with Rittershaus. The agreement can be terminated without notice by CureVac and with notice of three months to the end of the quarter by Rittershaus. In fiscal 2022, consulting fees of EUR 518k (2021: EUR 757k, 2020: EUR 990k) were paid to the Rittershaus. Prof. Dr. Christof Hettich is managing director of Rittershaus and was managing director at dievini until June 2022 as well.

Dietmar Hopp

During 2019, Dietmar Hopp, principal of dievini Hopp BioTech holding GmbH & Co. KG (dievini), the majority shareholder of the Group, granted two convertible loans to the Group which were terminated in July 2020 and fully repaid in August 2020. Additionally, in 2020, DH-LT Investments GmbH, a company beneficially owned by Dietmar Hopp, managing director of dievini, the Groups largest shareholder, purchased EUR 100,000k of the Group's common shares at the price of USD 16 per share. In 2022 a total of EUR 58k was paid to dievini Hopp BioTech Holding GmbH & Co. KG.

Antony Blanc

In 2020, a consulting agreement between CureVac AG and Clarentis SRL was made. Clarentis SRL is a wholly owned consulting company of Antony Blanc, PhD, the CBO of CureVac. After the transition of Antony Blanc to the Management Board in February 2021, the contract was no longer active, and no new orders were placed. In Q3 2021, a milestone payment, which related to the submission of the EMA dossier for CVnCoV and which amounted to EUR 100k was made to fulfil a contractual obligation from the consulting agreement in place before Antony Blanc joined the Management Board. In addition to his Management Board position at CureVac NV, Antony also took over the role as Management Director at CureVac Belgium SA. He executes this function by using Clarentis SRL. As it relates to these services in 2022, CureVac paid an amount of EUR 69k (2021: EUR 0k, 2020: EUR 0k). The amounts invoiced for this function/services are offset/deducted from his base compensation for his function on the Board of Management of CureVac N.V.

BePharBel Manufacturing S.A.

In December 2020, CureVac Manufacturing GmbH (formerly CureVac Real Estate GmbH) and BePharBel Manufacturing S.A., entered into a commercial supply agreement to develop and manufacture the diluent that was expected to be used to dilute the Group's first concentrated COVID-19 vaccine candidate, CVnCoV, to the amount specified by each dose level. Pursuant to the terms of the agreement, it was intended that BePharBel Manufacturing would manufacture and deliver to CureVac Manufacturing GmbH a low seven figure amount of commercial batches of diluent per year, in 2021 and 2022. Following the withdrawal of the CVnCoV in October 2021 due to COVID-19 virus drift, WHO COVID vaccine efficiency recommendation and market expectations, CureVac Manufacturinmg GmbH terminated the commercial and supply agreement with BePahrBel and entered into negotiations on a structured and rapid wind-down of the ordered production. The Parties agreed on a settlement in May 2022 of all claims resulting from the commercial and supply agreement for an amount of EUR 3,900k, which had beed recognized in provisions, based on estimate, as of December 31, 2021. In total an amount of EUR 4,016k was paid. Baron Jean Stéphenne, our supervisory board member, holds directly and indirectly 15.61% of BePharBel Manufacturing's equity and is a director of BePharBel Manufacturing, and Baron Jean Stéphenne's son, Vincent Stéphenne, holds 1.43% of BePharBel Manufacturing's equity and is a managing director of BePharBel Manufacturing.

Mariola Fotin-Mleczek

In 2022, a consulting agreement between CureVac N.V. and Mariola Fotin-Mleczek was made. In 2022 a total of EUR 20k was paid. Due to the exercise of the Old VAP award in December 2022, CureVac has a receivable position of EUR 131k as per year-end for the income tax and social security liability. CureVac has received the money in February 2023.

Florian von der Mülbe

Due to the exercise of the Old VAP award in December 2022, CureVac has a receivable position of EUR 559k as per year-end for the income tax and social security liability. CureVac has received the money in February 2023.

Dr. Ingmar Hörr

Due to the exercise of the Old VAP award in December 2022, CureVac has a receivable position of EUR 573k as per year-end for the income tax and social security liability. CureVac has received the money in February 2023.

Indemnification Agreements

The Company's articles of association require it to indemnify it's current and former managing directors and supervisory directors in relation to acts or omissions in the performance of their duties to the fullest extent permitted by law, subject to certain exceptions. We entered into indemnification agreements with all our managing directors and supervisory directors.

21. Business Combinations

Business Combination and Goodwill – Frame Acquisition

Effective July 1, 2022 ('closing date'), CureVac N.V. acquired all shares of Frame Pharmaceuticals B.V., Amsterdam, Netherlands ('Frame Pharmaceuticals'). Frame Pharmaceuticals focuses on the development of a proprietary platform enabling the identification of structural changes within the cancer genome and has strong competencies in antigen discovery as well as validation for personalized cancer vaccines. CureVac's management and supervisory board expect that the acquisition will contribute several key elements for the required end-to-end building blocks for CureVac's broader oncology strategy.

Frame Pharmaceuticals contributed no revenues and a loss of EUR 1.3 million to the 2022 consolidated net loss. Assuming an initial consolidation of Frame Pharmaceuticals on January 1, 2022, the Group's revenue would be unchanged, and the loss would have been EUR 3.9 million higher, respectively. In determining these amounts, management has assumed that the fair value adjustments made at the acquisition date would also have applied on January 1, 2022.

In the purchase price agreement ('SPA') dated June 8, 2022, total consideration of up to EUR 32.0 million, subject to certain adjustments for vested and non-vested employee options of the acquiree plus an amount of EUR 1.56 million for the assumption of an outstanding obligation resulting from advisory services, was agreed. The consideration consisted of the transfer of shares in CureVac N.V. ('CureVac Shares') and minor cash payments. The number of CureVac Shares to be issued as part of the consideration were agreed in the SPA based on EUR 16.44, the 60-trading day volume weighted average price through June 3, 2022 ('Signing Day Share Price').

The total consideration is split into three payments, two of which are contingent upon the achievement of defined milestones (contingent consideration). At the closing date, CureVac paid 50% of the total consideration, i. e., EUR 16.0 million plus the consideration for the outstanding obligation of EUR 1.56 million as follows:

- Issuance and transfer of 810,242 shares (EUR 11,040k) to former Frame shareholders. The respective share price of one CureVac Share was EUR 13.63 ('Closing Share Price').
- Issuance and transfer of further 48,254 shares (EUR 658k, valued at the Closing Share Price) as consideration for discharging the contractual obligations for the outstanding advisory agreements of EUR 1,560k.
- Payment of EUR 585k in cash, consisting of EUR 335k being the consideration for the settlement of the vested employee options, and an additional EUR 250k.

Payment of the remaining 50% of the total consideration is contingent upon the achievement of two milestones. A further 194,644 shares (representing 10% of EUR 32.0 million divided by the Signing Share Price) are issuable upon the achievement of a successful investigational new drug application filing for a product candiate of the Group that consists of at least one antigen based on frameshift-mutation identified by Frame's algorithms; ("Milestone 1") and a further 778,575 shares (representing 40% of EUR 32.0 million divided by the Signing Share Price) are issuable upon successful proof of mechanism in humans of that product candidate ("Milestone 2"). The fair value of these contingent payments was determined by considering the likelihood of the events occurring and totalled, based on the Closing Share Price, EUR 7,198k (Milestone 1: EUR 1,831k and Milestone 2: EUR 5,367k).

Consequently, the total consideration transferred for the business combination was determined to be EUR 19,481k, consisting of:

- Issuance and transfer of 858,496 CureVac shares with a fair value of EUR 11,697k,
- Payment of EUR 585k in cash, and
- Contingent consideration, classified as equity, with a fair value of EUR 7,198k. The contingent consideration will be settled by the issuance of a maximum of further 973,236 CureVac shares.

The contingent consideration of EUR 7,198k was valued by applying an estimated probability of the milestone being achieved to the payments due upon achievement. These probabilities were derived from third-party clinical development success rate studies.

In addition, 89,655 restricted stock unit awards (RSUs) were issued to certain employees to replace existing share-based payment awards of Frame Pharmaceuticals. This element is accounted for as a separately from the business combination as an equity-settled share-based transaction according to IFRS 2 (see Note 10). The total fair value of the grant was determined to be EUR 1,218k and will be expensed in the functional cost category to which the award recipient's costs are allocated (i.e., general and administrative expenses or research and development expenses) over the individual vesting periods for the 3 tranches, which run through June 30, 2023, June 30, 2024, and June 30, 2025.

Transactions costs in relation to the business combination amounting to EUR 500k were expensed and recognized within general and administrative expenses.

The final fair values in accordance with IFRS 3 of the identifiable net assets as of the date of acquisition were as follows:

in EUR thousands	Fair value recognized on acquisition
Non-current assets	**6,592**
Property, plant and equipment	206
Right-of-use assets	170
Intangible asset (Technology)	6,216
Current assets	**966**
Trade and other receivables	658
Cash and cash equivalents	308
Total assets	**7,558**
Non-current liabilities	**134**
Lease liabilities	114
Deferred tax liabilities (net of deferred tax assets)	20
Current liabilities	**406**
Lease liabilities	55
Accounts Payables	346
Other current liabilities	5
Total liabilities	**540**
Net assets acquired	**7,018**

The acquired receivables have since been collected in full except for EUR 24k related to rental deposits.

The technology intangible asset consists of a bioinformatical platform for cancer antigen discovery and validation for off-the-shelf and personalized cancer vaccines. The fair value of the technology of EUR 6,216k was determined by applying the replacement cost approach due to its early stage. The replacement cost was derived from historical costs incurred to create the technology.

As per July 1, 2022, a net deferred tax liability of EUR 20k has been recognized for the excess of deferred tax liabilities of EUR 1,550k on taxable temporary differences over deferred tax assets of EUR 1,530k arising mainly from tax loss carry forwards (of approximately EUR 5,800k).

Goodwill was recognized as a result of the acquisition as follows:

in EURk	
Consideration transferred	19,481
Net Assets acquired	(7,018)
Goodwill	**12,463**

The goodwill is mainly attributable to the synergies and an assembled workforce as well as the strategic benefits to the Group. The goodwill is not deductible for tax purposes.

Overview of cash flows on acquisition:	EURk
Transaction costs of the acquisition (included in **cash flows provided by(used in) operating activities**)	**(500)**
Payment of consideration in cash and cash equivalents	(585)
Cash acquired with the subsidiary (included in cash flows provided by (used in) investing activities)	308
Included in cash flows from investing activities	**(277)**
Net cash flows on acquisition	**(777)**

22. Subsequent events

Beginning of January 2023, positive preliminary data from ongoing Phase 1 clinical programs in COVID-19 and seasonal flu, assessing modified mRNA technology were published. The tested vaccine candidates are being developed in collaboration with GSK. The preliminary results generated by the broad technology approach, testing modified and unmodified nucleotides showed that vaccine candidates using a modified second-generation mRNA backbone produced promising immunogenicity and reactogenicity profiles in both indications. At the end of January, the Company published additional data with a focus on older adult age groups in both indications. The data further support the decision to advance updated versions of the modified mRNA COVID-19 and flu vaccine constructs to the next stage of clinical testing in 2023.

In February 2023, the Company closed a public offering by which it sold 27,027,028 common shares for aggregate gross proceeds to the company of $250.0 million (EUR 232.6 million) before underwriting discounts, commissions and offering expenses payable by the Company.

In the Extraordinary General Meeting of Shareholders of CureVac NV on March 28, 2023, Dr. Alexander Zehnder was elected as CEO of the Company effective April 1, 2023. This change of CEO was announced on January 6, 2023 and took place after a short transition phase as designated CEO. Dr. Alexander Zehnder followed Dr. Franz-Werner Haas, who with effect of March 31, 2023, resigned from office after more than 10 years as a member of the CureVac management board and a three-year tenure as CEO. In addition, the Shareholders confirmed the appointment of Dr. Myriam Mendila as Chief Development Officer effective February 1, 2023.

10. Company Financial Statement

CureVac N.V.

Company Financial Statements

for the Year ended
December 31, 2022

CureVac N.V.

Company Statement of Profit and Loss and Other Comprehensive Income (Loss)

(in thousands of EUR)	**Note**	**Years ended December 2021**	**2022**
General and administrative expenses	**3**	4.717	(2.919)
Other operating expenses		(1.116)	(1.146)
Total expenses		**3.601**	**(4.065)**
Net operating result		**3.601**	**(4.065)**
Other operating income		1.278	525
Other interest income and similar income	**4**	7.800	1.611
Interest expenses and similar expenses	**4**	(5.476)	(3.909)
Result before tax		**7.203**	**(5.839)**
Taxes	**12**	-	(225)
Share in results of investments in subsidiaries after tax	**5**	(418.919)	(242.966)
Result after tax		**(411.716)**	**(249.029)**
Foreign currency adjustments		(91)	(105)
Total comprehensive loss for the period		**(411.807)**	**(249.134)**

CureVac N.V.

Company Statement of Financial Position
(after appropriation of result)

(in thousands of EUR)	Note	December 31, 2021	December 31, 2022
Assets			
Non-current assets			
Investments in subsidiaries	**6**	303.494	80.092
Total non-current assets		**303.494**	**80.092**
Current assets			
Loans to subsidiaries	**7**	60	30.000
Receivables from subsidiaries	**7**	43.353	41.936
Prepaid expenses and other assets	**7**	27.448	18.892
Cash and cash equivalents	**8**	348.168	382.466
Other financial assets		-	560
Total current assets		**419.029**	**473.855**
Total assets		**722.523**	**553.946**
Equity and liabilities			
Equity	**9**		
Issued capital		22.454	23.400
Capital reserve		1.722.841	1.815.806
Accumulated deficit		(1.056.785)	(1.305.814)
Currency translation reserve		(34)	(139)
Total equity		**688.476**	**533.253**
Current liabilities			
Trade and other payables	**10**	3.913	895
Payables to subsidiaries	**10**	26.182	16.634
Other liabilities	**11**	3.952	3.165
Total current liabilities		**34.047**	**20.693**
Total liabilities		**34.047**	**20.693**
Total equity and liabilities		**722.523**	**553.946**

1. Corporate Information

CureVac N.V. ("CureVac" or "CV" or the "Company") is the parent company of CureVac Group ("Group") and, along with its subsidiaries, is a global biopharmaceutical company developing a new class of transformative medicines based on the messenger ribonucleic acid (mRNA) that has the potential to improve the lives of people.

The Company is incorporated in the Netherlands and is registered in the commercial register at the Netherlands Chamber of Commerce under RSIN 861149336, with statutory seat in Amsterdam. The Company's registered headquarters is Friedrich-Miescher-Strasse 15, 72076 Tuebingen, Germany. The major shareholder and ultimate parent company of the Group is dievini Hopp BioTech holding GmbH & Co. KG (dievini), which is an investment company dedicated to the support of companies in health and life sciences.

On August 14, 2020, the Company completed an initial public offering (IPO) on the Nasdaq Global Market; in connection with the IPO, the Company underwent a corporate reorganization by which CureVac N.V. became the parent holding company with 100% interest in CureVac AG. Prior to the reorganization, CureVac AG was the parent holding company of the Group; as part of the reorganization, CureVac B.V. was formed on April 7, 2020, and existing shareholders of CureVac AG subscribed for new common shares in CureVac B.V. and agreed to transfer their respective shares in CureVac AG to CureVac B.V. as a contribution in kind against issuance of the common shares in CureVac B.V. shares (share split) on a 1-to-133,0778 basis. As a result, CureVac B.V. became the holding company of CureVac AG, while the existing shareholders had a 100% shareholding in CureVac B.V. Effective with the IPO, CureVac B.V. changed its legal form and became CureVac N.V. and the common shares of CureVac B.V. were converted to common shares of CureVac N.V. In 2022, CureVac AG merged with CureVac Beteiligungsverwaltungs GmbH to CureVac SE in 2022. For further information please see note 1 of the consolidated financial statement.

Basis of preparation

The description of the activities and the structure of CureVac N.V. ("CureVac" or "CV" or the "Company") as included in the notes to the consolidated financial statements also apply to the Company Financial Statements.

The financial statements of CureVac N.V. included in this section are prepared in accordance with Part 9 of Book 2 of the Dutch Civil Code. Section 2:362 (8) of the Dutch Civil Code, allows companies that apply IFRS as endorsed by the European Union in their consolidated financial statements to use the same measurement principles in their company financial statements. The Company has prepared these Company financial statements using this provision.

The accounting policies are described in the Summary of significant accounting policies of the consolidated financial statements and are deemed incorporated and repeated herein by reference.

In case single balance sheet line items and profit and loss accounts are not further disclosed in the company financial statements, we refer to the disclosure to the consolidated financial statements.

Functional currency

The functional currency is the Euro, which is the reporting currency of CureVac.

Going Concern

These financial statements have been prepared on the basis of the going concern assumption.

2. Significant accounting policies

The accounting policies as included in the notes to the consolidated financial statements also apply to the company financial statements.

Investment in subsidiaries

Investments in subsidiaries refers to contractual and non-contractual involvement that exposes an entity to variability of returns from the performance of the other entity. An investment in subsidiaries can be evidenced by but is not limited to, the holding of equity or debt instruments as well as other forms of involvement such as the provision of funding, liquidity support, credit enhancement, and guarantees. It includes the means by which an entity has control or joint control of, or significant influence over, another entity. An entity does not necessarily have an interest in another entity solely because of a typical customer-supplier relationship.

Investments in subsidiaries are accounted using the equity method. For an overview of subsidiaries, please refer to note 6 and the consolidated financial statements.

Expected credit loss

Expected credit losses on intercompany receivables are offset against the intercompany receivables themselves.

Foreign currency translation

The functional currency is the Euro, which is the reporting currency of CureVac. Monetary assets and liabilities in a foreign currency are recognized at the exchange rate in effect on the date of the transaction and later at the rate in effect on the reporting date. Differences resulting from foreign currency translation are recognized in Other interest income and similar income and Interest expenses and similar expenses in the Company Statements of Profit and Loss account and Other Comprehensive Income (Loss).

NOTES TO THE COMPANY STATEMENT OF PROFIT AND LOSS AND OTHER COMPREHENSIVE INCOME

3. General and administrative expenses

General and administrative expenses include the following:

	2021	2022
	EURk	EURk
Personnel		
Wages and salaries (gross)	(1.952)	(2.304)
Social security charges (gross)	(20)	(56)
Share-based payment expenses (gross)	(2.596)	(6.921)
Legal and other professional services (gross)	(3.970)	(2.748)
Other (gross)	(7.782)	(10.716)
Total recharged to subsidiaries	21.037	19.826
Total (net)	**4.717**	**(2.919)**

Personnel expenses are for the seven Management Board Members of CureVac N.V. incurred since October 2021. All Board Members are employed outside of the Netherlands. As CureVac N.V. provides management services for the whole group, costs are charged to CureVac SE with a mark-up of 5% under the current service agreement. Legal and other professional services mainly consist of legal, tax and accounting services, for which an overview of fees paid to the statutory auditor Ernst & Young Accountants LLP and its network have been detailed below.

Other mainly consists of the insurance expenses of EURk 5.536 (2021: EURk 5.457). In addition, hereto an amount of EURk 2.019 (2021: EURk nil) was spend on commission costs relating to the At-the-market offering (ATM), resulting in an overall increase of the general and administrative expenses.

EY costs 2022

	Ernst & Young Accountants LLP	Other EY network	Total EY
	EUR	EUR	EUR
Statutory audit of financial statements	(166.000)	-	(166.000)
Other assurance services	-	(2.009.775)	(2.009.775)
Tax advisory services	-	(70.000)	(70.000)
Other non-audit services	-	(18.232)	(18.232)
Total	**(166.000)**	**(2.098.007)**	**(2.264.007)**

Ernst & Young Accountants LLP billed us approximately EURk 166 (2021: EURk 100) for local statutory audit services.

EY costs 2021

	Ernst & Young Accountants LLP	Other EY network	Total EY
	EUR	EUR	EUR
Statutory audit of financial statements	(100.000)	-	(100.000)
Other assurance services	-	(1.300.000)	(1.300.000)
Tax advisory services	-	(500.000)	(500.000)
Other non-audit services	-	-	-
Total	**(100.000)**	**(1.800.000)**	**(1.900.000)**

Other assurance fees

Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft billed us approximately EUR 2.0 million (2021: EUR 1.3 million) for audit services for fiscal 2022, including fees associated with the annual audit, consultations on various accounting issues, performance of local statutory audits and quarterly comfort letters relating to the at-the-market program, and review of offering documents filed with the SEC.

Ernst & Young Accountants LLP and/or Ernst & Young GmbH Wirtschaftsprüfungs-gesellschaft did not bill us for any other audit-related services for fiscal 2022 and 2021.

Tax advisory fees

Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft billed us approximately EUR 70k (2021: EURk 500) for tax fees, including fees associated with tax compliance, tax advice, and tax planning services for fiscal 2022, respectively.

Other non-audit fees

Ernst & Young GmbH Wirtschaftsprüfungsgesellschaft billed us EUR 18k for services other than those categorized in Audit Fees, Audit-Related Fees and Tax Fees described above for fiscal 2022 (2021: EURk 100).

4. Other interest income and similar income and Interest expenses and similar expenses

Financial income and expenses include the following:

	2021	2022
	EURk	EURk
Financial income	100	956
Foreign currency gains and (losses), net	7.082	561
Interest income from wholly owned subsidiaries	618	94
Financial expenses	(5.476)	(3.909)

Total	**2.324**	**(2.299)**

Interest income from wholly owned subsidiaries relates to the loan issued to CureVac SE in 2021 and CureVac Manufacturing GmbH in 2022. Financial expenses mainly include the foreign currency loss of EURk 2.942 (2021: EURk 2.990).

5. Share in results of investments in subsidiaries after tax

The share in results of subsidiaries has mainly decreased due to cost of sales expenses of the group compared to 2021. For further information we refer to note 3 of the consolidated financial statements.

NOTES TO THE COMPANY STATEMENT OF FINANCIAL POSITION

6. Non-current assets

Non-current assets consist of the Company's investment in its wholly-owned subsidiary CureVac SE (Tuebingen, Germany) of EURk 80.092 (2021: 303.494).

As of December 31, 2022, CureVac N.V. holds the following direct participating interests in subsidiaries:

Name	Location	Interest in %
CureVac SE	Tuebingen, Germany	100

CureVac AG merged with CureVac Beteiligungsverwaltungs GmbH to CureVac SE in 2022. For more information please see note 14 in the consolidated financial statement.

Through its direct participating interest in Curevac SE, the Company holds the following indirect participating interests:

Name	Location	Interest in %
CureVac Manufacturing GmbH	Tuebingen, Germany	100
CureVac Inc.	Boston, USA	100
CureVac Swiss AG	Basel, Switzerland	100
CureVac Corporate Services GmbH	Tuebingen, Germany	100
CureVac RNA Printer GmbH	Tuebingen, Germany	100
CureVac Belgium SA	Ottignies-Louvain-la-Neuve, BE	100
CureVac Netherlands B.V.	Amsterdam, Netherlands	100

CureVac N.V. operates and controls all of the business and affairs of the subsidiary and its respective subsidiaries.

Investments in subsidiaries 2022	**EURk**
Net book value per January 1, 2022	303.494
Movements in bookvalue 2022	
Capital contribution to Curevac SE	19.480
Share result from subsidiaries	(242.966)
Settlement of share-based payments on behalf of Curevac SE	(222)
Share-based-payments on subsidiary level	1.972
Income taxes recognized directly in equity	(1.646)
OCI on currency translation	(105)
Other	84
Total	80.092

7. Receivables and Prepaid Expenses

	2021	**2022**
	EURk	**EURk**
Loans to subsidiaries	60	30.000
Receivables from subsidiaries	43.353	41.936
Prepaid expenses and other assets	27.448	18.892
Total	70.861	90.829

The short-term loan to subsidiaries consists of the loan to CureVac Manufacturing GmbH which was repaid per April of 2023. Prepaid expenses are mostly driven by an amount of EURk 15.352 (2021: EURk 23.341) from VAT. In addition hereto the account includes an amount of EURk 3.236 (2021: EURk 3.228) for prepaid insurance costs. For the intercompany loan receivables, refer to Note 15.

Receivables from subsidiaries are mostly driven by EURk 21.071 recharge of Management services to subsidiaries and EURk 20.770 relating to the new VSOP (2021: EURk 21.600).

8. Cash and cash equivalents

Cash and cash equivalents amounted to EURk 382.466 (2021: EURk 348.168). EURk 168.127 (2021: EURk nil) is invested in short-term deposits with a maximum maturity of 3 months. The remaining cash is available for immediate use by the group, without any restrictions.

9. Equity

According to CureVac NV`s articles of association, which are effective as of August 14, 2020, the company`s authorized share capital amount to EUR 92.700.000. It is divided into 386.250.000 common shares and 386.250.000 preferred shares, each having a nominal

value of EUR 0,12. As of December 31, 2022, 194,997,091 common shares are outstanding, including 42,866 Treasury Shares held by CureVac N.V. and its subsidiary, and no preferred shares have been issued and all issued common shares issued and outstanding were fully paid. For further information we refer to the consolidated financial statements.

Common shares issued and outstanding at December 31, 2020	**180.460.565**
Follow-on public offering, incl. Greenshoe	5.750.000
Share option exercises	910.163
Common shares issued and outstanding at December 31, 2021	**187.120.728**
Shares issued as part of the at-the-market offering program	6.908.493
Shares issued to former shareholders of Frame Pharmaceuticals	858.496
Shares issued for LTIP option exercises and RSU deliveries	109.374
Common shares issued and outstanding at December 31, 2022	**194.997.091**

The development of equity is shown in the following tables.

(in thousands of EUR)	**Issued Capital**	**Capital Reserves**	**Treasury Shares**	**Accumulated Deficit**	**Currency Translation Reserve**	**Total Equity**
Balance as of January 1, 2021	**21.655**	**1.334.704**	**-**	**(645.069)**	**57**	**711.347**
Net loss	-	-	-	(411.716)	-	(411.716)
Other comprehensive income (loss)	-	-	-	-	(91)	(91)
Total comprehensive income (loss)	**-**	**-**	**-**	**(411.716)**	**(91)**	**(411.807)**
Share-based payment expense (Net of Taxes)	-	15.789	-	-	-	15.789
Exercise of options	109	3.077	-	-	-	3.186
Issuance of share capital (net of transaction costs)	690	403.372	-	-	-	404.062
Repurchase of common shares	-	(28.284)	(5.817)	-	-	(34.101)
Balance as of December 31, 2021	**22.454**	**1.728.658**	**(5.817)**	**(1.056.785)**	**(34)**	**688.476**

The main changes in 2022 can be summarized as follows:

(in thousands of EUR)	**Issued Capital**	**Capital Reserves**	**Treasury Shares**	**Accumulated Deficit**	**Currency Translation Reserve**	**Total Equity**
Balance as of January 1, 2022	**22.454**	**1.728.658**	**(5.817)**	**(1.056.785)**	**(34)**	**688.476**
Net loss	-	-	-	(249.029)	-	(249.029)
Other comprehensive income (loss)	-	-	-	-	(105)	(105)
Total comprehensive income (loss)	**-**	**-**	**-**	**(249.029)**	**(105)**	**(249.134)**
Share-based payment expense (Net of Taxes)	-	7.539	-	-	-	7.539
Issuance of share capital (net of transaction costs)	932	65.552	-	-	-	66.484
Share issuances and contingent consideration from business combinations	-	18.978	-	-	-	18.978
Exercise of options / Settlement of share-based payment awards	14	(3.440)	4.336	-	-	910
Balance as of December 31, 2022	**23.400**	**1.817.287**	**(1.481)**	**(1.305.814)**	**(139)**	**533.253**

On September 17, 2021, CureVac filed a prospectus for an "at-the-market" offering program to raise additional cash of up to USD 600,000k. The program was activated in June 2022. Through December 31, 2022, CureVac has issued 6,908,493 shares and raised gross proceeds of USD 69,139k. Offering costs for legal, accounting, printing and registration fees of EUR 1,058k were recognized as reduction to capital reserve against the proceeds from the offering.

On June 8, 2022, CureVac entered into a Share Purchase Agreement (SPA) to acquire all of the issued and outstanding shares of Frame Pharmaceuticals B.V., a research company focused on advanced genomics and bioinformatics, based in Amsterdam, Netherlands.

Under the SPA, the total consideration for the the purchase was up to EUR 34 million, conditioned on the meeting of certain development milestone payments. On the date of acquisition, July 1, 2022, CureVac issued 858,496 shares to the former shareholders of Frame Pharmaceuticals. For additional information we refer to note 21 of the consolidated financial statements.

A third 10 % portion of the (vested) virtual shares became exercisable on the second anniversary after IPO i. e., on August 14, 2022, because certain minimum trading volumes of the CureVac N.V. shares and liquidity levels were again reached. The beneficiaries declared the exercise of their then exercisable 777,260 virtual shares by Dec 12, 2022 and CureVac received 777,260 shares from the old shareholders on that day. On Dec 14, 2022, CureVac transferred 777,260 shares to the exercising beneficiaries. The portion of shares equaling the amount to be paid for (wage) tax and social security obligations were sold to pay for these amounts. For former employee’s CureVac shows a receivable position equaling

the amount to be paid for (wage) tax and social security obligations. The share price of CureVac on December 14, 2022 was EUR 6.96.

Share-based payments reflect the total share-based payment expense recognized and the recognized deferred tax assets which goes directly through equity on the level of CureVac SE, CureVac Manufacturing GmbH and CureVac Corporate Services GmbH (EURk 1,590). For more details on the deferred tax asset we refer to note 6 investment in associates and the deferred tax table of the consolidated financial statements, note 14 of the consolidated financial statements.

For a description of the effects of the share-based payments in total, as well as the main characteristics of the plans, reference is made to Note 10 of the consolidated financial statements.

As of December 31, 2021 Treasury shares held by wholly-owend subsidiaries of EURk 3.717. In March 2021 CureVac received 759,677 shares from the old shareholders and handed over 390,023 shares to the participants of the old VSOP plan. CureVac withheld 369,654 shares equaling the amount to be paid for income tax and social security tax. Another triggering event, minimum trading volume and liquidity was met one year after IPO. In October CureVac received 765,223 shares from the old shareholders and handed over 523,897 shares to the participants of the VSOP plan. CureVac withheld 241,326 shares equaling the amount to be paid for income tax and social security tax. As of December 31, 2021, the company still held 168,322 treasury shares.

During 2022 125,456 treasury shares were used thereof 110,689 for option exercises and 14,767 for RSU settlements. As of December 31, 2022, the company still held 42,866 treasury shares. For further information we refer to the consolidated financial statements.

Besides the minimum amount of share capital to be held under Dutch law and the currency translation reserve, there are no distribution restrictions applicable to equity of the Company. However, in certain events, Bill & Melinda Gates Foundation (BMGF) has the right to require the Company to redeem or facilitate the purchase by a third-party of all common shares it holds. For more details, we refer to the consolidated financial statements.

The General Meeting will be proposed to carry forward the loss after tax for 2022 and deduct EURk 249.029 from accumulated deficit.

10. Trade and other payables and Payables to subsidiaries

Trade payables and other payables are all due within one year and include the following:

	2021	2022
	EURk	EURk
Payables third parties	237	835
Payables to subsidiaries	26.182	16.634
Other payables	3.676	60
Total	**30.095**	**17.529**

Payables to subsidiaries are mostly due to payables in regard to the CureVac VAT group and to the buy back of treasury shares from its wholly-owned subsidiary, which are due within 12 months.

11. Other liabilities

Other current liabilities include the following:

	2021	2022
	EURk	EURk
Accruals for personnel	1.323	738
Accruals for audit	801	923
Accruals for invoices to be received	905	355
Accruals for other taxes	924	1.148
Total	**3.952**	**3.165**

12. Income tax

CureVac NV is considered a German-based entity for income tax purposes. In fiscal 2022 it has suffered tax losses in the amount of EURk 36.195 (2021: EURk 18.918) for corporate income tax and trade tax purposes by which EURk 36.070 (2021: EURk 22.590) relate to equity transaction costs that were debited directly to equity in the IFRS financial statements. Under German tax law, these tax loss carryforwards are available indefinitely for offsetting against future taxable income. Tax profits in a given year can be offset against tax loss carryforwards up to an amount of EURk 1.000. 60% of tax profit in excess of this amount can be offset against any remaining tax loss carryforwards. As a result, 40% of the profits in excess of EURk 1.000 are subject to taxation.

Tax loss carryforwards are examined by the German tax authorities and may be adjusted. Furthermore, significant changes in the shareholder and company structure can lead to a reduction in the loss carryforwards under the current provisions of German tax law, which can be used to calculate the annual amount for offsetting against the future taxable income.

In fiscal 2022, CureVac NV recorded no current income tax as in 2021. Deferred tax assets on tax loss carryforwards in 2022 EURk 10.651 (2021: EURk 10.991) and deductible temporary differences EURk 1.209 (2021: EURk 1.863) in excess of deferred tax liabilities EURk 130 (2021: EURk 178) for taxable temporary differences have not been capitalized as Management concluded that there is not sufficient probability as per IAS 12 that there will be future taxable profits available in the foreseeable future against which the unused tax losses can be utilized.

13. Remuneration

The emolument as referred to in Section 2:383(1) of the Netherlands Civil Code, charged in the financial period to the company can be detailed as follows.

Remuneration and Other Benefits to Supervisory and Managing Directors as of December 31, 2022

Our compensation policy authorizes our Supervisory Board to determine the amount, level, and structure of the compensation packages of our managing directors at the recommendation of our compensation committee. These compensation packages may

consist of a mix of fixed and variable compensation components, including base salary, short-term incentives, long-term incentives, fringe benefits, severance pay, and pension arrangements, as determined by our Supervisory Board.

Supervisory Board

Compensation of Supervisory Directors

For the year ended December 31, 2022, the aggregate compensation accrued or paid to our Supervisory directors for services in all capacities was EUR 1.179.092. The following table sets forth the aggregate compensation and benefits provided to our Supervisory Board Members in the year ended December 31, 2022.

	Fixed Compensation	**Share-based pament expenses**	**Total Compensation**
Name	*EUR*	*EUR*	*EUR*
Baron Jean Stéphenne	123.750	89.834	213.584
Ralf Clemens	89.164	68.793	157.957
Mathias Hothum	96.118	69.871	165.989
Hans Christoph Tanner	96.250	69.871	166.121
Friedrich von Bohlen und Halbach(1)	45.620	79.346	124.966
Craig A. Tooman	79.392	51.936	131.328
Dr. Viola Bronsema	68.750	-	68.750
Debra Barker(2)	68.368	33.324	101.693
Klaus Schollmeier(3)	34.177	14.528	48.705
Total	**701.589**	**477.503**	**1.179.092**

(1) Dr. von Bohlen und Halbach resigned from the Supervisory Board of CureVac N.V. on June 22, 2022.
(2) Dr. Barker joined the Supervisory Board of CureVac on June 22, 2022. Cash compensation includes services performed for CureVac AG and CureVac SE.
(3) Dr. Schollmeier joined the Supervisory Board of CureVac on June 22, 2022.

The Supervisory Board Members were awarded RSU's in 2022.

For the year ended December 31, 2021, the aggregate compensation accrued or paid to our Supervisory directors for services in all capacities was EUR 1.239.053. The following table sets forth the aggregate compensation and benefits provided to our Supervisory Board Members in the year ended December 31, 2021.

Name	Fixed Compensation	Share-based pament expenses	Total Compensation
	EUR	*EUR*	*EUR*
Baron Jean Stéphenne	123.750	224.989	348.739
Ralf Clemens	96.250	157.032	253.282
Mathias Hothum	96.250	49.581	145.831
Hans Christoph Tanner	96.250	49.581	145.831
Friedrich von Bohlen und Halbach	96.250	49.581	145.831
Timothy M. Wright (1)	26.631	-	26.631
Craig A. Tooman	68.750	35.408	104.158
Dr. Viola Bronsema	68.750	-	68.750
Total	**672.881**	**566.172**	**1.239.053**

(1) Mr. Wright resigned from the Supervisory Board per June 24, 2021

The Supervisory Board Members were awarded RSU's in 2021.

Management Board

Compensation of Managing Directors

For the year ended December 31, 2022, the aggregate compensation accrued or paid to our managing directors for services in all capacities was EUR 9.914.572. The following table sets forth the compensation and benefits provided to our Management Board in the year ended December 31, 2022.

Compensation of Managing Directors 2022

Name	Salary	Bonus (1)	Share-based payment expense	Other Compensation (2)	Total Compensation (3)
	EUR	*EUR*	*EUR*	*EUR*	*EUR*
Antony Blanc	342.500	59.904	2.883.170	64.809	3.350.383
Klaus Evardsen(6)	180.889	32.067	- (7)	30.103	243.059
Mariola Fotin-Mleczek(4)	26.666	64.896	-	3.487	95.049
Malte Greune(8)	342.500	29.952	325.347	54.448	752.247
Franz-Werner Haas(5)	417.500	79.040	684.806	89.172	1.270.518
Pierre Kemula	342.500	59.904	150.982	146.514	699.900
Igor Splawski	338.706	54.463	2.915.117	90.471	3.398.757
Total	**1.991.261**	**380.226**	**6.959.421**	**479.004**	**9.809.912**

(1) This amount represents the annual variable payment received based on a percentage of yearly gross remuneration for reaching certain targets agreed upon with the Supervisory Board. Performance criteria for bonus pay outs include a. ensure financing of CV group; b. Research & Development in all therapeutic areas; c. Technology Development & Manufacturing.
(2) All other compensation includes other monetary benefits and contributions to social security insurance, if any.
(3) This column does not include the virtual shares held by certain of the Management Board Members.
(4) Dr. Fotin-Mleczek resigned as a managing director of CureVac N.V. on January 31, 2022.
(5) Dr. Haas resigned as a managing director of CureVac N.V. on March 31, 2023.
(6) Dr. Edvardsen resigned as a chief development officer and as a managing director of CureVac N.V. on June 30, 2022.
(7) Expenses for Dr. Edvardsen were resolved as he resigned on June 30, 2022.
(8) Dr. Greune was formally appointed as a managing director of CureVac N.V. on June 22, 2022.

For the year ended December 31, 2021, the aggregate compensation accrued or paid to our managing directors for services in all capacities was € 15.770.332. The following table sets forth the compensation and benefits provided to our Management Board in the year ended December 31, 2021.

Compensation of Managing Directors 2021

Name	**Salary**	**Bonus (1)**	**Share-based payment expense**	**Other Compensation (2)**	**Total Compensation (3)**
	EUR	*EUR*	*EUR*	*EUR*	*EUR*
Antony Blanc	320.000	12.000	5.398.348	13.773	5.744.121
Klaus Edvardsen *(A)*	154.167	-	134.328	104.474	392.969
Mariola Fotin-Mleczek	320.000	102.000	32.056	25.557	479.613
Malte Greue *(B)*	160.000	-	102.696	10.319	273.015
Franz-Werner Haas	380.000	124.100	42.295	32.231	578.626
Pierre Kemula	320.000	112.500	32.056	133.496	598.052
Igor Splawski	327.300	60.005	6.930.696	13.976	7.331.977
Florian von der Mülbe *(C)*	202.151	116.250	-	53.558	371.959
Total	**2.183.618**	**526.855**	**12.672.475**	**387.384**	**15.770.332**

(A) Per august 1, 2021; (B) Per Juli 1, 2021; (C) Until August 18, 2021

(1) *This amount represents the annual variable payment received based on a percentage of yearly gross remuneration for reaching certain* targets agreed upon with the Supervisory Board.
(2) *All other compensation includes other monetary benefits and contributions to social security insurance if any.*
(3) This column does not include the virtual shares held by certain of the Management Board Members.

We did not provide pension, retirement, or similar benefits to our managing directors and Supervisory directors Board in the year ended December 31, 2022. Neither did we pay any dividends to our managing directors and Supervisory directors' Board.

Bonus Plan

We maintain and implement a management bonus plan for the Members of our Management. Under the Management bonus plan, we provide a variable bonus payment as a component of Management compensation that ranges from 45% to 55% of the individual's annual base salary, depending on Management level. We agree upon the respective individual amount of the target bonus with each employee on an individual contractual basis. The annual performance review is used to measure the achievement of objectives. In the individual's annual performance review, we measure the achievement of objectives for the past year and define the objectives for the coming year. The calculation of the respective bonus payment is based on the individual degree of target achievement, which is then calculated as a percentage of the annual base salary and is usually paid out in March of the following year. The bonus is calculated on a pro-rata basis if the individual joins or leaves CureVac during the year.

Equity Incentive Plans

Certain Members of our Management received share-based compensation under the legacy Management stock option plan, or Legacy Management Stock Option Plan, in the form of share option awards. The last Member of the Management Board that was part of the Legacy stock option plan resigned in 2021.

In addition to the Management share option awards described above, CureVac maintains a virtual share plan (Prior VSOP) for Members of the Management Board and other key employees of CureVac. For further information to the exercises under the Prior VSOP, we refer to note 10 of the consolidated financial statements.

CureVac also maintains a Long-term incentive plan and restricted stock units for the Board Member. For further information we refer to note 10 of the consolidated financial statements.

14. Employees

Since October 2021 the Management Board (seven employees) has been employed through CureVac NV. All Board Members are employed outside of the Netherlands.

15. Related Party transactions

Transactions with the CureVac Group companies

In prior years, December 2020 CureVac N.V. granted to CureVac SE a loan of EURk 149.310 at the rate of 0.50% p.a. repayable on or before June 30th, 2021. The loan agreement was extended and in October the loan and the interest fee accumulated up to September was used to increase the capital reserve within CureVac SE. Furthermore, a cash payment of EURk 250.000 into the capital reservce for CureVac SE was made by the end of October.

In the current year, in June 2022 a short-term loan was granted to CureVac Manufacturing GmbH of EURk 30.000 at the rate of 0.60% p.a. which was repaid per April of 2023.

16. Share-based payment

Regarding details of the individual plans, we refer to note 10 of the consolidated financial statements.

17. Contingent liabilities

CureVac NV represents and undertakes to procure that CureVac SE will receive adequate financial funding for the next year to ensure CureVac SE is financially and capital-wise

equipped in such a way that it is at all times in a position to meet all its payment obligations towards its creditors.

18. Subsequent Events

Regarding details of subsequent events, we refer to note 22 of the consolidated financial statements.

11. Other information

11.1 Independent Auditor's Report

11.2 Profit appropriation

In accordance with Article 35 of the Articles of Association, a distribution can only be made to the extent that the Company's equity exceeds the amount of the paid up and called up part of its capital plus the reserves which must be maintained by law.

Pursuant to the Company's articles of association, any profits shown in the adopted statutory annual accounts of the Company shall be appropriated as follows, and in the following order of priority:

a. to the extent that any preferred shares have been cancelled without full repayment as described in the articles of association and without such deficit subsequently having been paid in full, an amount equal to any such (remaining) deficit shall first be distributed to those who held those preferred shares at the moment of such cancellation becoming effective;

b. if preferred shares are issued and outstanding and to the extent that the mandatory annual distribution on the preferred shares (i.e., an amount equal to the applicable interest rate calculated over the aggregate amount paid up on those preferred shares, calculated in accordance with the relevant provisions of the articles of association), or part thereof, in relation to previous financial years has not yet been paid in full, an amount equal to any such (remaining) deficit shall be distributed on the preferred shares;

c. if preferred shares are issued and outstanding, the mandatory annual distribution (as described above under b.) payable on preferred shares shall then be distributed on the preferred shares;

d. following those distributions, the Management Board shall determine which part of the remaining profits shall be added to the Company's reserves; and

e. subject to a proposal by the Management Board to that effect, the remaining profits shall be at the disposal of the General Meeting for distribution on the ordinary shares.

See note 9 in the Notes to the Company Financial Statements (section 10) for the appropriation of profits realized during the financial year to which this Annual Report pertains.

11.3 Special rights of control under our articles

See sections 4.3, 5.1, 5.8.5 and 8 of this Annual Report for the special rights of KfW and dievini in relation to the Company pursuant to our articles of association. There are no other parties with special rights of control in relation to the Company pursuant to our articles of association.

11.4 Non-voting shares and shares carrying limited economic entitlement

The Company has not issued non-voting shares. The preferred shares in the Company's capital carry a limited entitlement to the Company's profit and reserves. As at December 31, 2022, no preferred shares in the Company's capital were issued.

11.5 Other establishments

The Company has no branch offices (*nevenvestigingen*).

Signature page to the Dutch statutory board report and financial statements of CureVac N.V. for the fiscal year ended December 31, 2022

Management Board

/s/ A. Zehnder
Name: A. Zehnder
Title : CEO

/s/ P.T.V. Kemula
Name: P.T.V. Kemula
Title : CFO

/s/ I. Splawski
Name: I. Splawski
Title : CSO

/s/ M.B. Greune
Name: M.B. Greune
Title : COO

/s/ A.Y.M. Blanc
Name: A.Y.M. Blanc
Title : CBO & CCO

/s/ M. Mendila
Name: M.Mendila
Title : CDO

Supervisory Board

/s/ Baron J.R.G. Stéphenne
Name: Baron J.R.G. Stéphenne
Title : Supervisory Board Member

/s/ R.L. Clemens
Name: R.L. Clemens
Title : Supervisory Board Member

/s/ M.P. Hothum
Name: M.P. Hothum
Title : Supervisory Board Member

/s/ H.C. Tanner
Name: H.C. Tanner
Title : Supervisory Board Member

/s/ K.C. Schollmeier
Name: K.C. Schollmeier
Title : Supervisory Board Member

/s/ C.A. Tooman
Name: C.A. Tooman
Title : Supervisory Board Member

/s/ V. Bronsema
Name: V. Bronsema
Title : Supervisory Board Member

/s/ D.S. Barker
Name: D.S. Barker
Title : Supervisory Board Member

Building a better working world

Publication of auditor's report

1 Conditions

Authorization to publish the auditor's report is granted subject to the following conditions:

- Further consultation with the auditor is essential if, after this authorization has been granted, facts and circumstances become known which materially affect the view given by the financial statements.
- The authorization concerns inclusion of the auditor's report in the annual report to be tabled at the Annual General Meeting (hereafter AGM) incorporating the financial statements as drawn up.
- The authorization also concerns inclusion of the auditor's report in the annual report to be filed with the Trade Registrar, provided consideration of the financial statements by the AGM does not result in any amendments.
- Financial statements for filing at the offices of the Trade Registrar which have been abridged in accordance with Section 397 of Book 2 of the Dutch Civil Code must be derived from the financial statements adopted by the AGM and a draft version of these financial statements for filing purposes must be submitted to us for inspection.
- The auditor's report can also be included if the financial statements are published electronically, such as on the internet. In such cases, the full financial statements should be published and these should be easily distinguishable from other information provided electronically at the same time.
- If the published financial statements are to be included in another document which is to be made public, authorization to include the auditor's report must again be granted by the auditor.

2 Explanations to the conditions

2.1 Board of supervisory directors and board of executive directors

The auditor usually forwards his report to the board of supervisory directors and to the board of executive directors. This is pursuant to Book 2 of the Dutch Civil Code, section 393 which stipulates inter alia: "The auditor sets out the outcome of his examination in a report". "The auditor reports on his examination to the board of supervisory directors and the board of executive directors".

2.2 Annual General Meeting (AGM)

Publication of the auditor's report will only be permitted subject to the auditor's express consent. Publication is understood to mean: making available for circulation among the public or to such group of persons as to make it tantamount to the public. Circulation among shareholders or members, as appropriate, also comes within the scope of the term "publication", so that inclusion of the auditor's report in the annual report to be tabled at the AGM similarly requires authorization by the auditor.

2.3 Auditor's reports and financial statements

The authorization concerns publication in the annual report incorporating the financial statements that are the subject of the auditor's report. This condition is based on the auditors' rules of professional practice, which state that the auditor will not be allowed to authorize publication of his report except together with the financial statements to which this report refers.
The auditor will also at all times want to see the rest of the annual report, since the auditor is not allowed to authorize publication of his report if, owing to the contents of the documents jointly published, an incorrect impression is created as to the significance of the financial statements.

2.4 Events between the date of the auditor's report and the AGM

Attention should be paid to the fact that between the date of the auditor's report and the date of the meeting at which adoption, as appropriate, of the financial statements is considered, facts or circumstances may have occurred which materially affect the view given by the financial statements. Under COS 560, the auditor must perform audit procedures designed to obtain sufficient audit evidence to ensure that all events occurring before the date of the auditor's report that warrant amendment of or disclosure in the financial statements have been identified.
If the auditor becomes aware of events that may be of material significance to the financial statements, the auditor must consider whether those events have been adequately recognized and sufficiently disclosed in the notes to the financial statements. If between the date of the auditor's report and the date of publication of the financial statements, the auditor becomes aware of a fact that may have a material impact on the financial statements, the auditor must assess whether the financial statements should be amended, discuss the matter with management and act as circumstances dictate.

2.5 Trade Registrar

The financial statements are tabled at the AGM (legal entities coming within the scope of Title 9 of Book 2 of the Dutch Civil Code table the directors' report and the other information as well). The AGM considers adoption of the financial statements. Only after the financial statements have been adopted, do they become the statutory (i.e., the company) financial statements. As a rule, the statutory financial statements will be adopted without amendment. The auditor's report must be attached to the statutory financial statements as part of the other information. As a rule, the text of this report will be the same as that issued earlier. The documents to be made public by filing at the offices of the Trade Registrar will consist of the statutory financial statements, the directors' report and the other information. The auditor's report which refers to the unabridged financial statements will then have to be incorporated in the other information. If consideration of the financial statements by the AGM does not result in any amendments, the auditor's report may be attached to the financial statements adopted, by the AGM and, provided the annual report and financial statements are filed promptly at the offices of the Trade Registrar, published as part of these annual report and financial statements.

2.6 Other manner of publication

The financial statements may also be published other than by filing at the offices of the Trade Registrar. In that event, too, inclusion of the auditor's report is permitted, provided the financial statements are published in full. If publication concerns part of the financial statements or if the financial statements are published in abridged form, publication of any report the auditor has issued on such financial statements will be prohibited, unless:

a. He has come to the conclusion that, in the circumstances of the case, the document concerned is appropriate
   Or
b. Based on legal regulations, publication of the document concerned is all that is required

If less than the full financial statements are published, further consultation with the auditor is essential. If the financial statements and the auditor's report are published on the internet, it should be ensured that the financial statements are easily distinguishable from other information contained on the internet site. This can be achieved, for example, by including the financial statements as a separate file in a read-only format or by including a warning message when the reader exits the financial statements document.

2.7 Inclusion in another document

If the published financial statements are to be included in another document which is to be made public, this is considered a new publication and authorization must again be obtained from the auditor. An example of this situation is the publication of an offering circular which includes the financial statements, after these financial statements have been filed at the office of the Trade Registrar together with the other annual reports. For each new publication, authorization must again be obtained from the auditor.

2.8 Events after the AGM

Even if facts and circumstances have become known after the adoption of the financial statements as a result of which they no longer give the statutory true and fair view, the auditor must stand by the report issued on the financial statements as adopted and by the auditor's report filed at the offices of the Trade Registrar. In that event, the legal entity is required to file a statement at the offices of the Trade Registrar on these facts and circumstances accompanied by an auditor's report. In this situation, too, further consultation with the auditor is essential.

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Independent auditor's report

To: the shareholders and supervisory board of CureVac N.V.

Report on the audit of the financial statements 2022 included in the annual report

Our opinion

We have audited the financial statements for the year 2022 of CureVac N.V. based in Amsterdam, the Netherlands.

The financial statements comprise the consolidated and company financial statements.

In our opinion:

- The accompanying consolidated financial statements give a true and fair view of the financial position of CureVac N.V. as at 31 December 2022 and of its result and its cash flows for 2022 in accordance with International Financial Reporting Standards as adopted by the European Union (EU-IFRS) and with Part 9 of Book 2 of the Dutch Civil Code
- The accompanying company financial statements give a true and fair view of the financial position of CureVac N.V. as at 31 December 2022 and of its result for 2022 in accordance with Part 9 of Book 2 of the Dutch Civil Code

The consolidated financial statements comprise:

- The consolidated statement of financial position as at 31 December 2022
- The following statements for 2022: the consolidated statements of operations and other comprehensive income (loss), changes in shareholders' equity and cash flows
- The notes comprising a summary of the significant accounting policies and other explanatory information

The company financial statements comprise:

- The company statement of financial position as at 31 December 2022
- The company statement of profit and loss and other comprehensive income (loss) for 2022
- The notes comprising a summary of the accounting policies and other explanatory information

Basis for our opinion

We conducted our audit in accordance with Dutch law, including the Dutch Standards on Auditing. Our responsibilities under those standards are further described in the Our responsibilities for the audit of the financial statements section of our report.

We are independent of CureVac N.V. in accordance with the EU Regulation on specific requirements regarding statutory audit of public-interest entities, the Wet toezicht accountantsorganisaties (Wta, Audit firms supervision act), the Verordening inzake de onafhankelijkheid van accountants bij assurance-opdrachten (ViO, Code of Ethics for Professional Accountants, a regulation with respect to independence) and other relevant independence regulations in the Netherlands. Furthermore, we have complied with the Verordening gedrags- en beroepsregels accountants (VGBA, Dutch Code of Ethics).

We believe the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Information in support of our opinion

We designed our audit procedures in the context of our audit of the financial statements as a whole and in forming our opinion thereon. The following information in support of our opinion and any findings were addressed in this context, and we do not provide a separate opinion or conclusion on these matters.

Our understanding of the business

CureVac N.V. is a global biopharmaceutical company developing transformative medicines based on messenger ribonucleic acid (mRNA). The group is structured in components and we tailored our group audit approach accordingly. We paid specific attention in our audit to a number of areas driven by the operations of the group and our risk assessment.

We determined materiality and identified and assessed the risks of material misstatement of the financial statements, whether due to fraud or error in order to design audit procedures responsive to those risks and to obtain audit evidence that is sufficient and appropriate to provide a basis for our opinion.

Materiality

Materiality	€10.2 million (2021: €38.3 million)
Benchmark applied	4% of operating expenses (2021: 4% of operating expenses)
Explanation	CureVac N.V. is a clinical-stage biopharmaceutical Group. Operating expenses is the key activity-based measure that is relevant for the users of the financial statements as the company is currently in its research and development phase. Following the decline in operating expenses, our 2022 materiality decreased compared to prior year. In relation, we assessed and confirmed the sufficiency of prior year audit procedures for the 2022 openings balance sheet.

We have also taken into account misstatements and/or possible misstatements that in our opinion are material for the users of the financial statements for qualitative reasons.

We agreed with the supervisory board that misstatements in excess of €508,000 which are identified during the audit, would be reported to them, as well as smaller misstatements that in our view must be reported on qualitative grounds.

Scope of the group audit

CureVac N.V. is the parent of a group of entities. The financial information of this group is included in the consolidated financial statements of CureVac N.V.

Because we are ultimately responsible for the opinion, we are also responsible for directing, supervising and performing the group audit. In this respect we have determined the nature and extent of the audit procedures to be carried out for group entities. Decisive were the size and/or the risk profile of the group entities or operations. On this basis, we selected group entities for which an audit or review had to be carried out on the complete set of financial information or specific items.

Our audit mainly focused on significant group entities. The group consists of nine components. Of these nine components, we identified 3 as significant components and we performed full-scope audit procedures on these components. These components are significant in size. In addition, for one component, we performed specified procedures. The other components are insignificant in size and risk. Elimination entries were evaluated on consolidated level.

In total the procedures over the significant entities represent 92.1% of the group's total assets, 90.2% of the group's operating expenses and 93.4% of the group's loss for the period.

By performing the procedures mentioned above at group entities, together with additional procedures at group level we have been able to obtain sufficient and appropriate audit evidence about the group's financial information to provide an opinion about the consolidated financial statements.

Teaming and use of specialists
We ensured that the audit teams both at group and at component levels included the appropriate skills and competences which are needed for the audit of a listed client in the biopharmaceutical industry. We included specialists in the areas of IT audit, forensics, income tax and share based payments and have made use of our own experts in the areas of valuations in relation to the business combination.

Our focus on fraud and non-compliance with laws and regulations

Our responsibility
Although we are not responsible for preventing fraud or non-compliance and we cannot be expected to detect non-compliance with all laws and regulations, it is our responsibility to obtain reasonable assurance that the financial statements, taken as a whole, are free from material misstatement, whether caused by fraud or error. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.

Our audit response related to fraud risks
We identify and assess the risks of material misstatements of the financial statements due to fraud. During our audit we obtained an understanding of CureVac N.V. and its environment and the components of the system of internal control, including the risk assessment process and management's process for responding to the risks of fraud and monitoring the system of internal control and how the supervisory board exercises oversight, as well as the outcomes. We refer to section 4.3 Risk factors of the Dutch statutory board report for management's fraud risk assessment.

We evaluated the design and relevant aspects of the system of internal control and in particular the fraud risk assessment, as well as the code of conduct and whistle blower procedures. We evaluated the design and the implementation of internal controls designed to mitigate fraud risks.

As part of our process of identifying fraud risks, we evaluated fraud risk factors with respect to financial reporting fraud, misappropriation of assets and bribery and corruption. We evaluated whether these factors indicate that a risk of material misstatement due to fraud is present.

We incorporated elements of unpredictability in our audit. We also considered the outcome of our other audit procedures and evaluated whether any findings were indicative of fraud or non-compliance.

As in all of our audits, we addressed the risks related to management override of controls. For these risks we have performed procedures among others to evaluate key accounting estimates for management bias that may represent a risk of material misstatement due to fraud, in particular relating to important judgment areas and significant accounting estimates as disclosed in Note 2 to the financial statements, including the provisions for contract termination costs. We have also used data analysis to identify and address high-risk journal entries and evaluated the business rationale (or the lack thereof) of significant extraordinary transactions, including those with related parties.

The following fraud risk identified did require significant attention during our audit:

Risks related to revenue recognition	
Fraud risk	We presumed that there are risks of fraud in revenue recognition. We evaluated determined the risk of premature recognition of revenue from performance obligations or achievement of milestones under the existing collaboration agreements in particular give rise to such risks.
Our audit approach	We describe the audit procedures responsive to the presumed risk of fraud in the description of our audit approach for the key audit matter "Revenue recognition".

We considered available information and made enquiries of relevant executives and the supervisory board.

The fraud risks we identified, enquiries and other available information did not lead to specific indications for fraud or suspected fraud potentially materially impacting the view of the financial statements.

Our audit response related to risks of non-compliance with laws and regulations
We performed appropriate audit procedures regarding compliance with the provisions of those laws and regulations that have a direct effect on the determination of material amounts and disclosures in the financial statements. Furthermore, we assessed factors related to the risks of non-compliance with laws and regulations that could reasonably be expected to have a material effect on the financial statements from our general industry experience, through discussions with the management board, reading minutes, inspection of whistleblower reports, and performing substantive tests of details of classes of transactions, account balances or disclosures.

We also inspected lawyers' letters and correspondence with regulatory authorities and remained alert to any indication of (suspected) non-compliance throughout the audit. Finally we obtained written representations that all known instances of non-compliance with laws and regulations have been disclosed to us.

Our audit response related to going concern

Management made a specific assessment of the company's ability to continue as a going concern and to continue its operations for the foreseeable future. As disclosed in section "Liquidity risk/ Capital management" in Note 16 to the financial statements. Based on its business as an active research group, CureVac N.V. has historically relied almost exclusively on equity funding by its shareholders and lenders as a means of financing itself prior to successful development and sales of a marketable product. As disclosed in section "Significant accounting policies, judgments, estimates, and assumptions" in Note 2 to the financial statements, the financial statements have been prepared on a going concern basis.

We discussed and evaluated the specific assessment with management exercising professional judgment and maintaining professional skepticism.

We considered whether management's going concern assessment, based on our knowledge and understanding obtained through our audit of the financial statements or otherwise, contains all events or conditions that may cast significant doubt on the company's ability to continue as a going concern.

Based on our procedures performed, we did not identify material uncertainties about going concern. If we conclude that a material uncertainty exists, we are required to draw attention in our auditor's report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify our opinion. Our conclusions are based on the audit evidence obtained up to the date of our auditor's report. However, future events or conditions may cause a company to cease to continue as a going concern.

Our key audit matters

Key audit matters are those matters that, in our professional judgment, were of most significance in our audit of the financial statements. We have communicated the key audit matters to the supervisory board. The key audit matters are not a comprehensive reflection of all matters discussed.

The key audit matter "Provisions for onerous contracts" which was included in our last year's auditor's report, is not considered a key audit matter for this year as the remaining amount per 31 December 2022 is not significant anymore. The key audit matters "Reimbursement of costs under government grants" and "Income from release of governmental contract liabilities and grant income" which were included in our last year's auditor's report, are not considered key audit matters for this year as there is no government grant anymore during 2022. Following the acquisition of Frame Pharmaceuticals B.V. during 2022 a new key audit matter "Business combinations-Frame acquisition" has been defined.

Revenue recognition (Reference is made to Note 2 and Note 3.1 of the consolidated financial statements)	
Risk	As described in Note 3.1 to the consolidated financial statements, the Company enters into licensing and development agreements with collaborative partners. The terms of these agreements contain multiple performance obligations which may include (i) licenses, or options to obtain licenses, (ii) research activities to be performed on behalf of the collaborative partner, and (iii) regulatory, development and sales milestones. Payments to the Company under these agreements may include upfront fees (which include license and option fees), payments for research activities, payments based upon the achievement of certain milestones and royalties on product sales. Per 2022, the Company recognized revenue of €67.4 million, which is made up of €44.8 million from amortization of upfront and milestone payments received under the collaboration agreements, €19.6 million for service revenue and reimbursement for R&D materials, and €3.0 million from product sales. We have determined the risk of premature recognition of revenue from performance obligations or achievement of milestones under the existing collaboration agreements as a fraud risk. Therefore we consider this a Key Audit Matter.
Our audit approach	In order to address the identified risk, we obtained an understanding of the revenue recognition process by performing a walkthrough of controls and evaluated the design of controls in this process. We performed the following substantive audit procedures: ▸ We obtained and inspected joint steering committee meeting minutes issued in 2022 up until our opinion date and inquired of project managers about the status and progress of the projects to ensure the amortization period of the associated upfront payments remains appropriate. ▸ We inquired management of the existence of contract modifications to the existing collaboration agreements in 2022. ▸ We recalculated the amortization of the upfront payments and agreed the reimbursable R&D costs incurred to supporting documentation. ▸ We tested service revenue and submitted costs for reimbursement to collaboration partners. ▸ We obtained the cash receipt of the milestone payments from collaboration partners and from service revenue and product sales. ▸ We assessed the adequacy of the Company's disclosure in Note 3.1 to the consolidated financial statements.
Key observations	Based on the audit procedures performed, we did not identify any material misstatements in the company's accounting for the collaboration agreements and conclude that the related disclosures in the financial statements are In accordance with EU-IFRS.

Provisions for contract termination costs (Reference is made to Note 2 and Note 12 of the consolidated financial statements)	
Risk	As described in Note 2 to the consolidated financial statements, the Company recognizes a provision for contract termination costs where it is probable that a liability exists as of the reporting date and a reliable estimate can be made. As described in Note 12 of the consolidated financial statements as of 31 December 2022, the Company recognized €61.3 million of provisions for the estimated costs of terminating Contract manufacturing organizations (CMOs) contracts. Auditing the provisions for CMO contracts, which have been terminated or are anticipated to be terminated, was complex and required significant judgment in determining a reliable estimate of the settlement cost for each agreement. Such provisions are judgmental and subjective due to potential variability in the amount required to be paid to ultimately release the Company from its remaining obligations under the CMO contracts, including as a result of arbitration. Therefore we consider this a Key Audit Matter.
Our audit approach	In order to address the identified risk, we obtained an understanding of the accounting for the contract termination provision and of management's process for estimating the amount required to release the Company from its remaining obligations under these contracts. We also obtained an understanding of the design of internal controls implemented in this process. We performed the following substantive audit procedures. ▶ We obtained and assessed the appropriateness of the termination settlement proposal calculation. EY has further compared the claim value raised by the CMOs to the provided management's best estimate of the settlement and challenged the risk coverage with management. ▶ We performed inquiries of management and obtained a legal assessment from the CureVac General counsel, as well as from external counsel. Their responses were consistent with the amounts the Company recognized. ▶ Where available, we inspected the court's arbitration timeline to evaluate whether additional proceedings were scheduled to have occurred and whether additional information, which might affect the estimates, may be available. ▶ We inspected cash disbursements as well as material billing related to the termination/settlement of CMO agreements concluded in 2022. ▶ We assessed the adequacy of the Company's disclosure in Note 11 to the consolidated financial statements.
Key observations	Based on the audit procedures performed, we did not identify any material misstatements in the company's accounting for the contract termination provision and conclude that the related disclosures in the financial statements are In accordance with EU-IFRS.

Business combinations - Frame acquisition (Reference is made to Note 2 and Note 21 of the consolidated financial statements)	
Risk	As described in Note 2 to the consolidated financial statements, the Company accounts for Business Combinations using the acquisition method. The cost of an acquisition is measured as the aggregate of the consideration transferred, which is measured at acquisition date fair value. Acquisition-related costs are expensed as incurred and included in general and administrative expenses in the statement of operations. As described in Note 21 of the consolidated financial statements, effective 1 July 2022, CureVac N.V. acquired all shares of Frame Pharmaceuticals B.V., Amsterdam, the Netherlands. Considering the complexity and management estimates involved in this business combination we consider this a Key Audit Matter.
Our audit approach	In order to address the identified risk, we obtained an understanding of the accounting for the business combination and of management's process for establishing the prospective financial information used as an input. We also obtained an understanding of the design of internal controls implemented in this process. We performed the following substantive audit procedures. ▶ We obtained and inspected the Frame sales and purchase agreement. ▶ We performed inquiries of the external management specialist and management to understand their evaluation method for accounting purposes. ▶ We reviewed the Purchase Price Allocation (PPA) report issued by the external management specialist. We reconciled the reported amounts for initial recognition to the recordings performed by the company. ▶ We involved EY valuation specialists as well as EY biotech experts evaluated the valuation method/approach and the reasonableness of the material assumptions and the probabilities applied for the contingent consideration. ▶ We assessed the adequacy of the Company's disclosure in Note 21 to the consolidated financial statements.
Key observations	Based on the audit procedures performed, we did not identify any material misstatements in the company's accounting for the business combination of Frame Pharmaceuticals B.V and conclude that the related disclosures in the financial statements are In accordance with EU-IFRS.

Report on other information included in the annual report

The annual report contains other information in addition to the financial statements and our auditor's report thereon.

Based on the following procedures performed, we conclude that the other information:

- Is consistent with the financial statements and does not contain material misstatements
- Contains the information as required by Part 9 of Book 2 of the Dutch Civil Code for the Dutch statutory board report and the other information as required by Part 9 of Book 2 of the Dutch Civil Code

We have read the other information. Based on our knowledge and understanding obtained through our audit of the financial statements or otherwise, we have considered whether the other information contains material misstatements. By performing these procedures, we comply with the requirements of Part 9 of Book 2 and the Dutch Standard 720. The scope of the procedures performed is substantially less than the scope of those performed in our audit of the financial statements.

Management is responsible for the preparation of the other information, including the Dutch statutory board report in accordance with Part 9 of Book 2 of the Dutch Civil Code and other information required by Part 9 of Book 2 of the Dutch Civil Code.

Report on other legal and regulatory requirements

Engagement

We were engaged by the general meeting as auditor of CureVac N.V. as of the audit for the year 2020 and have operated as statutory auditor ever since that date.

Description of responsibilities for the financial statements

Responsibilities of the management board and the supervisory board for the financial statements

Management is responsible for the preparation and fair presentation of the financial statements in accordance with EU-IFRS and Part 9 of Book 2 of the Dutch Civil Code. Furthermore, management is responsible for such internal control as management determines is necessary to enable the preparation of the financial statements that are free from material misstatement, whether due to fraud or error.

As part of the preparation of the financial statements, management is responsible for assessing the company's ability to continue as a going concern. Based on the financial reporting frameworks mentioned, management should prepare the financial statements using the going concern basis of accounting unless management either intends to liquidate the company or to cease operations, or has no realistic alternative but to do so. Management should disclose events and circumstances that may cast significant doubt on the company's ability to continue as a going concern in the financial statements.

The supervisory board is responsible for overseeing the company's financial reporting process.

Our responsibilities for the audit of the financial statements

Our objective is to plan and perform the audit engagement in a manner that allows us to obtain sufficient and appropriate audit evidence for our opinion.

Our audit has been performed with a high, but not absolute, level of assurance, which means we may not detect all material errors and fraud during our audit.

Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements. The materiality affects the nature, timing and extent of our audit procedures and the evaluation of the effect of identified misstatements on our opinion.

We have exercised professional judgment and have maintained professional skepticism throughout the audit, in accordance with Dutch Standards on Auditing, ethical requirements and independence requirements. The "Information in support of our opinion" section above includes an informative summary of our responsibilities and the work performed as the basis for our opinion.
Our audit further included among others:

- Performing audit procedures responsive to the risks identified, and obtaining audit evidence that is sufficient and appropriate to provide a basis for our opinion
- Obtaining an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the company's internal control
- Evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures made by management
- Evaluating the overall presentation, structure and content of the financial statements, including the disclosures
- Evaluating whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation

Communication

We communicate with the supervisory board regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant findings in internal control that we identify during our audit.

We provide the supervisory board with a statement that we have complied with relevant ethical requirements regarding independence, and to communicate with them all relationships and other matters that may reasonably be thought to bear on our independence, and where applicable, related safeguards.

From the matters communicated with the supervisory board, we determine the key audit matters: those matters that were of most significance in the audit of the financial statements. We describe these matters in our auditor's report unless law or regulation precludes public disclosure about the matter or when, in extremely rare circumstances, not communicating the matter is in the public interest.

Eindhoven, 30 May 2023

Ernst & Young Accountants LLP

Johannes René Frentz

Digitally signed by Johannes René Frentz
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J.R. Frentz