UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NO. 001-14888

INOVIO PHARMACEUTICALS, INC.
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

Delaware	**33-0969592**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
660 W. Germantown Pike, Suite 110 Plymouth Meeting, Pennsylvania	**19462**
(Address of principal executive offices)	**(Zip Code)**

REGISTRANT'S TELEPHONE NUMBER, INCLUDING AREA CODE: (267) 440-4200

SECURITIES REGISTERED PURSUANT TO SECTION 12(B) OF THE ACT:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
COMMON STOCK, $0.001 PAR VALUE	**INO**	**Nasdaq Global Select Market**

SECURITIES REGISTERED PURSUANT TO SECTION 12(G) OF THE ACT: NONE

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.☒

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity (which consists solely of shares of Common Stock) held by non-affiliates of the Registrant as of June 30, 2021 was approximately $1.9 billion based on $9.27 per share, the closing price on that date of the Registrant's Common Stock on the Nasdaq Global Select Market.

The number of shares outstanding of the Registrant's Common Stock, $0.001 par value, was 217,403,287 as of February 25, 2022.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2022 Annual Meeting of Stockholders (the "Proxy Statement') are incorporated by reference into Part III of this Report. Such Proxy Statement will be filed with the Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2021.

TABLE OF CONTENTS

Unless stated to the contrary, or unless the context otherwise requires, references to "INOVIO," "the company," "our company," "our," or "we" in this report include Inovio Pharmaceuticals, Inc. and its subsidiaries.

PART I

ITEM 1. BUSINESS

This Annual Report on Form 10-K (including the following section regarding Management's Discussion and Analysis of Financial Condition and Results of Operations), or this Annual Report, contains forward-looking statements regarding our business, financial condition, results of operations and prospects. Words such as "expects," "anticipates," "intends," "plans," "believes," "seeks," "estimates" and similar expressions or variations of such words are intended to identify forward-looking statements, but are not the exclusive means of identifying forward-looking statements in this Annual Report. Additionally, statements concerning future matters, including statements regarding our business, our financial position, the research and development of our products and other statements regarding matters that are not historical are forward-looking statements.

Although forward-looking statements in this Annual Report reflect the good faith judgment of our management, such statements can only be based on facts and factors currently known by us. Consequently, forward-looking statements are inherently subject to risks and uncertainties and actual results and outcomes may differ materially from the results and outcomes discussed in or anticipated by the forward-looking statements. Factors that could cause or contribute to such differences in results and outcomes include without limitation those discussed under the heading "Risk Factors" below, as well as those discussed elsewhere in this Annual Report. Readers are urged not to place undue reliance on these forward-looking statements, which speak only as of the date of this Annual Report. We undertake no obligation to revise or update any forward-looking statements in order to reflect any event or circumstance that may arise after the date of this Annual Report. Readers are urged to carefully review and consider the various disclosures made in this Annual Report, which attempt to advise interested parties of the risks and factors that may affect our business, financial condition, results of operations and prospects.

This Annual Report includes trademarks and registered trademarks of INOVIO Pharmaceuticals, Inc. Products or service names of other companies mentioned in this Annual Report may be trademarks or registered trademarks of their respective owners. References herein to "we," "our," "us," "INOVIO" or the "Company" refer to INOVIO Pharmaceuticals, Inc. and its subsidiaries. References herein to "DNA medicines" refers to INOVIO's product candidates for precancerous conditions, cancer and infectious diseases in development.

Summary Risk Factors

Our business is subject to a number of risks, including risks that may prevent us from achieving our business objectives or may adversely affect our business, financial condition, results of operations, cash flows and prospects. These risks are discussed more fully in Part I, Item 1A., "Risk Factors" herein. These risk factors include, but are not limited to, the following:

- We have incurred significant losses in recent years, expect to incur significant net losses in the foreseeable future and may never become profitable.
- We have limited sources of revenue and our success is dependent on our ability to develop our DNA vaccines, DNA immunotherapies, dMAbs and electroporation equipment.
- We will need substantial additional capital to develop our DNA vaccines, DNA immunotherapies and dMAb programs and electroporation delivery technology.
- None of our human vaccine candidates, including INO-4800, or our immunotherapy and DNA encoded monoclonal antibody product candidates have been approved for sale, and we may never develop commercially successful vaccine, immunotherapy or DNA encoded monoclonal antibody products.
- The Omicron SARS-CoV-2 variant and newly emerging SARS-CoV-2 variants will likely require us to modify our COVID-19 vaccine strategy, which will result in new and added risks, including whether there will continue to be a need for a COVID-19 vaccine.
- There can be no assurance that any of the products we are developing for COVID-19 would be granted an Emergency Use Authorization by the FDA or similar authorization by regulatory authorities outside of the United States if we were to decide to apply for such an authorization. The option of seeking an Emergency Use Authorization may no longer exist for our primary vaccine candidates, and if we cannot obtain such authorization or, if granted, it is terminated, we will be unable to sell our product in the near future and instead will be required to pursue the biologic licensure process in order to sell our product, which is lengthy and expensive.
- If we and the contract manufacturers upon whom we rely fail to produce our electroporation devices and product candidates in the volumes that we require on a timely basis, or at all, or fail to comply with their obligations to us or with stringent regulations, we may face delays in the development and commercialization of our electroporation equipment and product candidates.
- If we lose or are unable to secure collaborators or partners, or if our collaborators or partners do not apply adequate resources to their relationships with us, our product development and potential for profitability will suffer.

- We have agreements with government agencies, which are subject to termination and uncertain future funding.
- Our participation in the WHO Solidarity Trial Vaccines (STV) could result in adverse consequences. We do not have any control over clinical data, progress, and decisions regarding INO-4800's participation in STV, and as such, decisions regarding the clinical pathway for INO-4800 between the WHO and the Company may not always align.
- We are currently subject to litigation and may become subject to additional litigation, which could harm our business, financial condition and reputation.
- We face intense and increasing competition and steps taken by of our competitors, such as the introduction of a new, disruptive technology, may impede our ability to successfully commercialize our DNA medicines.
- It is difficult and costly to generate and protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.
- If we are sued for infringing intellectual property rights of third parties, it will be costly and time-consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Company Overview

We are a biotechnology company focused on bringing to market precisely designed DNA medicines and vaccines to help protect people from infectious diseases, including COVID-19, and to help treat people with cancer, and conditions associated with human papillomavirus ("HPV"). We have shown in clinical trials that our DNA vaccine candidates can be delivered into cells in the body via a proprietary smart device allowing the nucleic-acid delivered gene products to activate functional T cell and antibody responses against targeted pathogens and cancers.

Our DNA medicines pipeline is comprised of three types of product candidates: prophylactic DNA vaccines, therapeutic DNA immunotherapies, and DNA encoded monoclonal and bispecific antibodies ("dMAbs" and “dBTAs”), all of which utilize the two components of our integrated platform, SynCon® and CELLECTRA®.

Our proprietary SynCon® technology creates optimized plasmids, which are circular strands of DNA that instruct a cell to produce proteins or antigens to help the person’s immune system respond with antibodies and immune cells which recognize and then help block viruses and destroy cancerous or pre-cancerous cells.

Our patented CELLECTRA® smart delivery devices facilitate uptake of our DNA medicines into the cell, which has been a key limitation of historical DNA-based technology approaches. Human clinical trial data from more than 15,000 CELLECTRA® smart device administrations across more than 5,000 participants to date have shown a tolerable safety profile.

Our corporate strategy is to develop, seek regulatory approval for, and commercialize our novel DNA medicines to address unmet global health needs. We continue to advance and clinically validate an array of DNA medicine candidates that target infectious diseases, such as COVID-19, as well as HPV-associated diseases and cancer. We aim to advance our product candidates through commercialization and, where applicable, with third-party resources through collaborations and partnerships, including product license agreements.

Our partners and collaborators include ApolloBio Corporation, AstraZeneca, Advaccine Biopharmaceuticals Suzhou Co, The Bill & Melinda Gates Foundation (Gates), Coalition for Epidemic Preparedness Innovations ("CEPI"), Defense Advanced Research Projects Agency ("DARPA"), The U.S. Department of Defense ("DoD"), HIV Vaccines Trial Network, the U.S. Defense Threat Reduction Agency’s Medical CBRN Defense Consortium ("MCDC"), International Vaccine Institute ("IVI"), Kaneka Eurogentec, National Cancer Institute, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Ology Bioservices, the Parker Institute for Cancer Immunotherapy, Plumbline Life Sciences, Regeneron Pharmaceuticals, Richter-Helm BioLogics, Thermo Fisher Scientific, the University of Pennsylvania, the Walter Reed Army Institute of Research, and The Wistar Institute.

We or our collaborators are currently evaluating the feasibility of, conducting or planning clinical studies of our DNA medicines for COVID-19, which includes both homologous and heterologous boosting approaches; Middle East Respiratory Syndrome, or MERS; Lassa fever; Ebola; as well as HPV-associated precancers, including cervical, vulvar, and anal dysplasia; HPV-associated cancers, including head & neck, cervical, anal, penile, vulvar, and vaginal; other HPV-associated disorders, such as recurrent respiratory papillomatosis, or RRP; glioblastoma multiforme, or GBM; and prostate cancer.

Our DNA Medicines Platform

Overview of Our Platform

Our proprietary design and optimization process for our DNA plasmids is called SynCon®. These plasmids are delivered into cells intramuscularly or intradermally via our proprietary CELLECTRA® smart devices, which use brief electrical pulses to reversibly open small pores in the cell, enabling DNA plasmids to enter. Once inside the cell, the plasmids instruct the body’s cellular machinery to produce the target antigen or monoclonal antibody. We believe our DNA medicines platform offers

versatile capabilities, both in terms of addressing several disease targets as well as providing us with several product development opportunities.

The characteristics and core components of our DNA medicines platform include:

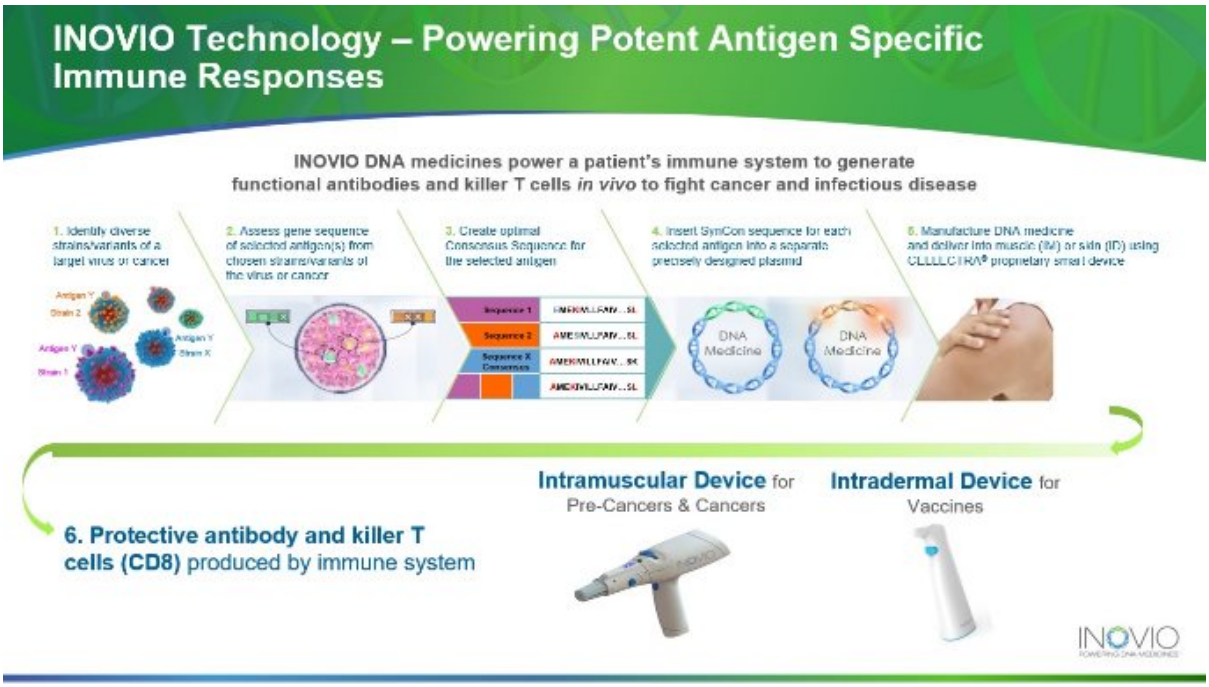
1. SynCon Design Process: SynCon uses a proprietary computer algorithm that has been designed to identify and optimize the DNA sequence of the target antigen, whether it is from a virus or a tumor.

2. CELLECTRA Smart Device: Once our DNA medicines are injected, the DNA medicines instruct the cell to produce the target antigen, monoclonal antibody, or therapeutic protein. The antigens are then processed naturally in the cell and induce the immune system to generate antibodies and T cells that perform preventive or therapeutic functions. Similarly, dMAbs® or dBTAs generated in this manner can also trigger desired immune system functions.

3. Our DNA medicines have generated *in vivo* (within the body) immune responses: With our core platform technology, we have developed a pipeline of clinical-stage product candidates that have generated *in vivo* immune responses, in particular $CD4^+$ and $CD8^+$ T cells that may be responsible for eliminating cancerous or infected cells.

4. Our DNA medicines work naturally with the immune system: Compared to some other technologies, our DNA medicines are designed to work with the immune system with reduced risk of unwanted inflammatory responses.

The mechanism of action for our DNA medicines and the process for administration of our DNA medicines are summarized in the following graphic:



Nucleic Acid Vaccines: Similarities and Differences between DNA and mRNA-based Approaches

The use of nucleic acid-based vaccines (DNA or mRNA) as an alternative to traditional immunization is a strategy that has been under development for many years. We believe that the U.S. Food and Drug Administration's (FDA) approval for emergency use authorization (EUA) of two messenger RNA (mRNA)-based vaccines for COVID-19 in 2020, as well as an EUA by Indian regulators for a DNA vaccine in 2021, suggests the benefit of using nucleic acids as vaccines.

Over the past decade, the scientific community and the vaccine industry have been asked to respond urgently to various epidemics, including but not limited to: H1N1 influenza, Ebola, Zika virus and, most recently, SARS-CoV-2, the virus that causes COVID-19. Today, multiple platforms have been used or are under development in the fight against COVID-19. Among those are DNA- and mRNA-based platforms, along with those developing viral vector and recombinant-subunit vaccines.

Our efforts to develop a DNA vaccine candidate for COVID-19 is based on the suitability and scalability of our DNA medicines platform, as well as our track record of generating clinical candidates to combat pandemic threats such as Ebola, Zika

virus, and Lassa Fever. We were the first company to advance a vaccine against MERS-CoV, a related coronavirus, into clinical evaluation in humans.

Our DNA Medicines' Differentiation from mRNA

While DNA and mRNA both use fragments of genetic materials that, once injected, instruct the body to fight pathogens, which cause cancer and infectious disease, there are key differentiating features of DNA vaccines. mRNA vaccines require colder storage temperature for transportation, necessitate complex LNP formulations for scaling, and are on average more expensive when considering manufacturing and distribution. We believe that our DNA vaccines offer several key potential advantages:

a. **Tolerability:** Our DNA vaccines appear to be well-tolerated when evaluated against multiple disease targets.

b. **Stability of Product:** Our DNA vaccines are stable for more than a year at room temperature or for more than a month at 37º C, have a five-year projected shelf life at normal refrigeration temperature and do not require frozen cold storage or shipping.

c. **Rapid Design and Manufacture:** Similar to mRNA vaccines, our DNA vaccines can be rapidly designed and scaled, which are critical aspects in addressing global pandemics like COVID-19.

d. **T Cell Responses:** Our DNA vaccines have demonstrated the ability to generate high levels of T cell ($CD4^+$ and $CD8^+$) responses along with antibody responses. The $CD8^+$ T cell responses, in particular, are regarded to be very important in their propensity to clear tumor cells in the body as well as to fight off infections. In the context of SARS-CoV-2 infection, $CD8^+$ T cells generated by our vaccine resemble those that the scientific and medical community have profiled and associated with mild COVID illness as opposed to severe illness, as well as convalescence. Furthermore, cellular responses have been preserved across different variants of SARS-CoV-2, suggesting that INO-4800 can elicit a cross-reactive immune profile.

e. **Ability to Readminister:** Our DNA vaccines have been used in clinical trials to boost our vaccines' immunity profile via repeat administration, suggesting that our DNA vaccines could be readministered if immunity wanes, offering the possibility for seasonal boosting usage without any concerns of generating an anti-vector response.

Our DNA Medicines Platform in Detail

The goal of our DNA medicines platform is to generate and deliver safe and effective therapeutics and preventive vaccines. Our technologies allow us to enable *in vivo* generation of functional immune responses to achieve desired therapeutic and preventive outcomes. Historically, we have focused primarily on *in vivo* production of disease-specific antigens in order to stimulate prophylactic or therapeutic immune responses. More recently, we have explored an additional new application for the platform: *in vivo* generation of monoclonal antibodies to achieve preventive and therapeutic outcomes complementary to our antigen-generating immunotherapies.

There are two components to our DNA medicines platform. The first is a **biological component (SynCon)**, by which we encode proteins (antigens, monoclonal antibodies, antibody fragments, and cytokines such as IL-12) into closed-circular DNA plasmids that are translated into proteins that are expressed to generate an immune response. The second component is **our proprietary CELLECTRA smart devices technology**, which facilitates delivery of the DNA plasmids.

The resulting immune responses from DNA medicine administration are designed to neutralize or eliminate infectious agents, such as viruses, bacteria, and other microorganisms, or abnormal cells, such as malignant tumors or infected cells. T cells can be "trafficked" to parts of the body where cells are displaying the target antigen. Memory cells are also created for durable effects.

SynCon® DNA Medicines Design

Our SynCon DNA medicines are designed to generate antigen-specific antibody and T cell responses. Based on extensive due diligence and pre-clinical and clinical data that we have evaluated, we first identify one or more antigens that we believe are the best targets, for directing the immune system toward a particular cancer or infectious disease. We then apply our SynCon design process, which uses the genetic make-up of the selected antigens from multiple variants of a cancer or strains of a virus.

For each antigen, we create a new genetic sequence that represents a nucleotide consensus sequence of the targeted antigen from multiple virus variants or strains. We can create a differentiated SynCon sequence to help the immune system better recognize a cancer self-antigen (from a cancerous cell grown in the body) and "break the tolerance" of those cancer cells within the body. We have generated immune responses with SynCon DNA medicines against different strains of certain infectious diseases in human clinical trials. Because the engineered SynCon sequences are substantially similar to the original sequences, without matching them exactly we believe they are patentable.

Once a SynCon sequence is engineered, it is then inserted into a circular DNA plasmid with its own promoter. The plasmid is optimized at the DNA level for codon usage and improved stability of mRNA and provided with enhanced and proprietary leader sequences for ribosome loading. It is optimized at the genetic level to enable high expression in human cells. We believe these design capabilities allow us to better target appropriate immune system mechanisms and produce a higher level of the coded antigen compared to traditional approaches, potentially enhancing the overall ability of the immunotherapy to induce the desired immune response.

The plasmids are then manufactured in a bacterial fermentation process using scalable manufacturing technology. Ultimately, the manufactured DNA medicines are designed to be stable under normal environmental conditions for extended periods of time.

Our DNA medicines platform allows for rapid design, pre-clinical testing, manufacturing at scale, and clinical development of both our DNA vaccine and DNA immunotherapy product candidates. Speed is an important feature, particularly as it relates to developing a response to globally emerging infectious diseases such as COVID-19. Responses to emerging infectious diseases that we have explored are described in more detail below.

CELLECTRA® Delivery Technology

Our DNA medicines are delivered directly into cells of the body intramuscularly (IM) or intradermally (ID) in a small, localized area of tissue using our proprietary CELLECTRA smart devices. CELLECTRA smart devices use brief electrical pulses to reversibly open small pores in the cell, enabling DNA plasmids to enter. Through this process, the cellular uptake of the DNA plasmids increases by more than 1,000-fold compared to the injection of a DNA plasmid alone without this delivery mechanism. This improved cellular uptake has enabled the immune responses observed in our clinical trials along with the efficacy results generated by these immune responses.

Our CELLECTRA portfolio consists of three devices. CELLECTRA 2000 is our clinical device that can perform both IM and ID injections. CELLECTRA 2000 has been used in almost all clinical trials to date. CELLECTRA 5PSP is our new IM device utilizing a prefilled drug CELLECTRA 5PSP is used in our Phase 3 (REVEAL1/REVEAL2) trials for cervical high squamous epithelial lesions (HSIL). Finally, CELLECTRA 3PSP is our next generation ID delivery device.

Alternative delivery approaches which typically involve or rely on virus-based vectors, bacteria, nanoparticles and lipids may be complex and expensive and, in some cases, may raise safety concerns. For example, because alternative delivery vectors themselves may possess additional antigens specific to the vector, they can attract unwanted immune responses that could compromise the vectors' ability to deliver their genetic "payload" and produce the desired immune response. In contrast, a DNA plasmid vector possesses no antigens of its own, as the plasmid results in production of only the target antigen.

We have published preclinical data in which we observed improved immune responses generated by our SynCon® DNA medicines delivered using CELLECTRA smart devices compared to a viral vector-based approach (Adenovirus type 5). The delivery of DNA medicines using CELLECTRA smart devices to date has shown a favorable tolerability and safety profile in clinical trials. Our CELLECTRA-based approach is designed to be tolerable without the need for an anesthetic.

There are several configurations in the CELLECTRA smart device family. The first configuration covers intramuscular (IM) delivery, while the second covers intradermal/subcutaneous (ID) delivery. Smart devices with these configurations have been validated, manufactured under Current Good Manufacturing Practices (cGMP) and are being used in human clinical trials. We have filed device master files with the FDA covering the use of the CELLECTRA smart devices in human clinical trials.

Our CELLECTRA smart devices combine the functionality of our current generation of ID and IM devices in clinical testing with enhanced form, design and portability. All components of the pulse generator and applicator are integrated into a cordless, rechargeable device. The rechargeable battery can enable immunization of several hundred participants, making the device useful for mass vaccinations. The devices are designed to accommodate different electrode arrays to meet the requirements of the particular DNA medicine and targeted tissue for delivery.

Next-Generation Smart Device Development

We are also advancing a new generation of small, portable, battery-powered ID delivery devices called CELLECTRA®-3PSP. Currently used ID devices penetrate no more than 3 mm into the target tissue, compared to IM devices that go deeper.

The medical arm of the U.S. Defense Threat Reduction Agency (DTRA) agreed to fund the further development of our CELLECTRA-3PSP device. DTRA provided $8.14 million of grant funding to support the development of CELLECTRA-3PSP, to be used in the administration of our vaccines and therapies, including DTRA-developed products.

In June 2020 we were awarded funding expected to be approximately $65.2 million from the U.S. Department of Defense (DoD) to support the large-scale manufacture of the CELLECTRA-3PSP smart device, the production of doses and the procurement of CELLECTRA 2000 devices. The DoD contract, from the JPEO-CRBND-EB through funding provided by the

Defense Health Program, builds upon two separate prior $5 million grants from the Bill & Melinda Gates Foundation and CEPI, to accelerate the testing of CELLECTRA-3PSP.

Background on DNA Medicines and Immuno-Oncology

Multiple technology advancements and product approvals have demonstrated the ability of immunotherapies to treat cancer. Monoclonal antibodies such as Herceptin® (anti-HER2) and its analogs have demonstrated therapeutic benefit in clinical trials and have been approved for use in a variety of cancers. While a significant step forward, monoclonal antibodies with ideal clinical characteristics have been difficult to design or identify and are expensive to produce, and the technology does not lend itself to designing mAbs for many diseases. Dendritic, or other cell-based therapies such as chimeric antigen receptor (CAR) T-cell therapies, are highly personalized medicines involving removing cells from the patient, modifying, manipulating and multiplying them, and then returning them to the body, which can be complex and costly.

Progress in the field of immune checkpoint inhibitors (ICIs) has resulted in optimism regarding the potential for new immunotherapies against a spectrum of cancers, specifically solid tumors, where cell-based therapies have not previously succeeded. The immune system relies on checkpoint mechanisms to prevent excessive or incorrectly directed immune responses. Many cancer cells can “hijack” these checkpoints and neutralize T cells sent by the immune system to eliminate them. ICIs prevent cancer cells from interfering with these safeguards and enable T cells (especially $CD8^+$ killer T cells) to complete their killing function against cancer cells. Clinical trials of ICIs have shown notable therapeutic impact against many cancers and have led to several approvals. However, ICIs may be less effective if there is not a high enough pre-existing level of antigen-specific $CD8^+$ T cells in the tumor micro-environment, meaning that the tumor is “cold” rather than “hot” (with a significant level of $CD8^+$ T cells). More recently, scientists have recognized that T cell-generating “active” immunotherapies may be able to transform a "cold" tumor into a "hot" tumor and in combination with ICIs may possess significant therapeutic potential to fight cancers.

More recently, a new category of immunotherapies called adoptive cell transfer, for example CAR-T technology, has provided further evidence of the merit of providing an enhanced T cell presence to fight cancer. CAR-T therapies have achieved dramatic results, most notably in B cell cancers. Unfortunately, they have also been associated with significant side effects. Additionally, these complex therapeutic products need to be manufactured and released for each patient, leading to expensive and timely manufacturing, as well as increased supply chain complexity.

While there have been significant clinical advances in recent years that better harness or activate capable killer T cells, we believe there is still significant potential to develop additional immunotherapies to fight cancers and infectious diseases.

We seek to advance product candidates that:

- Target disease-specific antigens or proteins unique to a cancer or infectious disease;
- Do not depend on complex manufacturing processes;
- Activate functional killer T cells;
- Generate robust T cell responses or a significant number of T cells that are persistent and durable over time (memory response);
- Do not induce toxic inflammatory responses; and
- Are capable of “breaking tolerance” of cancer cells in the body.

Data from our Phase 2b and REVEAL1 Phase 3 trial of VGX-3100, discussed below, suggest that our approach to activating significant antigen-targeted T cells may achieve these characteristics. Accordingly, we are advancing a pipeline of pre-clinical and clinical immunotherapy product candidates.

Our DNA Medicines in Development

The chart below summarizes the status of our active DNA medicines development programs, each of which is described in more detail following the chart.

VGX-3100 for the Treatment of HPV-Associated Precancerous Lesions

Overview and Background

Human papilloma virus (HPV) is a sexually-transmitted, persistent viral infection with one or more high-risk (HR) genotypes that can lead to pre-cancers and cancers, such as cervical, head and neck, anal and vulvar dysplasia and cancer. It is estimated that approximately 43% of the U.S. adult population is infected with HPV, and about 25% of adult men and 20% of adult women in the U.S. have a genital infection with one or more HR-HPV genotypes such as HPV-16 and HPV-18. HPV is the most common viral infection of the reproductive tract and HPV-16 and HPV-18 infections specifically are the major causes of cervical cancers globally. Almost 300 million women globally are estimated to be infected with HPV, with another 30 million additional cases that have progressed to the pre-cancerous stage. While most genital HPV infections are cleared naturally by the body's own immune system, persistent cervical infection with one or more HR-HPV genotypes can eventually lead to cervical high-grade dysplasia (HSIL) and eventually to cervical cancer. Researchers have estimated the global prevalence of clinically pre-cancerous cervical HSILs at between 28 and 40 million.

Current management options for cervical HSIL are limited and are associated with potential unwanted side effects. The “watch-and-wait” process associated with low-grade squamous intraepithelial lesions (LSIL, formerly called low-grade dysplasia or CIN 1) and in some young women with higher grade lesions (though only for the CIN 2 level of cervical HSIL) can be a stressful approach. The only available current treatment option for cervical HSIL is surgery, which involves ablating or cutting into a women’s cervix to remove the pre-cancerous or cancerous lesions. These treatments may lead to short-term adverse effects including cervical scarring, excess bleeding, and infection, or to longer-term reproductive risks such as pre-term birth, miscarriage, and perhaps infertility. More importantly, because surgery does not clear the underlying systemic HPV infection, there is a chance of high-grade pre-cancer lesion recurrence after surgery as a result of persistent HPV infection and/or incomplete removal of the lesion.

While there is currently a vaccine available to prevent HPV infection, challenges with acceptance, accessibility and compliance of vaccines to prevent HPV infection and their resulting pre-cancers and cancers have resulted in many vaccine-eligible people remaining unvaccinated and at risk; it is estimated that even in the United States, only 60% of the eligible population has been vaccinated against HPV. In addition, preventive HPV vaccines cannot treat or protect those already infected with the same HPV genotypes, which is a large population. Currently there is no viable immunotherapy or drug available to fight incident, prevalent, or persistent HPV infection or to treat cervical HSIL. We therefore believe that there is a significant market opportunity for our therapeutic product candidate VGX-3100.

VGX-3100 is designed to increase T cell immune responses against the E6 and E7 oncogenic proteins of high-risk HPV types 16 and 18 that can be present in both precancerous and cancerous cells transformed by these HPV types. E6 and E7 are oncogenes that play an integral role in transforming HPV-infected cells into precancerous and cancerous cells, thus making them appealing targets for T cell directed immunotherapy. The goal of VGX-3100 is to stimulate the body's immune system to

generate a T cell response strong enough to kill the cells producing the E6/E7 protein. The potential of such an immunotherapy would be to treat HSIL caused by these HPV types.

VGX-3100 for the Treatment of Cervical HSIL

We have completed randomized, blinded, placebo-controlled Phase 2b and Phase 3 clinical trials of VGX-3100 compared to placebo, in women with HPV-16 and HPV-18 cervical HSIL. Data from the Phase 2b trial supported our Phase 3 development program; in the Phase 2b trial, women treated with VGX-3100 were more likely to demonstrate resolution of cervical HSIL and HPV clearance from cervical lesions than those women receiving placebo. In addition, antigen-specific T cell levels in women treated with VGX-3100 were greater than those treated with placebo. All women were monitored for an additional 52 weeks following the primary endpoint to assess for safety; VGX-3100 was considered to be well-tolerated and there were no safety concerns observed. Immune endpoints were also assessed and women whose lesions regressed also had higher frequencies of HPV-specific $CD8^+$ T cells which co-expressed key molecules important in the T cell killing cascade and directly correlated with clinical efficacy. To our knowledge, this Phase 2b trial was the first study from which data was published indicating a direct correlation between antigen-specific $CD8^+$ T cells generated in vivo and clinical efficacy.

Phase 3 Trials (REVEAL1 and REVEAL2)

In preparation for Phase 3 development and potential commercialization, we completed a manufacturing technology-transfer to a commercial manufacturing facility and scaled up manufacturing of VGX-3100.

We also designed and manufactured a new smart delivery device, CELLECTRA®-5PSP, which is being used in our global Phase 3 clinical trial of VGX-3100. This smart device uses a cordless applicator and charges cordlessly in an improved base station that has been optimized for ease of use in the clinic.

Our Phase 3 program, named REVEAL, consists of a primary trial (REVEAL1; HPV-301) and confirmatory trial (REVEAL2; HPV-303), being conducted in parallel. The REVEAL trials are prospective, randomized (2:1), double-blind, placebo-controlled trials evaluating adult women with HPV 16/18 positive biopsy-proven cervical HSIL (CIN 2/3). The primary endpoint is regression of cervical HSIL and virologic clearance of HPV-16 and/or HPV-18 in the cervix, which was a secondary endpoint that was achieved in our Phase 2b trial. Overall, the Phase 3 trials are evaluating cervical tissue changes at approximately 9 months after beginning a three-dose regimen of VGX-3100 administered at months 0, 1 and 3.

In March 2021, we announced the result of the REVEAL1 trial of VGX-3100. The trial protocol-defined intention to treat (ITT) population (N=201) includes all randomized participants regardless of availability of endpoint data and defines those without endpoint data as non-responders. There were eight such participants (seven in the treatment group, one in the placebo group) in the ITT population. Including participants with missing endpoint data, the percentage of participants meeting the primary endpoint was 22.5% (31/138) in the treatment group, versus 11.1% (7/63) in the placebo group (p=0.029; 95%CI: -0.4,21.2), which was not statistically significant. All secondary endpoints were achieved except for regression of cervical HSIL alone (95%CI: -0.6,24.5).

For the protocol-defined mITT population (N=193) which includes all participants with endpoint data, we announced that VGX-3100 had achieved the primary and secondary endpoints among all evaluable participants. For the primary endpoint of histopathological regression of HSIL and virologic clearance of HPV-16 and/or HPV-18 at week 36, the percentage of responders was 23.7% (31/131) in the treatment group, versus 11.3% (7/62) in the placebo group (p=0.022; 95%CI: 0.4,22.5), thus achieving statistical significance. All secondary efficacy endpoints were achieved in this population. These endpoints were: a) regression of cervical HSIL to normal tissue combined with HPV16/18 viral clearance, b) regression of cervical HSIL alone, c) regression of cervical HSIL to normal tissue, and d) HPV 16/18 viral clearance alone. There were no treatment-related serious adverse events (SAEs) and most adverse events (AEs) were self-resolving and were considered to be mild to moderate, consistent with earlier clinical trials. These data were presented at the 2021 American Society for Colposcopy and Cervical (ASCCP) annual scientific meeting, and at the 34th International Papillomavirus Conference (IPVC) in November 2021.

We completed the 52-week safety follow-up of participants in REVEAL1 and showed that VGX-3100 remained well-tolerated through Week 88. In addition, participants treated with VGX-3100 who met the primary endpoint at Week 36 remained clear of HPV-16 and/or HPV-18 at Week 88.

REVEAL2 is the second of two Phase 3 trials and the confirmatory trial agreed upon by INOVIO and FDA. Endpoints for REVEAL2 are identical to those for REVEAL1; participants will be followed for up to 40 weeks. Enrollment of REVEAL2 was completed in the fourth quarter of 2021. Top-line efficacy and safety data are expected to be available in the second half of 2022.

VGX-3100 for the Treatment of Vulvar HSIL

HPV-16 and HPV-18 can cause precancerous and cancerous lesions of the vulva. These precancerous lesions, or vulvar HSIL, have less than a 5% rate of spontaneous or natural regression and there are no FDA-approved non-surgical treatments. Surgery, the most common treatment, is associated with high rates of disease recurrence and can cause disfigurement, long-term

pain, and psychological distress for women who undergo the procedure. Vulvar HSIL recurs in approximately one-half of patients who undergo surgical treatment.

We have also completed a Phase 2 trial (HPV-201) to evaluate the efficacy of VGX-3100 in participants with vulvar HSIL. This randomized, open-label Phase 2 clinical trial assessed the efficacy of VGX-3100 in 33 women with vulvar HSIL. VGX-3100 was administered with our CELLECTRA® -5PSP smart device. The primary endpoint of the trial was histologic clearance of high-grade lesions and virologic clearance of the HPV virus in vulvar tissue samples. The trial also evaluated the safety and tolerability of VGX-3100. In January 2021, we announced positive efficacy results from this trial. A 25% or more reduction in HPV-16/18-associated vulvar HSIL was observed for 63% of trial participants (12 of 19) treated with VGX-3100 at six months post-treatment. Three of the 20 participants with histology data (15%) resolved their vulvar HSIL and had no HPV-16/18 virus detectable in the healed area. VGX-3100 was well-tolerated in the Phase 2 trial.

We are evaluating future clinical steps for the vulvar HSIL program, including the potential for applying for U.S. FDA Orphan Drug Designation (ODD) for this indication. ODD is intended to encourage drug development for rare diseases by providing tax credits for qualified clinical trials, an exemption from user fees related to the New Drug Application or Biological License Application, and a potential of up to seven years of market exclusivity after approval. The FDA grants orphan drug status to medicines intended for the prevention, diagnosis, and treatment of rare diseases or conditions, as defined as a disease or condition with a prevalence of less than 200,000 patients in the United States annually.

VGX-3100 for the Treatment of Anal or Perianal HSIL

HPV-16 and HPV-18 can also cause precancerous lesions of the anus (anal HSIL). Left untreated, anal HSIL may progress to cancer. Spontaneous regression of anal HSIL is observed in approximately 20% of patients. Persistent infection with one or more high-risk HPV genotypes is responsible for a large portion of anal cancer. In the United States, about 55% to 80% of anal HSIL cases are associated with HPV-16/18, and worldwide about 80% of anal HSIL cases are associated with HPV-16/18. In the United States, over 90% of anal cancer is attributable to HPV, and about 87% of those HPV anal cancers are attributable to HPV-16/18 specifically.

There are no validated screening tests or a general screening recommendation consensus for anal HSIL. Treatment usually consists of repeated ablation, most commonly radiofrequency ablation (RFA), resections or laser therapy. However, recurrence rates are high, up to 49% one year after treatment, resulting in an unmet medical need.

We have completed a Phase 2 clinical trial (HPV-203) to evaluate VGX-3100 in participants who are HIV-negative with histologically confirmed anal or perianal HSIL, or anal intraepithelial neoplasia (AIN), associated with HPV-16 and/or HPV-18. This open-label trial enrolled 24 participants who received three doses of VGX-3100 delivered by our CELLECTRA®-5PSP device. The primary endpoint of the trial was histologic clearance of the high-grade lesions and virologic clearance of the HPV-16/18 virus in anal/perianal tissue samples. In December 2020, we announced positive Phase 2 efficacy results from this trial. One-half of participants treated with VGX-3100 (11/22) showed resolution of HPV-16/18-associated anal HSIL at six months following the start of treatment. VGX-3100 was well-tolerated in the trial. We plan to pursue a registrational Phase 3 clinical trial for HPV-16-/18-associated anal HSIL as well as to apply for ODD from the U.S. FDA.

In addition to the Phase 2 anal HSIL trial sponsored by us, a separate ongoing Phase 2 trial sponsored by the AIDS Malignancy Consortium (AMC-103) is evaluating VGX-3100 in participants with histologically confirmed anal or perianal HSIL associated with HPV-16 and/or HPV-18 who are HIV-positive. This open-label single-arm trial plans to enroll approximately 75 participants who will receive up to four doses of VGX-3100 delivered by CELLECTRA®-5PSP smart device. The primary endpoint of the trial is histological regression of high-grade anal lesions to low-grade SIL or normal histology.

VGX-3100 Immune Correlates and Biomarker Signatures

We are pursuing a biomarker signature for our VGX-3100 program. In May 2019, we entered into a collaboration with QIAGEN N.V. to co-develop a liquid biopsy-based diagnostic for this biomarker signature to identify women with HPV-16/18 cervical HSIL most likely to respond to VGX-3100. In February 2021, we announced an extension of our partnership with QIAGEN with a new master collaboration agreement to develop liquid biopsy-based companion diagnostic products based on next-generation sequencing technology to complement our therapies. QIAGEN is utilizing the Illumina NextSeq™ 550Dx platform for this biomarker, the first development based on a partnership QIAGEN and Illumina signed in October 2019.

In December 2021, we announced that we and QIAGEN have identified candidate biomarker signatures for VGX-3100 with the intent of selecting a final signature of a pre-treatment in vitro diagnostic to meet the specific characteristics desired to identify women with HPV-16/18 cervical HSIL most likely to respond to VGX-3100. This biomarker, if validated, may have the potential to identify those women who are more likely to have a favorable treatment outcome, specifically the regression of cervical HSIL and clearance of virus.

ApolloBio Collaboration Agreement for VGX-3100 within Greater China

In 2017, we entered into an agreement providing ApolloBio Corporation with the exclusive right to develop and commercialize VGX-3100 within Greater China (defined as China, Hong Kong, Macao and Taiwan). Additional details on the

ApolloBio Agreement are provided below under "License, Collaboration and Supply Agreements." In December 2021, ApolloBio dosed its first participant in a separate Phase 3 trial in China (HPV-303CHN).

INO-3107 for the Treatment of Recurrent Respiratory Papillomatosis (RRP)

RRP is a rare disease (estimated at about 7,000 active prevalent cases in the United States in 2018, including both juvenile and adult cases) that is characterized by the growth of tumors in the respiratory tract primarily caused by HPV-6 and/or HPV-11 genotypes. Although mostly benign, such papillomas can cause severe, sometimes life-threatening airway obstruction and respiratory complications. A distinguishing aspect of this disease is the tendency for the papilloma to recur after surgical procedures to remove them. If RRP develops in the lungs, affected individuals can potentially experience recurrent pneumonia, chronic lung disease (bronchiectasis) and, ultimately, progressive pulmonary failure. In extremely rare cases (less than 1%), RRP can develop into squamous cell carcinoma. Additional symptoms of RRP can include hoarse voice, difficulty in sleeping and swallowing, and chronic coughing. RRP symptoms are usually more severe in children than in adults. In children, the disorder is most often diagnosed at or around the age of four years. In adults, the disorder occurs most often in the third or fourth decade, though evidence exists for some incidence of new diagnoses in the sixth decade.

In February 2020, we commenced an open-label, multicenter Phase 1/2 trial that is evaluating the efficacy, safety, tolerability and immunogenicity of INO-3107, a DNA medicine candidate similar to INO-3106, but targeting HPV-6 and HPV-11 associated RRP and including INO-9112, encoding IL-12, in participants with HPV-6 and/or HPV-11-associated RRP. For this trial, adult participants will first undergo surgical removal of their papilloma(s) and then receive up to four doses of INO-3107, once every three weeks. The primary endpoint of this trial is safety and tolerability. The trial is also assessing efficacy as a function of the number of treatments required to treat RRP relative to the number of treatments required to control disease prior to enrollment in the trial. We began enrollment in November 2020, and completed enrollment of the first 32 participants in December 2021. All 32 adult participants first underwent surgical removal of their papilloma(s) and then received four doses of INO-3107, one every three weeks. We expect preliminary efficacy data from a portion of participants from this Phase 1/2 trial in the second half of 2022.

In July 2020, we announced that the U.S. FDA granted ODD for INO-3107.

INO-5401 for the Treatment of Glioblastoma Multiforme (GBM)

Glioblastoma multiforme (GBM) is the most common and aggressive type of brain cancer. In the United States, the median age at diagnosis is 65 years, and the incidence rate increases thereafter. Prognosis is extremely poor, and a limited number of new therapies have been approved over the last 10 years; median overall survival for U.S. patients receiving standard of care therapy was approximately eight months and the five-year survival was 6.8% for all ages combined. The annual incidence of GBM is estimated to be approximately 12,000 cases per year and increasing.

Our product candidate INO-5401 is an immunotherapy consisting of three synthetic DNA plasmids encoding for three tumor-associated antigens: human telomerase (hTERT), Wilms tumor gene-1 (WT1) and PSMA. The National Cancer Institute previously highlighted WT1, hTERT and PSMA among a list of important cancer antigens, designating them as high priorities for cancer immunotherapy development, as these three tumor-associated antigens are commonly expressed in human cancers.

In 2017, we reported data indicating that our SynCon® WT1 cancer antigen was capable of breaking immune tolerance, a major challenge to researchers striving to develop potent cancer therapies and induced neo-antigen-like T cell responses to cause tumor regression in pre-clinical studies. The results were published in the scientific journal Molecular Therapy.

While mice in the preclinical study did not mount an immune response to native mouse WT1 antigens, mice immunized with our SynCon WT1 antigen broke tolerance and generated robust neo-antigen-like T cells. The immunized mice also exhibited smaller tumors and prolonged survival in a tumor challenge study. SynCon WT1 DNA vaccination also broke tolerance and generated neo-antigen-like T cell immune responses in Rhesus monkeys, a species whose immune system closely resembles that of humans. The ability to overcome the immune system’s usual tolerance of WT1 antigen suggests the potential of our SynCon WT1 antigen to address multiple WT1-expressing cancer in humans. We previously reported similar results for our SynCon hTERT and PSMA cancer antigens.

We have completed a Phase 1/2 immuno-oncology trial of INO-5401 and INO-9012 (IL-12 plasmid) in participants with newly diagnosed GBM, in combination with cemiplimab (Libtayo®), a PD-1 inhibitor developed jointly by Regeneron Pharmaceuticals and Sanofi. This open-label trial began in 2018 and enrolled 52 newly diagnosed GBM participants. The primary endpoint was safety and tolerability, and the trial also evaluated immunogenicity and efficacy (overall survival). Data from the trial has been presented at several medical conferences. In November 2019, we provided interim results showing that 80% (16 of 20) of MGMT gene promoter methylated participants and 75% (24 of 32) of unmethylated participants, the more difficult to treat group, were progression-free at six months (PFS6) measured from the time of their first dose, exceeding historical standard-of-care data. This immunotherapy combination with a PD-1 checkpoint inhibitor also exhibited supportive safety, tolerability, and immunogenicity data and suggested a safety profile consistent with that of Libtayo as well as our other

product candidates. Most participants assessed had a T cell immune response to one or more tumor-associated antigens encoded by INO-5401, and immune responses to all three tumor-associated antigens were also observed in this trial.

In May 2020, we updated these results, showing that 85% (44 out of 52) of the participants in this trial were alive for at least 12 months following treatment. The updated results showed that 84.4% percent (27 of 32) of participants with MGMT promoter unmethylated tumors, and 85% (17 of 20) of participants with MGMT promoter methylated tumors, were alive at 12 months. Activated killer T cells directed towards one, two or all three cancer antigens in INO-5401 were detected in almost all participants tested.

In November 2020, additional data from the trial were presented at the Society for Neuro-Oncology (SNO) Annual Meeting. Survival data at 18 months showed that 70% (14/20) of MGMT promoter methylated GBM participants were alive, and 50% (16/32) of MGMT promoter unmethylated participants were alive after 18 months. Median overall survival in the unmethylated GBM participants was 17.9 months, which compares favorably to historical controls. An update on immunology data showed that in the MGMT promoter unmethylated cohort, 19 of 22 (86%) participants had an IFN-gamma T cell response that increased over baseline to one or more of the antigens encoded by INO-5401. In the MGMT promoter methylated cohort, 16 of 17 (94%) participants had an IFN-gamma response that increased over baseline to one or more of the antigens encoded by INO-5401.

In November 2021, updated data was presented at the Society for Immunotherapy of Cancer pre-conference workshop from the GBM-001 Phase 2 trial. Overall survival at 24 months was 22% (7/32) for the MGMT unmethylated cohort and 55% (11/20) for the MGMT methylated cohort. The trial showed that INO-5401+INO-9012 with cemiplimab and radiation/TMZ have an acceptable safety profile, are immunogenic, and may improve survival in newly diagnosed GBM.

INO-5151 (INO-5150 + INO-9012) for the Treatment of Prostate Cancer

We are developing INO-5151, which consists of DNA plasmids targeting Prostate Specific Antigen (PSA) and Prostate Specific Membrane Antigen (PSMA), combined with INO-9112, the IL-12 plasmid, for the treatment of prostate cancer. In the United States in 2022, there will be an estimated 268,490 new cases of prostate cancer and about 34,500 deaths due to this cancer. We previously completed a Phase 1 trial of INO-5150, DNA plasmids targeting PSA and PSMA. Data from this trial have been presented at several annual meetings, most recently at the 2018 European Society for Medical Oncology (ESMO) congress and have suggested that men treated with INO-5150 on the trial experienced a slowing of PSA doubling time, an important indicator of potential clinical benefit. Data presented at these conferences also showed immunogenicity and tolerability of INO-5150.

In 2019, we announced a clinical collaboration with Parker Institute for Cancer Immunotherapy (PICI) and the Cancer Research Institute (CRI) as part of which INO-5151 is being combined with an immune modulator (CDX-301, FLT3 ligand, a dendritic cell mobilizer) and a PD-1 immune checkpoint inhibitor (nivolumab) in participants with metastatic castration-resistant prostate cancer (mCRPC), in a PICI-sponsored platform trial (PORTER). This combination trial is an open-label, non-randomized, exploratory platform trial designed to assess the safety and antitumor activity of multiple immunotherapy-based combinations in participants with mCRPC who have received prior secondary androgen inhibition. This trial will evaluate biomarkers of immune activity and clinical outcomes using a multi-omic, multi-parameter approach. Our immunotherapy is one arm of this PICI-supported trial, and recruitment is ongoing. Under the agreement, PICI will design and conduct the clinical trial, working in collaboration with its established network of clinical academic and industry cancer centers, with funding support from CRI. We will provide financial contributions based on the actual costs of the trial, if INO-5151 reaches the initiation of a Phase 3 trial.

Infectious Disease Product Candidates

Our product development platform also allows for rapid design, pre-clinical testing, manufacturing and clinical development of our vaccine and immunotherapy product candidates. In 2016, we were the first entity able to advance a Zika virus vaccine into human clinical trials, 4.5 months after the World Health Organization, or WHO, declared the emerging Zika virus infections to be a Pandemic Health Emergency of International Concern. Previously, we led the development of the first MERS vaccine in human clinical trials. More recently, our DNA medicines platform and SynCon® capabilities allowed us to rapidly respond to the SARS-CoV-2 coronavirus outbreak in early 2020. We believe that our development platform is well positioned to support global health agencies to develop preparedness countermeasures against bioterrorism and/or emerging pandemic agents.

INO-4800 for COVID-19

Background

A novel strain of coronavirus emerged in the human population in Wuhan City, China in late 2019. The new virus is a member of the genus of Coronaviruses, which is comprised of seven known viruses that can infect and make humans ill, including Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Coronavirus

(SARS-CoV), as well as four other lower risk coronaviruses which can cause the common cold. The disease caused by the SARS-CoV-2 novel coronavirus was subsequently named COVID-19.

The virus quickly spread throughout China, Asia, and worldwide. As of February 2021, almost every country on earth had reported confirmed cases. As of January 2022, a total of nearly 320 million confirmed cases had been reported worldwide, with a total of more than 5,510,000 reported deaths directly due to this disease. Both the numbers of reported and estimated actual cases began to rise significantly in 2022 with the emergence of the Omicron variant of concern of the SARS-CoV-2 virus.

Presently, several major variants of concern (VOCs) of SARS-CoV-2 have evolved and spread significantly from several portions of the globe and quickly to many countries. These VOCs have the characteristics of at least having a significantly increased transmission rate compared to the original/main SARS-CoV-2 strain. Currently authorized vaccines may not be as effective at preventing disease due to these variants.

Phase 1 Clinical Trial

In December 2020, we announced the publication of peer-reviewed Phase 1 clinical data from the first cohort of 40 participants receiving INO-4800. In this trial, INO-4800 was immunogenic in all vaccinated participants, generating an immune response of humoral (including neutralizing antibodies) and/or cellular responses (both $CD4^+$ and $CD8^+$ T cells).

Additionally, Phase 1 clinical data found INO-4800 to have a favorable safety and tolerability profile with no serious adverse events reported. Six Grade 1 adverse events (AEs) were observed, primarily minor injection site reactions. These only occurred on the day of the first or second dosing, and the AEs did not increase in frequency with the second administration.

Phase 2/3 Clinical Trial – INNOVATE

In December 2020, we announced the dosing of the first participant in our Phase 2 clinical trial evaluating INO-4800, as part of our Phase 2/3 clinical trial, called INNOVATE (INOVIO INO-4800 Vaccine Trial for Efficacy). The Phase 2 segment of the trial has enrolled approximately 400 participants who are 18 years or older at 17 U.S. sites to evaluate safety and immunogenicity in order to confirm the dose(s) for the subsequent efficacy evaluation as part of the Phase 3 segment of the trial.

The Phase 2 segment of the trial, funded by the DoD, evaluated safety, tolerability and immunogenicity of INO-4800 in a two-dose regimen (1.0 mg or 2.0 mg), in a three-to-one randomization to receive either INO-4800 or placebo to confirm the more appropriate dosing level(s) for each of three age groups (18-50 years, 51-64 years and 65 years and older) at high risk of SARS-CoV-2 exposure for the subsequent Phase 3 efficacy evaluation. Results from the Phase 2 segment provided us with the information to select the dose level for the Phase 3 segment.

The global Phase 3 segment of INNOVATE is a randomized, blinded, placebo-controlled clinical trial to evaluate the safety and efficacy of INO-4800 in a two-dose regimen (2.0 mg per dose), administered one month apart, in a 2-to-1 randomization in men and non-pregnant women 18 years of age and older. The primary endpoint of this case-driven Phase 3 trial is virologically confirmed symptomatic COVID-19. The Phase 3 segment has received authorization to proceed in seven countries: Mexico, Brazil, Colombia, Thailand, India, Philippines, and the United States.

We conducted an in vitro assessment of the cross-reactivity of INO-4800 vaccine-induced immune responses against the Omicron variant of SARS-CoV-2. Testing was observed to provide full maintenance of T cell responses against the Omicron variant in clinical samples from participants who has received INO-4800, including CD8+ responses, in line with results observed with the vaccines of other developers, significantly decreased levels of both neutralizing and binding antibodies against Omicron. The maintenance and preservation of T cell responses continue to remain a consistent observation for INO-4800 against the ancestral COVID-19 virus and across all variants of concern (VOCs) tested to date, including Omicron. We believe this is a critical observation as T cell responses are thought to play an important role in protection against severe disease and death and may be central to the durability of vaccine protection.

In response to the dominance of the Omicron variant globally and the persistence of cross-reactive T cell responses generated by INO-4800, including CD8+, across all variants of concern to date, we plan to seek regulatory approval to amend the primary endpoint of INNOVATE from prevention of virologically confirmed COVID-19 disease to prevention of severe disease due to COVID-19. We believe INO-4800's ability to generate T cell responses could be critical in meeting the proposed amended primary endpoint.

In addition, to reflect the potential impact of the Omicron variant on INNOVATE, the Data Safety Monitoring Board (DSMB) recommended that we pause enrollment of new patients in the global Phase 3 clinical trial of INO-4800 in order to update the Informed Consent Form and Investigator Brochure. As a result of the DSMB’s recommendation, as well as our plans to seek approval to amend the trial’s primary endpoint, we have paused enrollment of new patients in INNOVATE. Interim efficacy data from INNOVATE will therefore not be available in the first half of 2022 as previously expected.

We are also evaluating the feasibility of an additional ex-US heterologous boost (vaccination with a different vaccine from the previous administration) trial with our COVID-19 DNA vaccine candidate, INO-4800, as a booster in a non-inferiority

clinical trial compared to approved viral vector and inactivated COVID-19 vaccines. Viral vector and inactivated COVID-19 vaccines have been the vaccine of choice, particularly in low-to-middle income countries where thermostability of a vaccine can be critical. Moreover, global demand for heterologous boosters may not be met with currently licensed vaccines (EUA or full authorization) or those not currently licensed but with Phase 3 efficacy data. While a clear regulatory pathway for a heterologous boost trial has not been defined, regulatory agencies in some countries have expressed consideration towards the use of heterologous boost vaccines in clinical trials, given the logistical challenges as well as vaccine hesitancy associated with some approved vaccines. We believe that second generation vaccines are needed to address issues such as vaccine equity and logistical challenges that are still left to be solved. At the same time, we recognize that there are regulatory hurdles to be cleared. Key features of our DNA vaccine technology which make it a potentially favorable booster candidate include generating T-cell responses against multiple variants of concern, lack of anti-vector immunity, tolerability of re-administration, thermostability for transport, storage, and distribution.

Phase 2/3 Clinical Trial – SOLIDARITY TRIAL VACCINES (STV)

INO-4800 is one of two initial COVID-19 vaccine candidates included in the WHO's Solidarity Trial Vaccines, which is designed to "rapidly evaluate the efficacy and safety of promising new candidate vaccines selected by an independent vaccine prioritization advisory group composed of leading scientists and experts." Recruitment for the trial has begun in Colombia, Mali and the Philippines; enrollment is expected at more than 40 sites across the three countries. According to the WHO, the trial "has the additional potential to uncover second-generation vaccines with greater efficacy, conferring greater protection against variants of concern offering longer duration of protection, and/or using needle-free routes of administration." The trial is sponsored by the WHO.

INO-4800 in China

In December 2020, we announced the dosing of the first participant in our Phase 2 clinical trial of INO-4800 in China. The Phase 2 clinical trial being conducted in China is independent of the INNOVATE Phase 2/3 clinical trial of INO-4800 and will enroll approximately 640 participants who are 18 years or older. Our collaborator Advaccine is conducting and funding the Phase 2 trial in China.

The Phase 2 clinical trial of INO-4800 in China has enrolled both 18-59 years old adults and older adults (60 years and older) with the primary endpoints of evaluating safety and immunogenicity within the Chinese population. The dosing regimen involves two vaccinations at 0 and 28 days with either 1.0 mg or 2.0 mg dosing levels and is similar to the Phase 2 segment of the INNOVATE trial.

Our partner Advaccine has completed enrollment of its 200-participant homologous and 267-participant heterologous boost trials in China. The trials are designed to evaluate safety, tolerability, and immunogenicity of INO-4800 as a homologous boost where INO-4800 was administered as the primary vaccine and as heterologous boost where an inactivated vaccine was administered as the primary vaccine.

COVID-19 dMAb®

In December 2020, we announced that we along with a team of scientists from The Wistar Institute, AstraZeneca, the University of Pennsylvania, and Indiana University received a $37.6 million grant from the U.S. Defense Advanced Research Projects Agency (DARPA), a research and development agency of the DoD and the JPEO-CBRND, to use our dMAb technology to develop anti-SARS-CoV-2-specific dMAbs that function as both a therapeutic and preventive treatment for COVID-19. See “Synthetic DNA-based Monoclonal Antibodies Program” below for more information about our dMAb technology.

As part of DARPA's two-year grant, our and Wistar's teams have constructed COVID-19 dMAb candidates mirroring AstraZeneca's traditional recombinant monoclonal antibody candidates currently being tested in clinical trials to treat COVID-19. These dMAb candidates can be quickly developed and produced *in vivo*, offering a cost-effective and scalable therapeutic and preventive option for treatment of SARS-CoV-2 virus infection. The dMAb® candidates will then be advanced into preclinical studies and then potentially into human clinical trials.

Global Manufacturing Consortium for INO-4800

In March 2020, we received a $5 million grant from the Bill & Melinda Gates Foundation to accelerate the testing and scale up of CELLECTRA® 3PSP proprietary smart devices for the intradermal delivery of INO-4800.

In April 2020, we announced an agreement to expand our manufacturing partnership with the German contract manufacturer Richter-Helm BioLogics GmbH & Co. KG, to support large-scale manufacturing of INO-4800.

In September 2020, we announced that Thermo Fisher Scientific signed a letter of intent to manufacture INO-4800. Thermo Fisher plans to manufacture INO-4800 drug substance as well as perform fill and finish of INO-4800 drug product at its commercial facilities in the United States.

In December 2020, we announced the execution of an agreement with Kaneka Eurogentec S.A., an affiliate of Kaneka Corporation, for Eurogentec to manufacture INO-4800 at their GMP plasmid production site in Belgium.

COVID-19 Variants of Concern (VOC)

We have been closely monitoring the development and evolution of SARS-CoV-2, with a particular focus on the Alpha (aka B.1.1.7 or "UK"), Beta (aka B.1.351 or original "South African"), Gamma (aka B.1.1.28.1 or "Brazilian"), Delta (aka B.1.617.2 or "Indian"), and Omicron (aka B.1.1.529 or newer "South African") variants of concern (VOCs) of the SARS-CoV-2 virus. We have been and are continuing to evaluate the impact of newly circulating strains of the SARS-CoV-2 virus on the immune profile of INO-4800 through an assessment of binding antibodies, neutralizing antibodies in both live and pseudo-type neutralization assays as well as assessing the impact of the INO-4800-generated T cell responses on these variants.

We are also developing next-generation, pan-COVID vaccine candidates, that could be tailored to the known and potentially the unknown SARS-CoV-2 variants. Using our SynCon® gene optimization algorithm to analyze the available sequence data from all existing circulating variants, we are seeking to create a synthetic SAR-CoV-2 spike protein gene design intended to protect against the known VOC as well the future unknown strains. Our DNA vaccines generate a balanced immune response, including T cell responses, which we believe could make our pan-COVID vaccine candidates less susceptible to changes in the genetic sequence of the virus. DNA vaccines can also be used for multiple boosts without being impacted by anti-vector immunity or an increase in reactogenicity. Moreover, pre-clinical studies and clinical trials have shown that DNA vaccines could also be used to boost the initial immune responses generated by multiple other vaccine platforms.

INO-4700 for Middle East Respiratory Syndrome (MERS)

Background on MERS

The Middle East Respiratory Syndrome or MERS is a viral respiratory illness first reported in Saudi Arabia in 2012. MERS appears to have been transmitted from an animal reservoir to humans but human to human transmission has been confirmed. The virus for this disease belongs to the Coronaviradea family (or a coronavirus – MERS-CoV), and was not shown to be a communicable virus spreading in a sustained way in communities, but rather via rapid spread in the nosocomial setting, such as emergency rooms and/or hospitals without adherence to state-of-the-art infection control practices, which can result in outbreaks with many cases, including super-spreading events. Like the severe acute respiratory syndrome (SARS) outbreak in 2003 linked to another coronavirus (SARS-CoV-1), which made approximately 8,000 people ill and was fatal in nearly 10% of those cases, MERS-CoV appears to cause severe lung infections. However, the case-fatality rate (death rate) of MERS has typically been between 30% and 40%, which is significantly higher than that of SARS. While the SARS epidemic in 2003 killed 10% of those who became ill from the SARS virus, MERS has killed approximately 34% of people who people who became ill from the MERS virus from 2012 to October 2021. MERS differs in that it also causes rapid kidney failure. Its high death rate has caused serious concern among global health officials.

Despite the continuing threat of MERS outbreaks, there are no approved vaccines or treatments for MERS.

Clinical Development – MERS

In April 2018, we announced a collaboration with CEPI under which we are developing vaccine candidates against MERS. CEPI will fund up to $56 million of costs to support our pre-clinical and clinical advancement through Phase 2 of our vaccine candidate INO-4700. The goal of the collaboration is for our MERS vaccine to be available as soon as possible for emergency use.

In April 2020, we announced interim data through week 16 from a Phase 1/2a trial of DNA vaccine INO-4700. Vaccine recipients had strong antibody and T cell immune responses after 2 or 3 doses with 0.6 mg, delivered intradermally with our CELLECTRA® device. The vaccination regimen was well-tolerated with no vaccine-associated SAEs. The researchers at the Wistar Institute, Seoul National University Hospital, and the International Vaccine Institute (IVI) collaborated on this trial.

For those receiving 0.6 mg of INO-4700, 88% seroconverted after a two-dose regimen at 0 and 8 weeks, while for those receiving a three-dose regimen given at 0, 4 and 12 weeks, 84% seroconverted after 2 doses and 100% after 3 doses, as measured by a binding antibody assay against the full-length S protein (ELISA). Additionally, 92% of the vaccine recipients in both groups displayed the ability to neutralize the virus using a pseudotype-based neutralization assay. Robust T cell responses were observed in 60% of vaccine recipients after the two-dose regimen and 84% of those in the three-dose group (ELISpot assay). A single dose of 0.6 mg of INO-4700 intradermal vaccination resulted in 74% binding antibody response rate and 48% neutralization antibody response rate.

We have dosed and completed enrollment for the first part (dose finding stage) of the Phase 2 trial (192 participants) of INO-4700. The multi-center Phase 2 trial is a randomized, double-blinded, placebo-controlled trial designed to evaluate the safety, tolerability, and immunogenicity of INO-4700 administered with CELLECTRA 2000 in approximately 500 healthy adult participants. The trial, which is sponsored by INOVIO and fully funded by CEPI, is being conducted at sites in Jordan, Lebanon, and Kenya where MERS cases have been reported.

INO-4201 for Ebola Virus Disease

Background on Ebola

The Ebola virus causes one of the most virulent viral diseases, with case fatality rates averaging 50% but approaching up to 90% in past outbreaks in areas with no or under-developed health care. Ebola can spread through human-to-human transmission by direct contact with the blood, secretions, organs or bodily fluids of an infected individual and with surfaces or materials that contain the contaminated fluids of an infected person, such as bedding and clothing. It is capable of causing death within two to twenty-one days of exposure. In November 2019, the first conditional approval was issued for a preventive vaccine against Ebola virus. This approval was from the European Medicines Agency (EMA) for the vaccine ERVEBO®. That same month, the WHO pre-qualified that vaccine for use in high-risk countries. In the next month, the FDA approved that vaccine. However, there are no proven effective therapeutic treatments for Ebola. In addition, various experimental approaches have already been associated with undesirable side effects and limited ability to scale manufacturing.

In 2018, two Ebola outbreaks occurred, both in the Democratic Republic of Congo (DRC). The second Ebola outbreak of 2018 in the DRC became the second largest Ebola outbreak in world history. This particular outbreak had a 66% case-fatality ratio (aka case-fatality rate) as of February 2020. On June 1, 2020 an additional Ebola outbreak was declared in the DRC, before the outbreak was declared over on November 18, 2020. More recently, Ebola outbreaks have occurred in Guinea (February to June, 2021) and in the DRC (October 2021 and still ongoing).

Clinical Development - Ebola

In March 2019, Phase 1 clinical data of our Ebola vaccine candidate INO-4201 was published in The Journal of Infectious Diseases. We believe that this trial, which is being fully funded by DARPA, further supports the advancement of the intradermal delivery platform for emerging infectious diseases. Significantly, intradermal (skin) administration with our CELLECTRA® smart delivery device resulted in 100% of evaluable participants in the trial generating antigen-specific antibody responses that persisted for more than one year in most participants and generated T cell responses equivalent to or better than the group that received intramuscular delivery. We believe these published data further validate the tolerability, potency, and product stability advantages of our vaccine and immunotherapy platform.

Our Ebola vaccine candidate was evaluated in five groups of healthy participants. Of 70 evaluated participants, 67 (96%) seroconverted and mounted a strong antibody response to the Ebola glycoprotein antigen following the three dose immunization regimen; 52 participants (74%) seroconverted after only two doses.

In the trial arm using intradermal (skin) administration, 13 of 13 evaluable participants (100%) generated antigen-specific antibody responses after only two doses and all remained seropositive after three immunizations.

In December 2021, we announced complete enrollment of a 46-participant Phase 1b trial in which INO-4201 will be assessed as a heterologous booster in healthy volunteers previously vaccinated with rVSV-ZEBOV (Ervebo®), an FDA- and EMA- approved viral vector-based Ebola vaccine. To date INO-4201 has been well-tolerated and has not demonstrated systemic SAEs, such as fever, joint pain, and low white blood cell counts, that have been reported in association with some viral vector-based Ebola vaccines currently in development.

INO-4500 for Lassa Fever

Background on Lassa Fever

Lassa fever, also known as Lassa hemorrhagic fever, is an acute viral disease which occurs mostly in West Africa. The disease can cause a range of outcomes including fever, vomiting, diarrhea, cough, swelling of the face, pain in the muscles, chest, back and abdomen, bleeding of various parts of the body including the eyes and nose, vagina, and gastrointestinal tract, and death. Of the survivors of Lassa fever, about one-third have sudden-onset hearing loss, with more than half of those cases resulting in permanent hearing loss. This infection is spread through contact with infected rodents. Person to person transmission is also possible, via bodily fluids, albeit less common. Lassa virus infection in West Africa is estimated to affect 100,000 to 300,000 people annually, resulting in approximately 5,000 deaths, as disease and infection surveillance has been poor. Because of difficulties in diagnosing Lassa fever and the remoteness of many areas in which the disease occurs, the numbers of cases and deaths are likely significantly under-reported. Though the majority (about 80%) of Lassa virus-infected persons are asymptomatic or have mild symptoms, the infection can be quite serious to fatal in others. There are no approved vaccines or treatments specifically for Lassa. The case-fatality ratio (aka case-fatality rate) (CFR) among patients hospitalized for Lassa fever is about 15% to 20%, and in some epidemics the CFR has reached 50% in hospitalized patients, such as in the 2015-2016 Nigeria portion of the West Africa outbreak. In lab confirmed cases in Nigeria from 2019 through 2020, the CFR was 21%. The CFR among pregnant women is particularly high, and in pregnant women infected with Lassa virus the fetal death rate due to spontaneous abortion rate is estimated to be about 95%.

Clinical Trials

In May 2019, we dosed our first participant in our Phase 1, first-in-human clinical trial to evaluate INO-4500, a DNA candidate vaccine to prevent infection from the Lassa virus. In 2019, we fully enrolled 60 volunteers in this placebo controlled, blinded, dose escalation trial evaluating INO-4500 for safety, tolerability and immune responses. This trial represents the first Lassa candidate vaccine to enter the clinic. Our sponsored trial, as well as our INO-4500 program, is fully funded through the global partnership with CEPI that we entered into in April 2018.

In October 2021, we announced that we have completed enrollment of a 220 participant Phase 1b trial in Accra, Ghana, which is the first vaccine clinical trial for Lassa Fever conducted in West Africa, where the viral illness is endemic. The dosing regimen involved two intradermal vaccinations at 0 and 28 days with either 1.0 mg or 2.0 mg doses. In addition to providing insights on the INO-4500 safety and immunogenicity profile, this trial will inform dose selection for subsequent Phase 2 trials in West Africa. If the result of this trial is positive, we expect to advance INO-4500 into a Phase 2 trial. If satisfactory Phase 2 data are achieved, CEPI, in cooperation with local regulatory authorities and the WHO, could elect to stockpile the vaccine for future use throughout the region.

Synthetic DNA-based Monoclonal Antibody Programs

Background on recombinant Monoclonal Antibodies (mAbs)

Recombinant mAbs have become one of the most valuable therapeutic technologies of recent years. In 2020, global sales of mAbs exceeded $100 billion.

mAbs are designed to bind to a very specific epitope (area) of an antigen or cell surface target and can bind to almost any selected target. They have the ability to alert the immune system to attack and kill specific cancer cells (as in the case of Yervoy®) or block certain biochemical pathways (such as those leading to rheumatoid arthritis, as in the case of Humira®). However, mAb technology has limitations. mAbs are manufactured outside the body and require costly large-scale laboratory development and production. Additional limitations include high cost to develop and manufacture, their limited duration of in vivo potency, and a pharmacokinetic profile that can result in toxicity. We have created DNA encoded monoclonal antibodies that we believe may overcome many of the limitations associated with conventional mAb technology.

Using our core platform technology, we insert the DNA sequence for a specific monoclonal antibody in a DNA plasmid. We deliver the plasmid directly into cells of the body using our CELLECTRA smart delivery system, enabling the electroporated cells to manufacture those mAbs in vivo, - unlike conventional mAb technology that requires manufacture outside of the body. We believe this approach provides potentially significant advantages in terms of design simplicity, rapidity of execution and lower production costs.

We expect to design dMAb® product candidates not only for new disease targets not currently addressable with conventional recombinant mAbs, but also targets of existing, commercially available mAb products. We have already designed and produced dMAb product candidates targeting cancer mechanisms including checkpoint inhibition, anti-cancer pathways and anti-Tregs, as well as prophylactic and therapeutic dMAb product candidates for infectious diseases including COVID-19, Ebola, influenza, antibiotic resistant bacteria, dengue and Chikungunya.

In February 2019, we announced that in collaboration with The Wistar Institute and the University of Pennsylvania, the first participant was dosed as part of the first-ever human trial of our dMAb technology. Funded fully by the Bill & Melinda Gates Foundation, this trial's focus is on the safety and tolerability of DNA plasmid encoding for a human anti-Zika antibody. This open-label trial is a single center, dose escalation trial that enrolled 24 healthy volunteers who received from one to four doses of INO-A002, our DNA plasmid encoding for a human anti-Zika antibody. Doses ranging from 0.5 mg to 4 mg of plasmids were injected per participant, independent of their body weight.

As described above, in December 2020, we and a team of scientists from The Wistar Institute, AstraZeneca, the University of Pennsylvania, and Indiana University received a $37.6 million grant from DARPA to use our DNA-encoded monoclonal antibody (dMAb) technology to develop anti-SARS-CoV-2-specific dMAbs which could offer versatile capabilities to function as both a therapeutic and preventive treatment for COVID-19.

License, Collaboration, Supply and Other Agreements

We have entered into various arrangements with corporate, academic, and government collaborators, licensors, licensees and others. The most material of these arrangements are summarized below.

Advaccine

On December 31, 2020, we entered into a Collaboration and License Agreement with Advaccine Biopharmaceuticals Suzhou Co., Ltd. (“Advaccine”), which was amended and restated on June 7, 2021 (as amended and restated, the “Advaccine Agreement”). Under the terms of the Advaccine Agreement, we granted to Advaccine the exclusive right to develop, manufacture and commercialize our vaccine candidate INO-4800 within the territories of China, Taiwan, Hong Kong and Macau (referred to collectively as “Greater China”) and 33 additional countries in Asia. Advaccine does not have the right to grant sublicenses, other than to affiliated entities, without our express prior written consent. As part of the collaboration,

Advaccine also granted to us a non-exclusive license to certain DNA vaccine manufacturing processes.

The June 2021 amendment relates to our collaboration with Advaccine to jointly conduct the global Phase 3 segment of our ongoing Phase 2/3 trial of INO-4800 and expand the existing collaboration to include the global Phase 3 trial. We will jointly participate in the trial and will equally share the global development costs for the trial, including our manufacturing costs to supply INO-4800. In certain instances, we will have the right to convert the exclusive license to a non-exclusive license in the licensed territories, other than Greater China, unless Advaccine agrees to pay us its full share of development costs in excess of a specified maximum. Notwithstanding the foregoing, Advaccine will be fully responsible for conducting the trial in Greater China, including its costs and expenses incurred in conducting the trial in Greater China. We will be fully responsible for our costs and expenses, if any, incurred solely as a result of our activities in connection with the performance of the trial in the United States. The parties may continue to conduct clinical trials of INO-4800 outside of the territories covered by the Advaccine Agreement.

In the event that a global purchasing entity desires to enter into a purchase agreement for INO-4800 in both parties' territories, the parties will enter into good faith negotiations for an arrangement to supply INO-4800 to such entity. In addition, we are permitted to enter into an agreement with a global purchasing entity to authorize the entity to conduct a portion of the global Phase 3 trial in the licensed territory outside of Greater China.

Under the Agreement, Advaccine made an upfront payment to us of $3.0 million in January 2021. In addition to the upfront payment, we are entitled to receive up to an aggregate of $206.0 million, payable upon the achievement of specified milestones related to the development, regulatory approval and commercialization of INO-4800, including the achievement of specified net sales thresholds for INO-4800 in Greater China and the additional covered territories, if approved. In December 2020 we earned a $2.0 million milestone payment based on the enrollment of the first participant in the Phase 2 clinical trial for the product in the Advaccine territory. We are also entitled to receive a royalty equal to a high single-digit percentage of annual net sales in each region within the licensed territory, subject to reduction in the event of competition from biosimilar products in a particular region and in other specified circumstances. Advaccine's obligation to pay royalties will continue, on a licensed product-by-licensed product basis and region-by-region basis, for ten years after the first commercial sale in a particular region within Greater China or, if later, until the expiration of the last-to-expire patent covering a given licensed product in a given region.

Beginning in the first calendar year following the first commercial sale of INO-4800 in the licensed territory outside of Greater China, Advaccine will pay us an annual maintenance fee of $1.5 million for a period of five years, which fee will be creditable against any royalties payable by Advaccine with respect to sales outside of Greater China.

Under the Advaccine Agreement, we will supply Advaccine's clinical requirements of INO-4800 and devices, although Advaccine may manufacture INO-4800 for its clinical use and may procure alternate suppliers. Advaccine is responsible for the manufacture and supply of INO-4800 itself or through a contract manufacturer for commercial use. Upon Advaccine's reasonable request, the parties may negotiate a separate clinical and/or commercial supply agreement.

The Advaccine Agreement will continue in force on a region-by-region basis until Advaccine has no remaining royalty obligations in such region. Either party may terminate the Advaccine Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party. In addition, we may terminate the agreement, upon prior written notice, if Advaccine (i) ceases all development or commercialization activities for at least nine months, subject to certain exceptions, or (ii) challenges the validity, enforceability or scope of any of the patents licensed by us to Advaccine under the Advaccine Agreement, subject to certain conditions. Advaccine may terminate the Advaccine Agreement at any time for convenience upon nine months' written notice to us, if such notice is provided before the first commercial sale of INO-4800 in the licensed territory, or 18 months' written notice thereafter; provided that we may accelerate the effectiveness of such termination to the extent permitted by law.

ApolloBio

In December 2017, we entered into an Amended and Restated License and Collaboration Agreement with Beijing Apollo Saturn Biological Technology Limited, a corporation organized under the laws of China, or ApolloBio. Under the terms of this License and Collaboration Agreement, which became effective in March 2018, we granted to ApolloBio the exclusive right to develop and commercialize VGX-3100, our DNA immunotherapy product candidate designed to treat pre-cancers caused by HPV, within the agreed upon territories. As part of the collaboration, ApolloBio will fund all clinical development costs within the licensed territory.

In addition to the upfront payment that we received in 2018, we are entitled to receive up to an aggregate of $20.0 million, less required income, withholding or other taxes, upon the achievement of specified milestones related to the regulatory approval of VGX-3100 in accordance with the Amended and Restated License and Collaboration Agreement. In the event that VGX-3100 is approved for marketing in these territories, we will be entitled to receive royalty payments based on a tiered percentage of annual net sales, with such percentage being in the low- to mid-teens, subject to reduction in the event of generic

competition in a particular territory. ApolloBio's obligation to pay royalties will continue for 10 years after the first commercial sale in a particular territory or, if later, until the expiration of the last-to-expire patent covering the licensed products in the specified territory. The License and Collaboration Agreement, once effective, will continue in force until ApolloBio has no remaining royalty obligations.

Competition

As we develop and seek to ultimately commercialize our product candidates, we face and will continue to encounter competition with an array of existing or development-stage drug and immunotherapy approaches targeting diseases we are pursuing. We are aware of various established enterprises, including major pharmaceutical companies, broadly engaged in vaccine/immunotherapy research and development. These include Janssen Pharmaceuticals (part of J&J), Sanofi-Aventis, GlaxoSmithKline plc, Merck, Pfizer, and AstraZeneca. There are also various development-stage biotechnology companies involved in different vaccine and immunotherapy technologies including but not limited to Advaxis, Bavarian Nordic, CureVac, Dynavax, Hookipa, Iovance, Nektar, Translate Bio, Zydus, and Vir Biotechnology. If these companies are successful in developing their technologies, it could materially and adversely affect our business and our future growth prospects.

Merck and GlaxoSmithKline have commercialized preventive vaccines against HPV to protect against cervical cancer. Some companies are seeking to treat early HPV infections or low- grade cervical dysplasia. Loop Electrosurgical Excision Procedure, commonly known as LEEP, is a surgical procedure and is the current standard of care for treating high-grade cervical dysplasia. Advaxis and Gilead Sciences have therapeutic cervical cancer product candidates under development. Many companies are pursuing different approaches to GBM, prostate, breast, lung and other cancers we are targeting.

A large number of companies are actively advancing COVID-19 vaccines through the clinic. Pfizer and BioNtech, Moderna Therapeutics, Janssen (J&J), Novavax, Zydus, and AstraZeneca have received conditional or complete approval for their COVID-19 vaccines from either the U.S., WHO, or European regulatory authorities. Additionally, several companies such as CanSino Biologics and Bharat Biotech are currently developing vaccine candidates in Phase 2 or Phase 3 clinical trials.

We also compete more specifically with companies seeking to utilize antigen-encoding DNA delivered with electroporation or other DNA delivery technologies such as viral vectors or lipid vectors to induce in vivo generated antigen production and immune responses to prevent or treat various diseases. These competitive technologies have shown promise, but they each also have their unique obstacles to overcome.

Viral Vaccine Delivery

This technology utilizes a virus as a carrier or vector to deliver genetic material into target cells. The method is efficient for delivering immunotherapy antigens and has the advantage of mimicking real viral infection so that the recipient will mount a broad immune response against the immunotherapy. The greatest limitation of the technology stems from problems with unwanted immune responses against the viral vector, limiting its use to patients who have not been previously exposed to the viral vector and making repeated administration difficult. In addition, complexity and safety concerns increase their cost and complicate regulatory approval.

Lipid DNA/RNA Delivery

A number of lipid formulations have been developed that increase the effect of DNA/RNA immunotherapies. These work by either increasing uptake of the DNA/RNA into cells or by acting as an adjuvant, alerting the immune system. While there has been significant progress in this field, including emergency use authorization of COVID-19 mRNA vaccines in 2020, lipid nanoparticle delivery of mRNA has thermal stability issues as well as the potential of adverse events from the lipid nanoparticle formulations.

DNA Immunotherapy Delivery with Electroporation

There are other companies with electroporation intellectual property and devices. We believe we have significant competitive advantages over other companies focused on electroporation for multiple reasons:

- We have an extensive history and experience in developing the methods and devices that optimize the use of electroporation in conjunction with DNA-based agents. This experience has been validated with multiple sets of interim data from multiple clinical studies assessing DNA-based immunotherapies and vaccines against cancers and infectious disease.
- We have a broad product line of electroporation instruments designed to enable DNA delivery in tumors, muscle, and skin.
- We have been proactive in filing for patents, as well as acquiring and licensing additional patents, to expand our global patent estate.

If any of our competitors develop products with efficacy or safety profiles significantly better than our product candidates, we may not be able to commercialize our products, and sales of any of our commercialized products could be harmed. Some of

our competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than we do. Competitors may develop products earlier, obtain FDA approvals for products more rapidly, or develop products that are more effective than those under development by us. We will seek to expand our technological capabilities to remain competitive; however, research and development by others may render our technologies or products obsolete or noncompetitive or result in treatments or cures superior to ours.

Our competitive position will be affected by the disease indications addressed by our product candidates and those of our competitors, the timing of market introduction for these products and the stage of development of other technologies to address these disease indications. For us and our competitors, proprietary technologies, the ability to complete clinical trials on a timely basis and with the desired results, and the ability to obtain timely regulatory approvals to market these product candidates are likely to be significant competitive factors. Other important competitive factors will include efficacy, safety, ease of use, reliability, availability and price of products and the ability to fund operations during the period between technological conception and commercial sales.

The FDA and other regulatory agencies may expand current requirements for public disclosure of DNA-based product development data, which may harm our competitive position with foreign and United States companies developing DNA-based products for similar indications.

Commercialization and Manufacturing

Because of the broad potential applications of our technologies, we intend to develop and commercialize products both on our own and through our collaborators and licensees. We intend to develop and commercialize products in well-defined specialty markets, such as infectious diseases and cancer. Where appropriate, we intend to rely on strategic marketing and distribution alliances.

We believe our plasmids can be produced in commercial quantities through uniform methods of fermentation and processing that are applicable to all plasmids. We believe we will be able to obtain sufficient supplies of plasmids for all foreseeable clinical investigations.

Intellectual Property

Patents and other proprietary rights are essential to our business. We file patent applications to protect our technologies, inventions and improvements to our inventions that we consider important to the development of our business. We file for patent registration extensively in the United States and in key foreign markets. Although our patent filings include claims covering various features of our products and product candidates, including composition, methods of manufacture and use, our patents do not provide us with complete protection, or guarantee, against the development of competing products. In addition, some of our know-how and technology are not patentable. We thus also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. We also require employees, consultants, advisors and collaborators to enter into confidentiality agreements, but such agreements may provide limited protection for our trade secrets, know-how or other proprietary information.

Our intellectual property portfolio covers our proprietary technologies, including CELLECTRA® delivery systems as well as immunotherapy and vaccine construct related technologies. As of December 31, 2021, our patent portfolio included 99 issued United States patents and over 651 issued foreign counterpart patents. We also have a number of patent applications pending in the United States and various foreign jurisdictions.

If we fail to protect our intellectual property rights adequately our competitors might gain access to our technology and our business would thus be harmed. In addition, defending our intellectual property rights might entail significant expense. Any of our intellectual property rights may be challenged by others or invalidated through administrative processes or litigation through the courts. In addition, our patents, or any other patents that may be issued to us in the future, may not provide us with any competitive advantages, or may be challenged by third parties. Furthermore, legal standards relating to the validity, enforceability and scope of protection of intellectual property rights are uncertain. Effective patent, trademark, copyright and trade secret protection may not be available to us in each country where we operate. The laws of some foreign countries may not be as protective of intellectual property rights as those in the United States, and domestic and international mechanisms for enforcement of intellectual property rights in those countries may be inadequate. Accordingly, despite our efforts, we may be unable to prevent third parties from infringing upon or misappropriating our intellectual property or otherwise gaining access to our technology. We may be required to expend significant resources to monitor and protect our intellectual property rights. We may initiate claims or litigation against third parties for infringement of our proprietary rights or to establish the validity of our proprietary rights. Any such litigation, whether or not it is ultimately resolved in our favor, would result in significant expense to us and divert the efforts of our technical and management personnel.

There may be rights we are not aware of, including applications that have been filed but not published that, when issued, could be asserted against us. These third parties could bring claims against us, and that would cause us to incur substantial expenses and, if successful against us, could cause us to pay substantial damages. Further, if a patent infringement suit were

brought against us, we could be forced to stop or delay research, development, manufacturing or sales of the product or biologic drug candidate that is the subject of the suit. As a result of patent infringement claims, or in order to avoid potential claims, we may choose or be required to seek a license from the third party. These licenses may not be available on acceptable terms, or at all. Even if we are able to obtain a license, the license would likely obligate us to pay license fees or royalties or both, and the rights granted to us might be non-exclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms. All of the issues described above could also impact our collaborators, which would also impact the success of the collaboration and therefore us.

Important legal issues remain to be resolved as to the extent and scope of available patent protection for biologic products, including vaccines, and processes in the United States and other important markets outside the United States, such as Europe and Japan. Foreign markets may not provide the same level of patent protection as provided under the United States patent system. We recognize that litigation or administrative proceedings may be necessary to determine the validity and scope of certain of our and others' proprietary rights. Any such litigation or proceeding may result in a significant commitment of resources in the future and could force us to interrupt our operations, redesign our products or processes, or negotiate a license agreement, all of which would adversely affect our revenue. Furthermore, changes in, or different interpretations of, patent laws in the United States and other countries may result in patent laws that allow others to use our discoveries or develop and commercialize our products.

We cannot guarantee that the patents we obtain or the unpatented technology we hold will afford us significant commercial protection.

Government Regulation

Government authorities in the United States at the federal, state and local level and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of biological products, or biologics, and medical devices, such as our product candidates. Generally, before a new biologic or medical device can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific to each regulatory authority, submitted for review and approved by the regulatory authority.

Review and Approval of Combination Products in the United States

Certain products may be comprised of components that would normally be regulated under different types of regulatory authorities, and frequently by different centers at the FDA. These products are known as combination products. Specifically, under regulations issued by the FDA, a combination product may be:

- A product comprised of two or more regulated components that are physically, chemically, or otherwise combined or mixed and produced as a single entity;
- Two or more separate products packaged together in a single package or as a unit and comprised of drug and device products;
- A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device or biological where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or
- Any investigational drug, device, or biological packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect.

Our product candidates are combination products comprising an electroporation device for delivery of a biologic. Under the Federal Food, Drug, and Cosmetic Act, or FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. That determination is based on the "primary mode of action" of the combination product, which means the mode of action expected to make the greatest contribution to the overall intended therapeutic effects. Thus, if the primary mode of action of a device-biologic combination product is attributable to the biologic product, that is, if it acts by means of a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, the FDA center responsible for premarket review of the biologic product would have primary jurisdiction for the combination product. We believe that all of our product candidates will have a biologic primary mode of action, with the device component reviewed under a Device Master File.

U.S. Biological Product Development

In the United States, the FDA regulates biologics under FDCA, and the Public Health Service Act, or PHSA, and their implementing regulations. Biologics are also subject to other federal, state, and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

Our product candidates must be approved by the FDA through the Biologics License Application, or BLA, process before they may be legally marketed in the United States. The process required by the FDA before a biologic may be marketed in the United States generally involves the following:

- Completion of extensive nonclinical, sometimes referred to as pre-clinical laboratory tests, pre-clinical animal studies and formulation studies in accordance with applicable regulations, including the FDA's Good Laboratory Practice, or GLP, regulations;
- Submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND and other clinical trial-related regulations, sometimes referred to as good clinical practices, or GCPs, to establish the safety and efficacy of the proposed product candidate for its proposed indication;
- Submission to the FDA of a BLA;
- Satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities where the product is produced to assess compliance with the FDA's current good manufacturing practice, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality, purity and potency;
- Potential FDA audit of the pre-clinical and/or clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

The data required to support a BLA is generated in two distinct development stages: pre-clinical and clinical. The pre-clinical development stage generally involves laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which support subsequent clinical testing. The conduct of the pre-clinical studies must comply with federal regulations, including GLPs. The sponsor must submit the results of the pre-clinical studies, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND is a request for authorization from the FDA to administer an investigational drug product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials and places the IND on clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a product candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that could cause the trial to be suspended or terminated.

The clinical stage of development involves the administration of the product candidate to healthy participants under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCPs, which include the requirement that all research participants provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, participant selection and exclusion criteria, and the parameters to be used to monitor participant safety and assess efficacy. Each protocol, and any subsequent amendments to the protocol, must be submitted to the FDA as part of the IND. Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial participant or his or her legal representative and must monitor the clinical trial until completed.

There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products, including biologics, are required to register and disclose specified 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 disclose the results of their clinical trials after completion.

Clinical trials are generally conducted in three sequential phases that may overlap, known as Phase 1, Phase 2 and Phase 3 clinical trials. Phase 1 clinical trials generally involve a small number of healthy volunteers who are initially exposed to a product candidate. The primary purpose of these clinical trials is to assess the action, side effect tolerability and safety of the product candidate and, if possible, to gain early evidence on effectiveness. Phase 2 clinical trials typically involve studies in patients to determine the dose required to produce the desired benefits. At the same time, safety and preliminary evaluation of efficacy is assessed. Phase 3 clinical trials generally involve large numbers of patients at multiple sites, in multiple countries (from several hundred to several thousand participants) and are designed to provide the data necessary to demonstrate the efficacy of the product for its intended use, its safety in use, and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product approval. Phase 3 clinical trials may include comparisons with placebo and/or other comparator treatments. The duration of treatment is often extended to mimic the actual use of a product during marketing. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of a BLA.

Post-approval trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may grant conditional approval of a BLA on the sponsor's agreement to conduct additional clinical trials, such as these post-approval trials, to further assess the biologic's safety and effectiveness after BLA approval.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse, findings from other studies suggesting a significant risk to humans exposed to the drug, findings from animal or *in vitro* testing suggesting a significant risk to humans, and any clinically important rate increase of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research participants 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 drug has been associated with unexpected serious harm to patients. 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 provides authorization for whether or not a trial may move forward at designated intervals based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA and FDA Review Process

Following trial completion, trial data is analyzed to assess safety and efficacy. The results of pre-clinical studies and clinical trials are then submitted to the FDA as part of a BLA, along with proposed labeling for the product and information about the manufacturing process and facilities that will be used to ensure product quality, results of analytical testing conducted on the chemistry of the product candidate, and other relevant information. The BLA is a request for approval to market the biologic for one or more specified indications and must contain proof of safety, purity, potency and efficacy, which is demonstrated by extensive pre-clinical and clinical testing. The application includes positive findings from pre-clinical and clinical trials as well as ambiguous or negative results. Data may come from company-sponsored clinical trials intended to test the safety and efficacy of a use of a product, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee, which is adjusted on an annual basis. PDUFA also imposes an annual program fee for approved products. 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.

Once a BLA has been accepted for filing, which occurs, if at all, sixty days after the BLA's submission, the FDA's goal is to review BLAs within ten months of the filing date for standard review or six months of the filing date for priority review, if the application is for a product intended for a serious or life-threatening condition and the product, if approved, would provide a significant improvement in safety or effectiveness. The review process is often significantly extended by FDA requests for additional information or clarification. If not accepted for filing, the sponsor must resubmit the BLA and begin the FDA's

review process again, including the initial sixty-day review to determine if the application is sufficiently complete to permit substantive review.

After the BLA submission is accepted for filing, the FDA reviews the BLA to determine, among other things, whether the proposed product candidate is safe and effective for its intended use, and whether the product candidate is being manufactured in accordance with cGMP to assure and preserve the product candidate's identity, strength, quality, purity and potency. The FDA may refer applications for novel drug product candidates or drug product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA will likely re-analyze the clinical trial data, which could result in extensive discussions between the FDA and us during the review process. The review and evaluation of a BLA by the FDA is extensive and time consuming and may take longer than originally planned to complete, and we may not receive a timely approval, if at all.

Before approving a BLA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMPs. The FDA will not approve the product 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. In addition, before approving a BLA, the FDA may also audit data from clinical trials to ensure compliance with GCP requirements. After the FDA evaluates the application, manufacturing process and manufacturing facilities, it 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. A Complete Response Letter indicates that the review cycle of the application is complete and the application will not be approved in its present form. A Complete Response Letter usually describes all of the specific deficiencies in the BLA identified by the FDA. The Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, pre-clinical studies or manufacturing. 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. Even if such data and information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data.

There is no assurance that the FDA will ultimately approve a product for marketing in the United States and we may encounter significant difficulties or costs during the review process. If a product receives marketing approval, the approval may be significantly limited to specific populations, severities of allergies, and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or may condition the approval of the BLA on other changes to the proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-market testing or clinical trials and surveillance to monitor the effects of approved products. For example, the FDA may require Phase 4 testing which involves clinical trials designed to further assess the product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized. The FDA may also place other conditions on approvals including the requirement for a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the product. 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 an approved REMS, if required. A REMS 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. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

Post-Marketing Requirements

Following approval of a new product, a manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting to the applicable regulatory authorities of adverse experiences with the product, providing the regulatory authorities with updated safety and efficacy information, product sampling and distribution requirements, and complying with promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, also known as off-label use, limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available drugs and biologics for off-label uses, manufacturers may not market or promote such off-label uses. Modifications or enhancements to the product or its labeling or changes of the site of manufacture are often subject to the approval of the FDA and other regulators, which may or may not be received or may result in a lengthy review process. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use.

In the United States, once a product is approved, its manufacture is subject to comprehensive and continuing regulation by the FDA. The FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP. Moreover, the constituent parts of a combination product retain their regulatory status, for example, as a biologic or device, and as such, we may be subject to additional requirements in the Quality System Regulation, or QSR, applicable to medical devices, such as design controls, purchasing controls, and corrective and preventive action. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products 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 and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. These regulations also impose certain organizational, procedural and documentation requirements with respect to manufacturing and quality assurance activities. BLA holders using contract manufacturers, laboratories or packagers are responsible for the selection and monitoring of qualified firms, and, in certain circumstances, qualified suppliers to these firms. These firms and, where applicable, their suppliers are subject to inspections by the FDA at any time, and the discovery of violative conditions, including failure to conform to cGMP, could result in enforcement actions that interrupt the operation of any such facilities or the ability to distribute products manufactured, processed or tested by them. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, recall or withdrawal of the product from the market.

The FDA also may require post-approval testing, sometimes referred to as Phase 4 testing, REMS and post-marketing surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures. Also, 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.

Coverage and Reimbursement

Patients in the United States and elsewhere generally rely on third-party payors to reimburse part or all of the costs associated with their prescription drugs and vaccines. Accordingly, a pharmaceutical company's ability to commercialize its products successfully depends in part on the extent to which private health insurers, other third-party payors, and governmental authorities, including Medicare and Medicaid, establish appropriate coverage and reimbursement levels for its product candidates and related treatments. As a threshold for coverage and reimbursement, third-party payors generally require that products be approved for marketing by the FDA.

Coverage decisions may not favor new products when more established or lower cost therapeutic alternatives are available. The process for obtaining coverage for a product or service is separate from the process to obtain the associated reimbursement. Reimbursement levels can affect the adoption of products and services by physicians and patients. Additionally, products used in connection with medical procedures may not be reimbursed separately, but their cost may instead be bundled as part of the payment received by the provider for the procedure only. Separate reimbursement for a product or the treatment or procedure in which the product is used may not be available.

Coverage and reimbursement policies for drug products and vaccines can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for drug products among third-party payors in the United States. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time consuming and costly which may require the provision of scientific and clinical support for the use of the product to each payor separately, with no assurance that coverage or adequate reimbursement will be obtained.

A significant trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular products and services. Third-party payors are increasingly challenging the effectiveness of and prices charged for medical products and services. Moreover, the U.S. government, state legislatures and foreign governmental entities have shown significant interest in implementing cost containment programs to limit the growth of government paid healthcare costs, including price controls, restrictions on reimbursement and coverage and requirements for substitution of generic products for branded prescription drugs.

Healthcare Reform

In both the United States and certain foreign jurisdictions there have been, and continue to be, a number of legislative and regulatory changes to the healthcare system that impact the ability to sell pharmaceutical products profitably. In the United States, the federal government enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA. Among the ACA's provisions of importance to the pharmaceutical industry are that it:

- Created an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- Increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- Created new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected;
- Expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- Expanded the entities eligible for discounts under the Public Health program;
- Created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- Established a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending that began on January 1, 2011; and
- Created a licensure framework for follow on biologic products.

There remain judicial and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry qualifying health insurance coverage for all or part of a year. In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax, and, effective January 1, 2021, also eliminated the health insurer tax. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the Affordable Care Act is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the Affordable Care Act will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA 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 Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2031 with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. Additionally, 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. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24,

2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, 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 implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinded the Most Favored Nation model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other reform initiatives. Further, at the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

Healthcare Laws

Certain federal, state, local and foreign healthcare laws and regulations pertaining to fraud and abuse, transparency, patients' rights, and privacy are applicable to the business of a pharmaceutical company. The laws that may affect a pharmaceutical company's ability to operate include:

- The federal healthcare program Anti-Kickback Statute, which prohibits, among other things, people from soliciting, receiving or providing remuneration, directly or indirectly, to induce or reward either the referral of an individual, or the purchasing, ordering, or leasing of an item, good, facility or service, for which payment may be made by a federal healthcare program such as Medicare or Medicaid;
- Federal civil and criminal false claims laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain individuals and entities;
- the Physician Payments Sunshine Act, created under the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with certain exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and other healthcare professionals (such as physicians assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- The FDCA, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples;
- The U.S. Foreign Corrupt Practices Act, which, among other things, prohibits companies issuing stock in the U.S. from bribing foreign officials for government contracts and other business; and
- State law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state and local laws requiring the registration of pharmaceutical sales and medical representatives, and state laws governing the privacy

and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and

- Additional state and local laws such as laws in California and Massachusetts, which mandate implementation of compliance programs, compliance with industry ethics codes, and spending limits, and other state and local laws, such as laws in Vermont, Maine, and Minnesota which require reporting to state governments of gifts, compensation, and other remuneration to physicians.

A pharmaceutical company will need to spend substantial time and money to ensure that its business arrangements with third parties comply with applicable healthcare laws and regulations. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, which require strict compliance in order to offer protection, it is possible that governmental authorities may conclude that its business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws. If a pharmaceutical company's operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to it, it may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, integrity and/or other oversight obligations, contractual damages, reputational harm and the curtailment or restructuring of operations.

Other Regulations

We also are subject to various federal, state and local laws, regulations, and recommendations relating to safe working conditions, laboratory and manufacturing practices, the experimental use of animals, and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with our research. The extent of government regulation that might result from any future legislation or administrative action cannot be accurately predicted.

Significant Customers and Research and Development

During the year ended December 31, 2021, we derived 43% of our revenue from the procurement contract with the DoD that we entered into in June 2020 and 14% of our revenue from our collaborator Plumbline Life Sciences, a company of which we are an approximately 19% stockholder. During the year ended December 31, 2020, we derived 68% of our revenue from Advaccine and 18% our our revenue from Plumbline Life Sciences. During the year ended December 31, 2019, we derived 78% of our revenue from AstraZeneca. Our collaboration agreement with AstraZeneca was terminated in 2021.

Since our inception, virtually all of our activities have consisted of research and development efforts related to developing our electroporation technologies and immunotherapies. Research and development expense consists of expenses incurred in performing research and development activities including salaries and benefits, facilities and other overhead expenses, clinical trials, contract services and other outside expenses. Our research and development expense was $249.2 million in 2021, $94.2 million in 2020 and $88.0 million in 2019.

Geographic Information

All of our revenue for the years ended December 31, 2021, 2020 and 2019 was earned in the United States. All of our long-lived assets are located in the United States.

Corporate Information

Our corporate headquarters are located at 660 W. Germantown Pike, Suite 110, Plymouth Meeting, Pennsylvania 19462, and our main telephone number is (267) 440-4200.

Available Information

Our Internet website address is *www.inovio.com*. In addition to the information contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

We make our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, or the Exchange Act, available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. The SEC maintains an Internet site (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC, including us.

Information regarding our corporate governance, including the charters of our audit committee, our nomination and corporate governance committee and our compensation committee, our Code of Business Conduct and Ethics, our Corporate Governance Guidelines, our Corporate Governance Policy and information for contacting our board of directors is available on our website.

Our Code of Business Conduct and Ethics includes our Code of Ethics applicable to our Chief Executive Officer and Chief Financial Officer, who also serves as our principal accounting officer. Any amendments to or waivers of the Code of Ethics will be promptly posted on our website or in a report on Form 8-K, as required by applicable law.

Employees and Human Capital Resources

As of February 2022, we employed 317 people on a full-time basis. Of the total, 256 were in product research, which includes research and development, quality assurance, clinical, engineering and manufacturing, and 61 were in general and administrative functions, which includes corporate development, information technology, legal, commercial, investor relations, finance and corporate administration. About 50% of our workforce is comprised of women and approximately 50% is comprised of individuals with ethnically diverse backgrounds. In addition, three of the eight members of our board of directors are women. None of our employees are subject to collective bargaining agreements. We consider our relationship with our employees to be good.

We compete in the highly competitive biotechnology industry. Attracting, developing and retaining talented people in research, quality assurance, clinical, engineering, manufacturing and other positions is crucial to executing our strategy and our ability to compete effectively. Our ability to recruit and retain such talent depends on several factors, including compensation and benefits, talent development and career opportunities, and work environment. To that end, we invest in our employees to be an employer of choice.

Employee Engagement

As we work to make an impact on how healthcare is delivered, we believe it is critical that our employees are informed and engaged. We communicate frequently and transparently with our employees through a variety of communication methods, including video and written communications, town hall meetings, employee surveys and our company intranet, and acknowledge individual contributions to INOVIO through several rewards and recognition initiatives. We believe these engagement efforts keep employees informed about our strategy, culture and purpose and motivated to do their best work. As a result of the COVID-19 pandemic, we also further strengthened our digital communication platform. Our employee communications during the pandemic have kept our employees informed on critical priorities and important actions being taken by management in response to the pandemic.

Health, Safety and Wellness

The physical health, financial well-being, life balance and mental health of our employees is vital to our success. In 2021, we launched a company wide comprehensive wellness program inclusive of financial, physical, and mental well-being.

The environmental, health and safety team stays abreast of local, regional and global concerns and trends and ensures safety procedures are in place to mitigate workplace injuries and safety risks. Employees are required to complete training in various safety procedures for the laboratories and manufacturing facilities and specialized safety training based on particular job duties. Designated Safety Officers and response teams oversee safety-related initiatives and a safety committee provides input on safety procedures, practices, and policies. Employees are required to wear personal protective equipment relevant for their particular job duties. Occupational injuries at the workplace are extremely low and are always investigated to determine if any environmental or other changes need to be implemented.

Since the onset of the COVID-19 pandemic, strict safety protocols have been put in place for employees working on-site, including following federal and local guidelines and mandates to ensure the safety of the workforce. In addition to providing the necessary personal protective equipment, special engineering controls have been installed at the facilities to further protect workers. Regular communication and training about the virus and how individuals can protect themselves and others is ongoing with employees.

ITEM 1A. RISK FACTORS

You should carefully consider the following factors regarding information included in this Annual Report. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. If any of the following risks actually occur, our business, financial condition and operating results could be materially adversely affected.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses in recent years, expect to incur significant net losses in the foreseeable future and may never become profitable.

We have experienced significant operating losses over the last several years. As of December 31, 2021 our accumulated deficit was $1.2 billion. We have generated limited revenues, primarily consisting of license revenue, grant funding and interest income. We expect to continue to incur substantial additional operating losses for at least the next several years as we advance our clinical trials and research and development activities. We may never successfully commercialize our DNA vaccine and DNA immunotherapy product candidates or electroporation-based synthetic vaccine delivery technology and thus may never have any significant future revenues or achieve and sustain profitability.

We have limited sources of revenue and our success is dependent on our ability to develop our DNA vaccines, DNA immunotherapies, dMAbs and electroporation equipment.

We do not sell any products and may not have any other products commercially available for several years, if at all. Our ability to generate future revenues depends heavily on our success in:

- developing and securing United States and/or foreign regulatory approvals for our product candidates, including securing regulatory approval for conducting clinical trials with product candidates;
- developing our electroporation-based DNA delivery technology; and
- commercializing any products for which we receive approval from the FDA and foreign regulatory authorities.

Our electroporation equipment and product candidates will require extensive additional clinical study and evaluation, regulatory approval in multiple jurisdictions, substantial investment and significant marketing efforts before we generate any revenues from product sales. We are not permitted to market or promote our electroporation equipment and product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities. If we do not receive regulatory approval for and successfully commercialize any products, we will not generate any revenues from sales of electroporation equipment and products, and we may not be able to continue our operations.

A small number of licensing partners and government contracts currently account for a substantial portion of our revenue.

We currently derive, and in the past we have derived, a significant portion of our revenue from a limited number of licensing partners and government grants and contracts. Revenue can fluctuate significantly depending on the timing of upfront and event-based payments and work performed. If we fail to sign additional future contracts with major licensing partners and the government, if a contract is delayed or deferred, or if an existing contract expires or is canceled and we fail to replace the contract with new business, our revenue would be adversely affected.

We will need substantial additional capital to develop our DNA vaccines, DNA immunotherapies and dMAb programs and electroporation delivery technology.

Conducting the costly and time-consuming research, pre-clinical studies and clinical testing necessary to obtain regulatory approvals and bring our product candidates and delivery technology to market will require a commitment of substantial funds in excess of our current capital. Our future capital requirements will depend on many factors, including, among others:

- the progress of our current and new product development programs;
- the progress, scope and results of our pre-clinical and clinical testing;
- the time and cost involved in obtaining regulatory approvals;
- the cost of manufacturing our products and product candidates;
- the cost of prosecuting, enforcing and defending against patent infringement claims and other intellectual property rights;
- debt service obligations;
- competing technological and market developments; and
- our ability and the related costs to establish and maintain collaborative and other arrangements with third parties to assist in potentially bringing our products to market.

Additional financing may not be available on acceptable terms, or at all. Domestic and international capital markets have from time to time experienced heightened volatility, particularly in light of the COVID-19 pandemic and geopolitical turmoil, making it more difficult in many cases to raise capital through the issuance of equity securities. Volatility in the capital markets can also negatively impact the cost and availability of credit, creating illiquid credit markets and wider credit spreads. Concern about the stability of the markets generally and the strength of counterparties specifically has led many lenders and institutional investors to reduce, and in some cases cease to provide, funding to borrowers. To the extent we are able to raise additional capital through the sale of equity securities, or we issue securities in connection with another transaction in the future, the ownership position of existing stockholders could be substantially diluted. If additional funds are raised through the issuance of preferred stock or debt securities, these securities are likely to have rights, preferences and privileges senior to our common stock and may involve significant fees, interest expense, restrictive covenants and the granting of security interests in our assets. Fluctuating interest rates could also increase the costs of any debt financing we may obtain. Raising capital through a licensing or other transaction involving our intellectual property could require us to relinquish valuable intellectual property rights and thereby sacrifice long-term value for short-term liquidity.

Our failure to successfully address ongoing liquidity requirements would have a substantially negative impact on our business. If we are unable to obtain additional capital on acceptable terms when needed, we may need to take actions that adversely affect our business, our stock price and our ability to achieve cash flow in the future, including possibly surrendering our rights to some technologies or product opportunities, delaying our clinical trials or curtailing or ceasing operations.

Risks Related to Product Development, Manufacturing and Regulatory Approval

If we are unable to obtain FDA approval of our products, we will not be able to commercialize them in the United States.

We need FDA approval prior to marketing our electroporation equipment and product candidates in the United States. If we fail to obtain FDA approval to market our electroporation equipment and product candidates, we will be unable to sell our products in the United States, which will significantly impair our ability to generate any revenues.

This regulatory review and approval process, which includes evaluation of preclinical studies and clinical trials of our products as well as the evaluation of our manufacturing processes and our third-party contract manufacturers' facilities, is lengthy, expensive and uncertain. To receive approval, we must, among other things, demonstrate with substantial evidence from well-controlled clinical trials that our electroporation equipment and product candidates are both safe and effective for each indication for which approval is sought. To the extent that our product candidates are manufactured at multiple sites or using different processes, we will also need to demonstrate comparability across the manufacturing batches in order to obtain regulatory approval. Satisfaction of the approval requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the product. We do not know if or when we might receive regulatory approvals for our electroporation equipment and any of our product candidates currently under development. Moreover, any approvals that we obtain may not cover all of the clinical indications for which we are seeking approval, or could contain significant limitations in the form of narrow indications, warnings, precautions or contra-indications with respect to conditions of use. In such event, our ability to generate revenues from such products would be greatly reduced and our business would be harmed.

The FDA has substantial discretion in the approval process and may either refuse to consider our application for substantive review or may form the opinion after review of our data that our application is insufficient to allow approval of our electroporation equipment and product candidates. If the FDA does not consider or approve our application, it may require that we conduct additional clinical, preclinical or manufacturing validation studies and submit that data before it will reconsider our application. Depending on the extent of these or any other studies, approval of any applications that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be successful or considered sufficient by the FDA for approval or even to make our applications approvable. If any of these outcomes occur, we may be forced to abandon one or more of our applications for approval, which might significantly harm our business and prospects.

It is possible that none of our products or any product we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or our collaborators to commence product sales. Any delay in obtaining, or an inability to obtain, applicable regulatory approvals would prevent us from commercializing our products, generating revenues and achieving and sustaining profitability.

Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

Clinical testing is expensive and can take many years to complete, and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our products may not be predictive of the results of later-stage clinical trials. Results from one study may not be reflected or supported by the results of similar studies. Results of an animal study may not be indicative of results achievable in human studies. Human-use equipment and 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 testing. The time required to obtain approval by the FDA and similar foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials, depending upon numerous factors. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change. We have not obtained regulatory approval for any human-use products.

Our products could fail to complete the clinical trial process for many reasons, including the following:

- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that our electroporation equipment or product candidate is safe and effective for any indication;
- the results of clinical trials may not meet the level of clinical or statistical significance required by the FDA or comparable foreign regulatory authorities for approval, for example, the results for the ITT population in the REVEAL 1 Phase 3 clinical trial were not statistically significant, which could result in the FDA requiring that we conduct another clinical trial before submitting a BLA for VGX-3100;
- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may not be successful in enrolling a sufficient number of participants in clinical trials;
- we may be unable to demonstrate that our electroporation equipment or product candidates' clinical and other benefits outweigh their safety risks;
- we may be unable to demonstrate that our electroporation equipment or product candidate presents an advantage over existing therapies, or over placebo in any indications for which the FDA requires a placebo-controlled trial;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a new drug application or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of us or third-party manufacturers with which we or our collaborators contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

Our product candidates are combination products regulated under both the biologic and device regulations of the Public Health Service Act and Federal Food, Drug, and Cosmetic Act. Third-party manufacturers may not be able to comply with cGMP regulations, regulations applicable to biologic/device combination products, including applicable provisions of the FDA's drug cGMP regulations, device cGMP requirements embodied in the QSR or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates.

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities 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 sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; and
- lack of adequate funding to continue the clinical trial.

If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for our electroporation equipment and our product candidates may be harmed and our ability to generate product revenues will be delayed or eliminated altogether. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Further, delays in the commencement, conduct or completion of clinical trials may adversely affect the trading price of our common stock.

Delays in the commencement, conduct or completion of clinical testing could result in increased costs to us and delay or limit our ability to generate revenues.

Delays in the commencement, conduct or completion of clinical testing could significantly affect our product development costs. We do not know whether planned clinical trials will begin on time or be completed on schedule, if at all. In addition, ongoing clinical trials may not be completed on schedule, or at all, and could be placed on a hold by the regulators for

various reasons. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- obtaining regulatory approval to commence a clinical trial;
- adverse results from third party clinical trials involving gene-based therapies and the regulatory response thereto;
- reaching agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- future bans or stricter standards imposed on clinical trials of gene-based therapy;
- manufacturing sufficient quantities of our electroporation equipment and product candidates for use in clinical trials;
- obtaining institutional review board, or IRB, approval to conduct a clinical trial at a prospective site;
- slower than expected recruitment and enrollment of patients to participate in clinical trials for a variety of reasons, including competition from other clinical trial programs for similar indications or, with respect to our clinical trials for INO-4800, mass vaccination efforts;
- conducting clinical trials with sites internationally due to regulatory approvals and meeting international standards;
- retaining patients who have initiated a clinical trial but may be prone to withdraw due to side effects from the therapy, lack of efficacy or personal issues, or who are lost to further follow-up;
- collecting, reviewing and analyzing our clinical trial data; and
- global unrest including geopolitical risks emanating from countries such as Russia and China, global pathogen outbreaks or pandemics, terrorist activities, and economic and other external factors beyond our control.

Clinical trials may also be delayed as a result of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, the FDA, the IRB overseeing the clinical trial at issue, any of our clinical trial sites with respect to that site, or other regulatory authorities 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 sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- unforeseen safety issues; and
- lack of adequate funding to continue the clinical trial.

If we experience delays in completion of, or if we terminate, any of our clinical trials, the commercial prospects for our electroporation equipment and our product candidates may be harmed and our ability to generate product revenues will be delayed or eliminated altogether. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. Further, delays in the commencement, conduct or completion of clinical trials may adversely affect the trading price of our common stock.

None of our human vaccine candidates, including INO-4800, or our immunotherapy and DNA encoded monoclonal antibody product candidates have been approved for sale, and we may never develop commercially successful vaccine, immunotherapy or DNA encoded monoclonal antibody products.

Our human vaccine programs, which includes our COVID-19 vaccine candidate INO-4800, our immunotherapy programs and our DNA encoded monoclonal antibodies program are in various stages of research and development, and currently include product candidates in discovery, preclinical studies and Phase 1, 2 and 3 clinical trials. There are limited data regarding the efficacy of synthetic vaccine candidates and immunotherapy candidates compared with conventional vaccines, and we must conduct a substantial amount of additional research and development before the FDA or any comparable foreign regulatory authority will approve any of our vaccine product candidates, including INO-4800. The success of our efforts to develop and commercialize our product candidates, including INO-4800, could be delayed or fail for a number of reasons. For example, we could experience delays in product development and clinical trials. Our product candidates could be found to be ineffective or unsafe, or otherwise fail to receive necessary regulatory clearances to proceed with further clinical development or to be approved for marketing. Our products, even if they are deemed to be safe and effective by regulatory authorities, could be difficult to manufacture on a large scale or uneconomical to market, or our competitors could develop superior products more quickly and efficiently or more effectively market their competing products. The ability to manufacture sufficient quantities of INO-4800 on a large scale is particularly challenging and will require substantial resources and the engagement of third parties, which we may not be able to obtain on a timely basis, or at all.

In addition, adverse events, or the perception of adverse events, relating to vaccine and immunotherapy candidates and delivery technologies may negatively impact our ability to develop commercially successful products. For example, pharmaceutical companies have been subject to claims that the use of some pediatric vaccines has caused personal injuries, including brain damage, central nervous system damage and autism. These and other claims may influence public perception of the use of vaccine and immunotherapy products and could result in greater governmental regulation, stricter labeling requirements and potential regulatory delays in the testing or approval of our potential products.

Our planned Phase 3 clinical trial of INO-4800 in the United States as a potential COVID-19 vaccine was previously placed on partial clinical hold by the U.S. FDA. Even though the hold has been lifted, we may experience delays in our ability to conduct clinical trials in the United States.

Our planned clinical development of INO-4800 in the United States as a potential COVID-19 vaccine was previously placed on partial clinical hold by the U.S. FDA until we satisfactorily resolved the FDA's questions relating to our CELLECTRA 2000 device to be used in the trial. This clinical hold meant that we were not permitted to commence a Phase 3 clinical trial in the United States until the hold was lifted. The FDA notified us in November 2021 that the clinical hold had been lifted, allowing us to proceed with the Phase 3 segment of our INNOVATE trial. Although the partial clinical hold did not prevent us from starting our planned Phase 3 clinical trials outside of the United States, foreign regulatory authorities may impose similar requirements before we can commence or complete the portion of our Phase 3 clinical trial to be conducted in foreign countries.

Delays in completion of ongoing clinical testing for INO-4800, because of a clinical hold, our current pause on enrolling new patients for INNOVATE, our ability to obtain regulatory approval to amend the primary endpoint of INNOVATE or otherwise, could significantly affect our product development costs. We do not know whether our planned Phase 3 clinical trial will be completed on schedule, if at all. In addition, our ongoing clinical trials for INO-4800 may not be completed on schedule, or at all, and could be placed on additional holds by regulators either in the United States or in foreign jurisdictions for reasons unrelated to our current hold. If we experience delays in completion of, or if we terminate, any of our clinical trials relating to INO-4800, the commercial prospects for our product candidate may be harmed and our ability to generate product revenues will be delayed or eliminated altogether. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate.

The Omicron SARS-CoV-2 variant and newly emerging SARS-CoV-2 variants has required us to modify our COVID-19 vaccine strategy, which will result in new and added risks, including whether there will continue to be a need for a COVID-19 vaccine.

The emergence and current dominance of the Omicron SARS-CoV-2 variant may reduce the effectiveness of INO-4800 in preventing COVID-19. We conducted an in vitro assessment of the cross-reactivity of INO-4800 vaccine-induced immune responses against Omicron. Testing demonstrated a maintenance of T cell responses, including CD8+ responses, but significantly decreased levels of both neutralizing and binding antibodies against Omicron. As a consequence, we plan to seek regulatory approval to amend the protocol for the INNOVATE clinical trial by changing the primary endpoint from prevention of virologically confirmed COVID-19 disease to prevention of severe disease due to COVID-19. There can be no assurance that we will receive regulatory approval for such amendment and we do not know what other requirements and conditions may be imposed on the conduct of INNOVATE that may affect its timing, cost and outcome. If we are not able to obtain regulatory approval to amend the primary endpoint, INO-4800 may not achieve the primary endpoint of the INNOVATE trial, making marketing approvals less likely.

In addition, our COVID-19 vaccine strategy and prospects would be adversely affected if a weakened version of SARS-CoV-2 becomes the dominant variant, obviating the need for any vaccine.

As part of our modified COVID-19 vaccine strategy, we are also evaluating the feasibility of an additional ex-US heterologous boost (vaccination with a different vaccine from the primary series) trial with INO-4800. However, a clear regulatory pathway for a heterologous boost trial has not been defined and such a regulatory strategy may be difficult to navigate and ultimately may not be successful.

There can be no assurance that any of the products we are developing for COVID-19 would be granted an Emergency Use Authorization by the FDA or similar authorization by regulatory authorities outside of the United States if we were to decide to apply for such an authorization. The option of seeking an Emergency Use Authorization may no longer exist for our primary vaccine candidates, and if we cannot obtain such authorization or, if granted, it is terminated, we will be unable to sell our product in the near future and instead will be required to pursue the biologic licensure process in order to sell our product, which is lengthy and expensive.

We may seek an Emergency Use Authorization, or EUA, from the FDA or similar authorization from regulatory authorities outside of the United States, such as conditional marketing authorization from the EMA. If we apply for an EUA and it is granted, an EUA would authorize us to market and sell our COVID-19 vaccine under certain conditions of authorization as long as the public health emergency exists. The FDA expects that companies which receive an EUA for COVID-19 vaccines will proceed to licensure of their vaccine products under a full Biologics License Application. The FDA may issue an EUA during a Public Health Emergency if the agency determines that the potential benefits of a product outweigh the potential risks and if other regulatory criteria are met.

There is no guarantee that we will apply for an EUA or other similar authorization or, if we do apply, that we will be able to obtain such authorization. For example, we may no longer be able to obtain an EUA for INO-4800 as a primary vaccine, since several of our competitors' COVID-19 vaccines have already obtained full approval. As a result, we may only be able to seek an EUA for INO-4800 as a heterologous booster vaccine candidate, which strategy may not be successful. We would need to seek full biologics licensure for INO-4800 as a primary vaccine, which is a lengthy and expensive process. Even if an EUA

or other authorization is ultimately granted, we will rely on the FDA or other applicable regulatory authority policies and guidance governing vaccines authorized in this manner in connection with the marketing and sale of our product. If these policies and guidance change unexpectedly and/or materially or if we misinterpret them, potential sales of our product could be adversely impacted. An EUA authorizing the marketing and sale of our product will terminate upon expiration of the Public Health Emergency, which is a determination made by the Secretary of Health and Human Services. The FDA may also terminate an EUA if safety issues or other concerns about our product arise or if we fail to comply with the conditions of authorization. If we apply for an EUA or similar authorization from regulatory authorities outside of the United States, the failure to obtain such authorization or the termination of such an authorization, if obtained, would adversely impact our ability to market and sell our COVID-19 vaccine, which could adversely impact our business, financial condition and results of operations.

If we and the contract manufacturers upon whom we rely fail to produce our electroporation devices and product candidates in the volumes that we require on a timely basis, or at all, or fail to comply with their obligations to us or with stringent regulations, we may face delays in the development and commercialization of our electroporation equipment and product candidates.

We manufacture some components of our electroporation devices and utilize the services of contract manufacturers to manufacture the remaining components of these devices. We also rely on third party contract manufacturers to produce our product candidates for use in our clinical trials and potentially for commercial distribution, if any product candidate is approved by regulatory authorities. The manufacture of these devices and our product candidates requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers often encounter difficulties in production, particularly in scaling up for commercial production. These problems include difficulties with production costs and yields, quality control, including stability of the equipment and product candidates and quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations.

If we or our manufacturers were to encounter any of these difficulties or our manufacturers otherwise fail to comply with their obligations to us, our ability to provide our electroporation equipment to our partners and to supply product candidates for clinical trials or to commercially launch a product would be jeopardized. For example, we previously relied on VGXI to manufacture DNA plasmids for our product candidates, including INO-4800. In 2020, VGXI notified us that they would be unable to produce the necessary plasmids to meet this timeline due to a lack of manufacturing capacity. As a result, we have engaged several additional third-party contract manufacturers to support the planned large-scale manufacturing of INO-4800. However, there can be no assurance that we will be able to secure adequate additional manufacturing capacity on commercially reasonable terms. Our inability to secured sufficient manufacturing capacity, or our inability to transfer necessary manufacturing know-how to third parties, would adversely affect our commercialization plans and could also harm our reputation.

Furthermore, any delay or interruption in the supply of clinical trial supplies for INO-4800 or any of our other product candidates could delay the completion of our clinical trials, increase the costs associated with maintaining our clinical trial program and, depending upon the period of delay, require us to commence new trials at significant additional expense or terminate the trials completely.

In addition, all manufacturers of our products must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include, among other things, quality control, quality assurance and the generation and maintenance of records and documentation. Manufacturers of our products may be unable to comply with these cGMP requirements and with other FDA, state and foreign regulatory requirements. We have little control over our manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of any product is compromised due to our or our manufacturers' failure to adhere to applicable laws or for other reasons, we may not be able to obtain regulatory approval for or successfully commercialize our products, and we may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of our products, entail higher costs or result in our being unable to effectively commercialize our products. Furthermore, if our manufacturers fail to deliver the required commercial quantities on a timely basis, pursuant to provided specifications and at commercially reasonable prices, we may be unable to meet demand for our products and would lose potential revenues.

We are devoting significant resources to the scale-up, development and commercialization of our COVID-19 vaccine.

We continue to work toward the large-scale technical development, manufacturing scale-up and larger scale deployment of our COVID-19 vaccine candidates. The number of doses of these vaccines that we are able to produce and distribute is dependent on our ability, and the ability of our contract manufacturers, to successfully and rapidly scale up manufacturing capacity. To support the scale-up, we have expended and will need to continue to expend significant resources and capital. We may need to divert resources and capital from our other programs. We may also seek and secure significant additional funding

through contractual arrangements and collaborations with third parties. We may be unable to enter into such arrangements on favorable terms, or at all, which would adversely affect our ability to develop, manufacture and distribute the COVID-19 vaccine.

We are dependent on single-source suppliers for some of the components and materials used in, and the processes required to develop, our products, development candidates and investigational medicines.

We currently depend on single-source suppliers for some of the components and materials used in, and manufacturing processes required to develop and commercialize, our products, development candidates and investigational medicines. We cannot ensure that these suppliers or service providers will remain in business, have sufficient capacity or supply to meet our needs, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to work with us. Our use of single-source suppliers of raw materials, components, key processes, and finished goods exposes us to several risks, including disruptions in supply, price increases, or late deliveries. There are, in general, relatively few alternative sources of supply for substitute components. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components, materials, and processes could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any single-source supplier or service provider could lead to supply delays or interruptions which would damage our business, financial condition, results of operations, and prospects.

If we have to switch to a replacement supplier, the manufacture and delivery of our products, development candidates or investigational medicines could be interrupted for an extended period, which could adversely affect our business. Establishing additional or replacement suppliers for any of the components or processes used in our products or investigational medicines, if required, may not be accomplished quickly. If we are able to find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. While we seek to maintain adequate inventory of the single-source components and materials used in our products, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to supply our investigational medicines.

Our reliance on these suppliers, service providers, and manufacturers subjects us to a number of risks that could harm our reputation, business, and financial condition, including, among other things:

- delays to the development timelines for our development candidates or investigational medicines;
- interruption of supply resulting from modifications to or discontinuation of a supplier's operations;
- delays in product shipments resulting from uncorrected defects, reliability issues, or a supplier's variation in a component;
- a lack of long-term supply arrangements for key components with our suppliers;
- inability to obtain adequate supply in a timely manner, or to obtain adequate supply on commercially reasonable terms;
- difficulty and cost associated with locating and qualifying alternative suppliers for our components in a timely manner;
- production delays related to the evaluation and testing of components from alternative suppliers, and corresponding regulatory qualifications;
- delay in delivery due to our suppliers' prioritizing other customer orders over ours;
- damage to our reputation caused by defective components produced by our suppliers; and
- fluctuation in delivery by our suppliers due to changes in demand from us or their other customers.

If any of these risks materialize, costs could significantly increase and our ability to meet demand for our products could be impacted.

Even if our products receive regulatory approval, they may still face future development and regulatory difficulties.

Even if United States regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies. This governmental oversight may be particularly strict with respect to gene-based therapies. Our products will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, record keeping and submission of safety and other post-market information. For example, the FDA strictly regulates the promotional claims that may be made about medical 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. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. However, companies may in certain circumstances share truthful and not misleading information that is otherwise consistent with the product's FDA approved labeling. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and

other regulatory authorities for compliance with current good manufacturing practices, or cGMP, regulations. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates, or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue Warning Letters or untitled letters;
- impose civil or criminal penalties;
- suspend regulatory approvals;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products or require us to initiate a product recall.

Even if our products receive regulatory approval in the United States, we may never receive approval or commercialize our products outside of the United States.

In order to market any electroporation equipment and product candidates outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval, and the regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. For example, in connection with our planned Phase 3 clinical trials of INO-4800 to be conducted outside of the United States, some regulatory authorities have indicated concerns with placebo-controlled efficacy trials of a COVID-19 vaccine, which means that we would not be able to open clinical trial sites in those countries. Furthermore, regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects detailed above regarding FDA approval in the United States. Such effects include the risks that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and have an adverse effect on their commercial potential or require costly, post-marketing follow-up studies.

DNA medicines are a novel approach, and negative perception of the efficacy, safety, or tolerability of any investigational medicines that we develop could adversely affect our ability to conduct our business, advance our investigational medicines, or obtain regulatory approvals.

No DNA medicines have been granted EUA or have been approved to date by the FDA. Adverse events in clinical trials of our investigational medicines or in clinical trials of others developing similar products and the resulting publicity, as well as any other adverse events in the field of DNA medicine, or other products that are perceived to be similar to DNA medicines, such as those related to gene therapy or gene editing, could result in a decrease in the perceived benefit of one or more of our programs, increased regulatory scrutiny, decreased confidence by patients and clinical trial collaborators in our investigational medicines, and less demand for any product that we may develop. Our large pipeline of development candidates and investigational medicines could result in a greater quantity of reportable adverse events, including suspected unexpected serious adverse reactions, other reportable negative clinical outcomes, manufacturing reportable events or material clinical events that could lead to clinical delay or hold by the FDA or applicable regulatory authority or other clinical delays, any of which could negatively impact the perception of one or more of our programs, as well as our business as a whole. In addition, responses by U.S., state, or foreign governments to negative public perception may result in new legislation or regulations that could limit our ability to develop any investigational medicines or commercialize any approved products, obtain or maintain regulatory approval, or otherwise achieve profitability. More restrictive statutory regimes, government regulations, or negative public opinion would have an adverse effect on our business, financial condition, results of operations, and prospects and may delay or impair the development of our investigational medicines and commercialization of any approved products or demand for any products we may develop.

Because we are developing some of our development candidates or investigational medicines for the treatment of diseases in which there is little clinical experience and, in some cases, using new endpoints or methodologies, the FDA or other regulatory authorities may not consider the endpoints of our clinical trials to provide clinically meaningful results.

There are no pharmacologic therapies approved to treat the underlying causes of many diseases that we currently attempt to address or may address in the future. There has been limited clinical trial experience for the development of pharmaceuticals to treat these rare diseases in general, and we are not aware of a registrational trial that led to approval of a drug to treat these

diseases. There have been some historical trials with other agents which may have utilized clinical endpoints that are less applicable to our efforts that address the underlying defect. As a result, the design and conduct of clinical trials of investigational medicines for the treatment of these disorders and other disorders may take longer, be more costly, or be less effective as part of the novelty of development in these diseases.

Even if the FDA does find our success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance in any pivotal or other clinical trials we or our strategic collaborators may conduct for our programs. Further, even if we do achieve the pre-specified criteria, our trials may produce results that are unpredictable or inconsistent with the results of the more traditional efficacy endpoints in the trial. The FDA also could give overriding weight to other efficacy endpoints over a primary endpoint, even if we achieve statistically significant results on that endpoint, if we do not do so on our secondary efficacy endpoints. 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 licensure. Other regulatory authorities in Europe and other countries may make similar findings with respect to these endpoints.

We have obtained Orphan Drug Designation for one of our product candidates. As part of our business strategy, we may continue to seek Orphan Drug Designation for additional product candidates, and we may be unsuccessful in obtaining new designations or may be unable to obtain or maintain the benefits associated with Orphan Drug Designation, including the potential for orphan drug exclusivity.

We have obtained Orphan Drug Designation from the FDA for INO-3107 for the treatment of recurrent respiratory papillomatosis. We have sought and may continue to seek Orphan Drug Designation for one or more of our other product candidates, including but not limited to VGX-3100 for the treatment of HPV-16-/18-associated anal dysplasia, although we may be unsuccessful in doing so. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as tax advantages and user fee waivers. Opportunities for grant funding toward clinical trial costs may also be available for clinical trials of drugs for rare diseases, regardless of whether the drugs are designated for the orphan use. In addition, if a product that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same product for the same indication for seven years, except in limited circumstances.

Although we have obtained Orphan Drug Designation for INO-3107 for the treatment of recurrent respiratory papillomatosis, and even if we obtain Orphan Drug Designation for our other product candidates in specific indications, we may not be the first to obtain marketing approval of these product candidates for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. If a competitor with a product that is determined by the FDA to be the same as one of our product candidates obtains marketing approval before us for the same indication we are pursuing and obtains orphan drug exclusivity, our product candidate may not be approved until the period of exclusivity ends unless we are able to demonstrate that our product candidate is clinically superior. Even after obtaining approval, we may be limited in our ability to market our product. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or 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. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different principal molecular structural features can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug with the same principal molecular structural features for the same condition if the FDA concludes that the later drug is safer, more effective or makes a major contribution to patient care. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek Orphan Drug Designation for some of our product candidates, we may never receive such designations.

Tax reform legislation enacted in 2017 reduced the amount of the qualified clinical research costs for a designated orphan product that a sponsor may claim as a credit from 50% to 25%. This reduction could further limit the advantage of, and may impact our future business strategy with respect to, seeking the Orphan Drug Designation.

A breakthrough therapy designation or fast track designation by the FDA for a drug may not lead to a faster development or regulatory review or approval process, and it would not increase the likelihood that the drug will receive marketing approval.

We may seek a breakthrough therapy designation for one or more of our investigational medicines. A breakthrough therapy is defined as a drug 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 drug 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 drugs 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. Drugs designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the regulatory submission.

Designation as a breakthrough therapy is at the discretion of the FDA. Accordingly, even if we believe that one of our investigational medicines 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 drug may not result in a faster development process, review, or approval compared to drugs considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. Even if we are successful in obtaining accelerated approval in the United States or under comparable pathways in other jurisdictions, we may face requirements and limitations that will adversely affect our prospects. For example, we may be approved only for a very limited indication, we may not successfully complete required post-approval trials, such trials may not confirm the clinical benefit of our drug, or approval of the drug may be withdrawn. In addition, even if one or more of our investigational medicines qualify as breakthrough therapies, the FDA may later decide that the investigational medicine no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened.

Risks Related to Reliance on Third Parties

If we lose or are unable to secure collaborators or partners, or if our collaborators or partners do not apply adequate resources to their relationships with us, our product development and potential for profitability will suffer.

We have entered into, and may continue to enter into, distribution, co-promotion, partnership, sponsored research and other arrangements for development, manufacturing, sales, marketing and other commercialization activities relating to our products. For example, in the past we have entered into license and collaboration agreements to develop, obtain regulatory approval for and commercialize our product candidates for specified indications, including in jurisdictions outside of the United States. The amount and timing of resources applied by our collaborators are largely outside of our control.

If any of our current or future collaborators breaches or terminates our agreements, or fails to conduct our collaborative activities in a timely manner, our commercialization of products could be diminished or blocked completely. We may not receive any event-based payments, milestone payments or royalty payments under our collaborative agreements if our collaborative partners fail to develop products in a timely manner or at all. It is possible that collaborators will change their strategic focus, pursue alternative technologies or develop alternative products, either on their own or in collaboration with others. Further, we may be forced to fund programs that were previously funded by our collaborators, and we may not have, or be able to access, the necessary funding. The effectiveness of our partners, if any, in marketing our products will also affect our revenues and earnings.

We desire to enter into new collaborative agreements. However, we may not be able to successfully negotiate any additional collaborative arrangements and, if established, these relationships may not be scientifically or commercially successful. Our success in the future depends in part on our ability to strategically enter into agreements with other organizations. This can be difficult due to internal and external constraints placed on these organizations. Some organizations may have insufficient administrative and related infrastructure to enable collaborations with many companies at once, which can extend the time it takes to develop, negotiate, implement and execute a collaboration. Once news of discussions regarding possible collaborations are known in the medical community, regardless of whether the news is accurate, failure to announce a collaborative agreement or the entity's announcement of a collaboration with another entity may result in adverse speculation about us, resulting in harm to our reputation and our business.

Disputes could also arise between us and our existing or future collaborators, as to a variety of matters, including financial and intellectual property matters or other obligations under our agreements. These disputes could be both expensive and time-consuming and may result in delays in the development and commercialization of our products or could damage our relationship with a collaborator.

We have agreements with government agencies, which are subject to termination and uncertain future funding.

We have entered into agreements with government agencies, such as the NIAID, DARPA and the DoD, and we intend to continue entering into these types of agreements in the future. Our business is partially dependent on the continued performance by these government agencies of their responsibilities under these agreements, including adequate continued funding of the agencies and their programs. We have no control over the resources and funding that government agencies may devote to these agreements, which may be subject to annual renewal and which generally may be terminated by the government agencies at any time. For example, in April 2021 we were notified by the DoD that they will discontinue funding for the Phase 3 segment of our INNOVATE trial.

Government agencies may fail to perform their responsibilities under these agreements, which may cause them to be terminated by the government agencies. In addition, we may fail to perform our responsibilities under these agreements. Many of our government agreements are subject to audits, which may occur several years after the period to which the audit relates. If

an audit identifies significant unallowable costs, we could incur a material charge to our earnings or reduction in our cash position. As a result, we may be unsuccessful entering, or ineligible to enter, into future government agreements.

We and our collaborators rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we and our collaborators may not be able to obtain regulatory approval for or commercialize our product candidates.

We and our collaborators have entered into agreements with CROs to provide monitors for and to manage data for our on-going clinical programs. We and the CROs conducting clinical trials for our electroporation equipment and product candidates are required to comply with current good clinical practices, or GCPs, regulations and guidelines enforced by the FDA for all of our products in clinical development. The FDA enforces GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or the CROs conducting clinical trials of our product candidates fail to comply with applicable GCPs, the clinical data generated in the clinical trials may be deemed unreliable and the FDA may require additional clinical trials before approving any marketing applications.

If any relationships with CROs terminate, we or our collaborators may not be able to enter into arrangements with alternative CROs. In addition, these third-party CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our on-going clinical programs or perform trials efficiently. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies or other drug development activities, which could harm our competitive position. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical 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. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed. Cost overruns by or disputes with our CROs may significantly increase our expenses.

We enter into various contracts in the normal course of our business in which we agree to indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically agree to indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our or our sub licensees' exercise of rights under the agreement. With respect to our commercial agreements, we have agreed to indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party. With respect to consultants, we typically agree to indemnify them from claims arising from the good faith performance of their services.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage or not covered by insurance, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator or other third party to indemnify us and the collaborator or other third party is denied insurance coverage or otherwise does not have assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

Our participation in the WHO Solidarity Trial Vaccines (STV) could result in adverse consequences. We do not have any control over clinical data, progress, and decisions regarding INO-4800's participation in STV, and as such, decisions regarding the clinical pathway for INO-4800 between the WHO and the Company may not always align.

Our COVID-19 vaccine candidate INO-4800 is one of two vaccine candidates initially selected by the WHO for its randomized, global Phase 3 clinical trial, STV, being conducted initially in Columbia, Mali and the Philippines. We are supplying INO-4800 to WHO for the STV clinical trial. Because STV and our other ongoing Phase 2/3 global clinical trial of INO-4800, INNOVATE, have similar protocols and endpoints, we believe that the data generated by STV could support a potential EUA or licensure application for INO-4800. STV is entirely independent of INNOVATE and is being conducted at different clinical trial sites with separate investigators, IRBs and DSMBs. We have no influence on the conduct of STV other than providing INO-4800 for the trial. As a result, we do not have any control over clinical data, clinical trial progress or decisions regarding INO-4800's inclusion in STV. All decisions regarding STV are and will be made by the WHO, which has the ability to terminate, pause or otherwise control the conduct of STV without seeking our consent. If WHO does not modify the endpoints of STV, or modifies the endpoints in such a manner that results in INO-4800 not showing efficacy in STV, it could negatively affect the prospects of INO-4800 as a vaccine candidate.

Risks Related to Commercialization of Our Product Candidates

We currently have a small marketing organization and no sales organization. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our products, we may not be able to generate product revenues.

We currently have a small sales organization for the marketing, sales and distribution of our electroporation equipment and product candidates. In order to commercialize any products, we must build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. We contemplate establishing our own sales force or seeking third-party partners to sell our products. The establishment and development of our own sales force to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel. To the extent we rely on third parties to commercialize our approved products, if any, we will receive lower revenues than if we commercialized these products ourselves. In addition, we may have little or no control over the sales efforts of third parties involved in our commercialization efforts. In the event we are unable to develop our own marketing and sales force or collaborate with a third-party marketing and sales organization, we would not be able to commercialize our product candidates which would negatively impact our ability to generate product revenues.

If products for which we receive regulatory approval do not achieve broad market acceptance, the revenues that we generate from their sales will be limited.

The commercial success of our electroporation equipment and product candidates for which we obtain marketing approval from the FDA or other regulatory authorities will depend upon the acceptance of these products by both the medical community and patient population. Coverage and reimbursement of our product candidates by third-party payors, including government payors, generally is also necessary for optimal commercial success. The degree of market acceptance of any of our approved products will depend on a number of factors, including:

- our ability to provide acceptable evidence of safety and efficacy;
- our biomarker being developed to identify women with HPV 16/18 cervical HSIL, may not be validated by the FDA or other regulatory bodies, which could adversely affect the commercial viability ofVGX-3100;
- the relative convenience and ease of administration, including the acceptance and usage of our electroporation equipment by the medical community;
- the prevalence and severity of any actual or perceived adverse side effects;
- limitations or warnings contained in a product's FDA-approved labeling, including, for example, potential “black box” warnings
- availability of alternative treatments;
- pricing and cost effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- the public perception of new therapies and the reputational challenges that the vaccine industry is facing related to the growing momentum of the anti-vaccine movement, including with respect to COVID-19 vaccines;
- our ability to obtain sufficient third-party coverage and adequate reimbursement; and
- the willingness of patients to pay out of pocket in the absence of third-party coverage.

If our electroporation equipment and product candidates are approved but do not achieve an adequate level of acceptance by physicians, healthcare payors and patients, we may not generate sufficient revenue from these products, and we may not become or remain profitable. In addition, our 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.

We are subject to uncertainty relating to coverage and reimbursement policies which, if not favorable to our product candidates, could hinder or prevent our products' commercial success.

Patients in the United States and elsewhere generally rely on third-party payors to reimburse part or all of the costs associated with their prescription drugs and medical treatments. Accordingly, our ability to commercialize our electroporation equipment and product candidates successfully will depend in part on the extent to which governmental authorities, including Medicare and Medicaid, private health insurers and other third-party payors establish appropriate coverage and reimbursement levels for our product candidates and related treatments. As a threshold for coverage and reimbursement, third-party payors in the United States generally require that drug products and vaccines have been approved for marketing by the FDA.

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. Coverage decisions may not favor new products when more established or lower cost therapeutic alternatives are already available. Even if we obtain coverage for a given product, the associated reimbursement rate may not be adequate to cover our costs, including research, development, intellectual property, manufacture, sale and distribution expenses,

or may require co-payments that patients find unacceptably high. Patients are unlikely to use our products unless reimbursement is adequate to cover all or a significant portion of the cost of our drug products.

Additionally, some of our products, if approved, will be provided under the supervision of a physician. When used in connection with medical procedures, our product candidates may not be reimbursed separately but their cost may instead be bundled as part of the payment received by the provider for the procedure only. Separate reimbursement for the product itself or the treatment or procedure in which our product is used may not be available. A decision by a third-party payor not to cover or separately reimburse for our product candidates or procedures using our product candidates, could reduce physician utilization of our products once approved.

Coverage and reimbursement policies for products can differ significantly from payor to payor as there is no uniform policy of coverage and reimbursement for products among third-party payors in the United States. There may be significant delays in obtaining coverage and reimbursement as the process of determining coverage and reimbursement is often time consuming and costly which will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage or adequate reimbursement will be obtained. It is difficult to predict at this time what government authorities and third-party payors will decide with respect to coverage and reimbursement for our products.

A significant trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular products and services. Third-party payors are increasingly challenging the effectiveness of and prices charged for medical products and services. Moreover, the U.S. government, state legislatures and foreign governmental entities have shown significant interest in implementing cost containment programs to limit the growth of government paid healthcare costs, including price controls, restrictions on reimbursement and coverage and requirements for substitution of generic products for branded prescription drugs. We may not be able to obtain third-party payor coverage or reimbursement for our products in whole or in part.

Risks Related to Managing Our Growth and Employee and Operational Matters

We are currently subject to litigation and may become subject to additional litigation, which could harm our business, financial condition and reputation.

We may have actions brought against us by stockholders relating to past transactions, changes in our stock price or other matters. For example, during 2020, numerous purported shareholder class action complaints were filed against us, naming us and our directors and executive officers as defendants, and alleging that we made materially false and misleading statements regarding the development of our INO-4800 vaccine candidate against COVID-19 in violation of certain federal securities laws. We may also become party to litigation with third parties as a result of our business activities. In 2020, we filed a lawsuit against one of our contract manufacturers, who then filed a counterclaim against us alleging that we had breached our contract with them, among other claims. These litigation matters, described in this report, are ongoing, and even though we intend to vigorously defend ourselves in these actions, there can be no assurance that we will ultimately prevail. These and any potential future actions against us could give rise to substantial damages, which could have a material adverse effect on our financial position, liquidity or results of operations. Even if an action is not resolved against us, the uncertainty and expense associated with litigation could harm our business, financial condition and reputation, as litigation is often costly, time-consuming and disruptive to business operations. The defense of our existing and potential future lawsuits could also result in diversion of our management's time and attention away from business operations, which could harm our business.

Our business could be adversely affected by the effects of health epidemics, including the global COVID-19 pandemic.

In response to the COVID-19 pandemic, in 2020 a number of governmental orders and other public health guidance measures were implemented across much of the United States, including in the locations of our offices, laboratories, clinical trial sites and third parties on whom we rely. As a result, our expected clinical development timelines could be negatively affected by COVID-19, which could then materially and adversely affect our business, financial condition and results of operations. Further, we have implemented a work from home policy allowing employees who can work from home to do so, while those needing to work in laboratory facilities work in shifts to reduce the number of people gathered together at one time. We have also implemented a mask-wearing mandate for all on-site activities. Non-essential business travel has been suspended and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, while work in laboratories has been organized to reduce risk of COVID-19 transmission. Our increased reliance on personnel working from home may negatively impact our productivity, or could disrupt, delay or otherwise adversely impact our business. For example, with our personnel working from home, some of our research activities that require our personnel to be in our laboratories could be delayed.

In addition, as local jurisdictions continue to put restrictions in place or reinstitute restrictions they had previously lifted, our ability to continue to conduct and enroll patients in our clinical trials, manufacture our product candidates and pursue collaborations may also be limited. Such events may result in business and manufacturing disruption, and in reduced operations, any of which could materially affect our business, financial condition and results of operations. The COVID-19 pandemic has caused supply chain disruptions and supply shortages globally. As a result, we have experienced delays and disruptions in

obtaining clinical supplies, manufacturing supplies and components, and have had to secure new vendors for certain supplies and components at higher prices. Some manufacturing supplies and components remain in limited supply with uncertain delivery dates.

The spread of COVID-19, which has caused a broad impact globally, could also affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, it has resulted in significant disruption of global financial markets, which could reduce our ability to access capital. Although we have raised significant funds from the sale of our common stock in the public markets during the pandemic, there can be no guarantee that we will be able to continue to so, which could negative affect our future liquidity. In addition, if a global economic recession results following the spread of COVID-19, including newly emerging SARS-CoV-2 variants, its impact could materially affect our business and the value of our common stock.

The continued spread of COVID-19, including newly emerging SARS-CoV-2 variants globally, has affected and could continue to adversely affect our clinical trial operations, including our ability to initiate and conduct our planned trials on their expected timelines and to recruit and retain participants and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 if an outbreak occurs in their geography. For example, COVID-19 adversely impacted the timeline for data collection for our VGX-3100 program. An increasing number of trial participants are either not able or do not feel safe going into healthcare facilities, which is necessary for the collection and completion of data samples for this trial. As a result, it is taking longer than anticipated to complete the data collection process. Further, the COVID-19 outbreak could result in delays in our clinical trials due to prioritization of hospital resources toward the outbreak, restrictions in travel, potential unwillingness of participants to enroll in trials, participants withdrawing from trials following enrollment as a result of contracting COVID-19 or other health conditions, or the inability of participants to comply with clinical trial protocols as quarantines and travel restrictions impede participant movement or interrupt healthcare services. In addition, we rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the outbreak may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. These restrictions may delay the conduct of multiple clinical trials including our Phase 1 through 3 clinical trials.

Additionally, COVID-19 may also result in delays in receiving approvals from local and foreign regulatory authorities, delays in necessary interactions with local and foreign regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or forced furloughs of government employees, and refusals to accept data from clinical trials conducted in these affected geographies.

The global outbreak of COVID-19 continues to evolve. The extent to which COVID-19 may impact our business, operations and clinical trials will depend on future developments, including travel restrictions to, from and within the United States and other countries, the effectiveness of actions taken in the United States and other countries to contain and treat the disease, including mass vaccination efforts, and whether the United States and additional countries are required to move to complete lock-down status. The ultimate long-term impact of COVID-19 is highly uncertain.

We face intense and increasing competition and steps taken by our competitors such as the introduction of a new, disruptive technology may impede our ability to successfully commercialize our DNA medicines.

If any of our competitors develop products with efficacy or safety profiles significantly better than our products and introduce new, disruptive technology, we may not be able to commercialize our products, and sales of any of our commercialized products could be harmed. Some of our competitors and potential competitors have substantially greater product development capabilities and financial, scientific, marketing and human resources than we do. Competitors may develop products earlier, obtain FDA approvals for products more rapidly, or develop products that are more effective than those under development by us. We will seek to expand our technological capabilities to remain competitive; however, research and development by others may render our technologies or products obsolete or noncompetitive, or result in treatments or cures superior to ours.

Many other companies are pursuing other forms of treatment or prevention for diseases that we target. For example, many of our competitors are working on developing and testing COVID-19 vaccines, cancer vaccines and immunotherapies, and several products such as the CAR-Ts developed by our competitors have been approved for human use. Some of our competitors have already received regulatory approval for their COVID-19 vaccines and have mass vaccination efforts underway in our target markets. For example, multiple COVID-19 vaccines and boosters have been approved by regulators in the United States and Europe and in August 2021 the world's first DNA vaccine against COVID-19 was approved for emergency use by India's regulators. The earlier market entry of these other vaccines, and their actual or perceived efficacious or success relative to our own, has led to and may continue to lead to diversion of funding away from us, a declining market for COVID-19 vaccines, decreased demand for INO-4800, if approved, and difficulty in finding participants for our clinical trials. All of these factors could substantially impact our ability to complete the development of, commercialize and generate revenues from INO-4800.

In addition, our competitors and potential competitors include large pharmaceutical and more established biotechnology companies. These companies have significantly greater financial and other resources and greater expertise than us in research and development, securing government contracts and grants to support research and development efforts, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and marketing. This may make it easier for them to respond more quickly than us to new or changing opportunities, technologies or market needs. Many of these competitors operate large, well-funded research and development programs and have significant products approved or in development. Small companies may also prove to be significant competitors, particularly through collaborative arrangements with large pharmaceutical companies or through acquisition or development of intellectual property rights. Our potential competitors also include academic institutions, governmental agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for product and clinical development and marketing. Research and development by others may seek to render our technologies or products obsolete or noncompetitive.

Our failure to successfully acquire, develop and market additional product candidates or approved products would impair our ability to grow.

We may acquire, in-license, develop and/or market additional products and product candidates. The success of these actions depends partly upon our ability to identify, select and acquire promising product candidates and products.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with us for the license or acquisition of product candidates and approved products. We have limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into our current infrastructure. Moreover, we may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or we may fail to realize the anticipated benefits of such efforts. We may not be able to acquire the rights to additional product candidates on terms that we find acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

- exposure to unknown liabilities;
- disruption of our business and diversion of our management's time and attention to develop acquired products or technologies;
- incurrence of substantial debt or dilutive issuances of securities to pay for acquisitions;
- higher than expected acquisition and integration costs;
- increased amortization expenses;
- difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel;
- impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and
- inability to retain key employees of any acquired businesses.

Further, any product candidate that we acquire may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

We depend upon key personnel who may terminate their employment with us at any time and we may need to hire additional qualified personnel in order to obtain financing, pursue collaborations or develop or market our product candidates.

The success of our business strategy will depend to a significant degree upon the continued services of key management, technical and scientific personnel and our ability to attract and retain additional qualified personnel and managers, including personnel with expertise in clinical trials, government regulation, manufacturing, marketing and other areas. Competition for qualified personnel is intense among companies, academic institutions and other organizations. If we are unable to attract and retain key personnel and advisors, it may negatively affect our ability to successfully develop, test, commercialize and market our products and product candidates.

Changes in funding for the FDA and other government agencies could prevent new products from being developed or commercialized in a timely manner, 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, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency 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 new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days from December 2018 to January 2019, 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. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

We are dependent on information technology and our systems and infrastructure face certain risks, including from cybersecurity breaches and data leakage.

We rely to a large extent upon sophisticated information technology systems to operate our businesses, some of which are managed, hosted provided and/or used for third-parties or their vendors. We collect, store and transmit large amounts of confidential information (including personal information and pseudonymized information), and we deploy and operate an array of technical and procedural controls to maintain the confidentiality and integrity of such confidential information. A significant breakdown, invasion, corruption, destruction, interruption, or unavailability of critical information technology systems or infrastructure, by our workforce, others with authorized access to our systems or unauthorized persons could negatively impact operations. Hardware, software, or applications we develop or obtain from third parties may contain defects in design or manufacture or other supply chain problems that could unexpectedly compromise our information and network security. The ever-increasing use and evolution of technology, including cloud-based computing, creates opportunities for the unintentional dissemination or intentional destruction of confidential information stored in our or our third-party providers' systems, portable media or storage devices. We could also experience a business interruption, theft of confidential information or reputational damage from industrial espionage attacks, malware or other cyber-attacks (including ransomware), which may compromise our system infrastructure or lead to data leakage, either internally or at our third-party providers. While we have invested in the protection of data and information technology, there can be no assurance that our efforts will prevent service interruptions or security breaches. Any such interruption or breach of our systems could adversely affect our business operations and/or result in the loss of critical or sensitive confidential information or intellectual property, and could result in financial, legal, business and reputational harm to us. In addition, as the regulatory environment related to information security, data collection and use, and privacy becomes increasingly rigorous, with new and constantly changing requirements applicable to our business, compliance with those requirements could also result in additional costs.

We face potential product liability exposure and, if successful claims are brought against us, we may incur substantial liability.

The use of our electroporation equipment and DNA vaccine, DNA immunotherapy and dMAb candidates in clinical trials and the sale of any products for which we obtain marketing approval expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. For example, pharmaceutical companies have been subject to claims that the use of some pediatric vaccines has caused personal injuries, including brain damage, central nervous system damage and autism, and these companies have incurred material costs to defend these claims. If we cannot successfully defend ourselves against product liability claims, we could incur substantial liabilities. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- decreased demand for our product candidates;
- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- inability to commercialize our products.

We have obtained product liability insurance coverage for our clinical trials, but our insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action lawsuits based on products that had unanticipated side effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our business.

Healthcare reform measures could hinder or prevent our products' commercial success.

In both the United States and certain foreign jurisdictions there have been, and we anticipate there will continue to be, a number of legislative and regulatory changes to the healthcare system that could impact our ability to sell any of our products

profitably. In the United States, the federal government enacted healthcare reform legislation, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA. Among the ACA's provisions of importance to the pharmaceutical industry are that it:

- imposed an annual excise tax of 2.3% on any entity that manufactures or imports medical devices offered for sale in the United States, with limited exceptions, although the effective rate paid may be lower. However, the 2020 federal spending package permanently eliminated, effective January 1, 2020, this ACA-mandated medical device tax;
- created an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;
- created new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for certain drugs and biologics that are inhaled, infused, instilled, implanted or injected;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expanded the entities eligible for discounts under the Public Health program;
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- established a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending that began on January 1, 2011; and
- created a licensure framework for follow on biologic products.

There have been executive, judicial, and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry qualifying health insurance coverage for all or part of a year. In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage, and, effective January 1, 2021, also eliminated the health insurer tax. On June 17, 2021 the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges, and the healthcare reform measures of the Biden administration will impact the ACA and our business. Additionally, 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. Further, Congress is considering additional health reform measures as part of the budget reconciliation process.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. On August 2, 2011, the Budget Control Act of 2011 was signed into law, which, among other things, included reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect through 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequester. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing,

review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that seek to implement several of the administration's proposals. As a result, the FDA released a final rule and guidance in September 2020, providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the Department of Health and Human Services, or 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 implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing the Trump administration's Most Favored Nation (MFN) executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the MFN model, on December 27, 2021, CMS published a final rule that rescinded the MFN model interim final rule. In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. Further, at the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. It is also possible that additional governmental action is taken in response to the COVID-19 pandemic.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to make and implement healthcare reforms may adversely affect:

- our ability to set a price we believe is fair for our products;
- our ability to generate revenues and achieve or maintain profitability;
- the availability of capital; and
- our ability to obtain timely approval of our products.

If we fail to comply with applicable healthcare regulations, we could face substantial penalties and our business, operations and financial condition could be adversely affected.

Certain federal, state, local and foreign healthcare laws and regulations pertaining to fraud and abuse, transparency, patients' rights, and privacy are applicable to our business. The laws that may affect our ability to operate include:

- the federal healthcare program Anti-Kickback Statute, which prohibits, among other things, people from soliciting, receiving or providing remuneration, directly or indirectly, to induce or reward either the referral of an individual, or ordering, or leasing of an item, good, facility or service, for which payment may be made by a federal healthcare program such as Medicare or Medicaid. The intent standard under the federal healthcare program Anti-Kickback Statute was amended by the ACA to a stricter standard such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. Further, the ACA codified case law that a claim including items or services resulting from a violation of the federal healthcare program Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- federal civil and criminal false claims laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- HIPAA, which prohibits, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal healthcare program Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and related regulations, which impose certain requirements relating to the privacy, security and transmission of individually identifiable health information on certain individuals and entities;

- the Physician Payments Sunshine Act, created under the ACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with certain exceptions, to report annually to CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), other healthcare professionals (such as physicians assistants and nurse practitioners) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members;
- the FDCA, which among other things, strictly regulates drug product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples;
- the U.S. Foreign Corrupt Practices Act, which, among other things, prohibits companies issuing stock in the U.S. from bribing foreign officials for government contracts and other business;
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state and local laws requiring the registration of pharmaceutical sales and medical representatives, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts; and
- additional state and local laws such as laws in California and Massachusetts, which mandate implementation of compliance programs, compliance with industry ethics codes, and spending limits, and other state and local laws, such as laws in Vermont, Maine, and Minnesota which require reporting to state governments of gifts, compensation, and other remuneration to physicians.

The shifting regulatory environment, along with the requirement to comply with multiple jurisdictions with different compliance and/or reporting requirements, increases the possibility that a company may run afoul of one or more laws.

We will be required to spend substantial time and money to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations. Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, which require strict compliance in order to offer protection, it is possible that governmental authorities may conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable healthcare laws. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, integrity and/or other oversight obligations, contractual damages, reputational harm, and the curtailment or restructuring of our operations. Any such penalties could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

Our business involves the use of hazardous materials and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our and our third-party manufacturers' activities involve the controlled storage, use and disposal of hazardous materials, including the components of our product candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In the event of an accident, state or federal authorities may curtail the use of these materials and interrupt our business operations. If we are subject to any liability as a result of our or our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected.

We have entered into collaborations with Chinese companies and conduct certain research and development activities in China. Uncertainties regarding the interpretation and enforcement of Chinese laws, rules and regulations, a trade war, political unrest or unstable economic conditions in China could materially adversely affect our business, financial condition and results of operations.

We conduct research and development activities in China through our collaboration with Advaccine, which is conducting and funding the Phase 2 trial of INO-4800 in China. In addition, we are party to a license and collaboration agreement with China-based company ApolloBio, pursuant to which ApolloBio has the exclusive right to develop and commercialize VGX-3100 in China, Hong Kong, Macao and Taiwan. The Chinese legal system is a civil law system based on written statutes. Unlike the common law system, prior court decisions may be cited for reference but have limited precedential value. In addition, the Chinese legal system is based in part on government policies and internal rules, some of which are not published on a timely basis or at all, and which may have a retroactive effect. As a result, we may not be aware of our violation of these policies and rules until after the occurrence of the violation. Any administrative and court proceedings in China may be protracted, resulting in substantial costs and diversion of resources and management attention. Because Chinese administrative and court authorities have significant discretion in interpreting and implementing statutory and contractual terms, it may be

more difficult to evaluate the outcome of administrative and court proceedings and the level of legal protection we enjoy than in more developed legal systems. Furthermore, we are exposed to the possibility of disruption of our research and development activities in the event of changes in the policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, a trade war could lead to increased costs for clinical materials that are manufactured in China. These interruptions or failures could also impede commercialization of our product candidates and impair our competitive position. Further, we may be exposed to fluctuations in the value of the local currency in China. These uncertainties may impede our ability to enforce the contracts we have entered into and our ability to continue our research and development activities and could materially and adversely affect our business, financial condition and results of operations.

Our employees, principal investigators, and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, and consultants. Misconduct by these parties could include intentional failures to comply with FDA regulations or the regulations applicable in the EU 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; or 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. Sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. 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 these 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.

Employee litigation and unfavorable publicity could negatively affect our future business.

Our employees may, from time to time, bring lawsuits against us regarding injury, creating a hostile work place, discrimination, wage and hour disputes, sexual harassment, or other employment issues. In recent years there has been an increase in the number of discrimination and harassment claims generally. Coupled with the expansion of social media platforms and similar devices that allow individuals access to a broad audience, these claims have had a significant negative impact on some businesses. Certain companies that have faced employment- or harassment-related lawsuits have had to terminate management or other key personnel, and have suffered reputational harm that has negatively impacted their business. If we were to face any employment-related claims, our business could be negatively affected.

Risks Related to Our Intellectual Property

It is difficult and costly to generate and protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent, trademark, trade secret, and other intellectual property protection relating to our electroporation equipment and product candidates, as well as successfully defending these intellectual property rights against third-party challenges.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. The laws and regulations regarding the breadth of claims allowed in biotechnology patents have evolved over recent years and continues to undergo review and revision, both in the United States and abroad. The biotechnology patent situation outside the United States can be even more uncertain depending on the country. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our licensed patents, our patents or in third-party patents, nor can we predict the likelihood of our patents surviving a patent validity challenge.

The degree of future protection for our intellectual property rights is uncertain, because legal decision-making can be unpredictable, thereby often times resulting in limited protection, which may not adequately protect our rights or permit us to gain or keep our competitive advantage, or resulting in an invalid or unenforceable patent. For example:

- we, or the parties from whom we have acquired or licensed patent rights, may not have been the first to file the underlying patent applications or the first to make the inventions covered by such patents;

- the named inventors or co-inventors of patents or patent applications that we have licensed or acquired may be incorrect, which may give rise to inventorship and ownership challenges;
- others may develop similar or alternative technologies, or duplicate any of our products or technologies that may not be covered by our patents, including design-arounds;
- pending patent applications may not result in issued patents;
- the issued patents covering our products and technologies may not provide us with any competitive advantages or have any commercial value;
- the issued patents may be challenged and invalidated, or rendered unenforceable;
- given the nature of the COVID-19 pandemic, governments in the United States or abroad may prevent us from enforcing patents on our vaccines, which could prevent us from excluding competitors from those markets;
- the issued patents may be subject to reexamination, which could result in a narrowing of the scope of claims or cancellation of claims found unpatentable;
- we may not develop or acquire additional proprietary technologies that are patentable;
- our trademarks may be invalid or subject to a third party's prior use; or
- our ability to enforce our patent rights will depend on our ability to detect infringement, and litigation to enforce patent rights may not be pursued due to significant financial costs, diversion of resources, and unpredictability of a favorable result or ruling.

We depend, in part, on our licensors and collaborators to protect a portion of our intellectual property rights. In such cases, our licensors and collaborators may be primarily or wholly responsible for the maintenance of patents and prosecution of patent applications relating to important areas of our business. If any of these parties fail to adequately protect these products with issued patents, our business and prospects would be harmed significantly.

We also may rely on trade secrets to protect our technology, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisors may unintentionally or willfully disclose our trade secrets to competitors. Enforcing a claim that a third-party entity illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we or our licensors fail to obtain or maintain patent protection or trade secret protection for our product candidates or our technologies, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and attain profitability.

From time to time, U.S. and other policymakers have proposed reforming the patent laws and regulations of their countries. In September 2011 the America Invents Act (the Act) was signed into law. The Act changed the current “first-to-invent” system to a system that awards a patent to the “first-inventor-to-file” for an application for a patentable invention. The Act also created a procedure to challenge newly issued patents in the patent office via post-grant proceedings and new inter parties reexamination proceedings. These changes may make it easier for competitors to challenge our patents, which could result in increased competition and have a material adverse effect on our product sales, business and results of operations. The changes may also make it harder to challenge third-party patents and place greater importance on being the first inventor to file a patent application on an invention.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time-consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Other companies may have or may acquire intellectual property rights that could be enforced against us. If they do so, we may be required to alter our technologies, pay licensing fees or cease activities. If our products or technologies infringe the intellectual property rights of others, they could bring legal action against us or our licensors or collaborators claiming damages and seeking to enjoin any activities that they believe infringe their intellectual property rights.

Because patent applications can take many years to issue, and there is a period when the application remains undisclosed to the public, there may be currently pending applications unknown to us or reissue applications that may later result in issued patents upon which our products or technologies may infringe. There could also be existing patents of which we are unaware that our products or technologies may infringe. In addition, if third parties file patent applications or obtain patents claiming products or technologies also claimed by us in pending applications or issued patents, we may have to participate in interference or derivation proceedings in the United States Patent and Trademark Office to determine priority or derivation of the invention. If third parties file oppositions in foreign countries, we may also have to participate in opposition proceedings in foreign tribunals to defend the patentability of our filed foreign patent applications.

If a third party claims that we infringe its intellectual property rights, it could cause our business to suffer in a number of ways, including:

- we may become involved in time-consuming and expensive litigation, even if the claim is without merit, the third party's patent is invalid or we have not infringed;
- we may become liable for substantial damages for past infringement if a court decides that our technologies infringe upon a third party's patent;
- we may be enjoined by a court to stop making, selling or licensing our products or technologies without a license from a patent holder, which may not be available on commercially acceptable terms, if at all, or which may require us to pay substantial royalties or grant cross-licenses to our patents; and
- we may have to redesign our products so that they do not infringe upon others' patent rights, which may not be possible or could require substantial investment or time.

If any of these events occur, our business could suffer and the market price of our common stock may decline.

We have not yet registered our trademarks in all of our potential markets, and failure to secure those registrations could adversely affect our business.

Our trademark applications may not be allowed for registration, and our registered trademarks may not be maintained or enforced. During trademark registration proceedings, we may receive rejections. Although we are 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 do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would.

Risks Related to an Investment in Our Common Stock

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, we cannot assure you that an active trading market for our shares will continue to be sustained. If an active market for our common stock is not sustained, it may be difficult for investors in our common stock to sell shares without depressing the market price for the shares or to sell the shares at all.

The price of our common stock has been and may continue to be volatile, and an investment in our common stock could decline substantially in value.

In light of our small size and limited resources, as well as the uncertainties and risks that can affect our business and industry, our stock price has been and may continue to be highly volatile and has been and may in the future be subject to substantial drops, with or even in the absence of news affecting our business. Period to period comparisons are not indicative of future performance. The following factors, which are not exhaustive, in addition to the other risk factors described in this report, and the potentially low volume of trades in our common stock, may have a significant impact on the market price of our common stock, some of which are beyond our control:

- developments concerning any research and development, clinical trials, manufacturing, and marketing efforts or collaborations, particularly developments concerning the prospects of INO-4800 as a potential vaccine candidate against COVID-19;
- fluctuating public or scientific interest in the potential for our vaccines or other product candidates to address COVID-19 or other diseases;
- our announcement of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- fluctuations in our operating results;
- announcements of technological innovations;
- new products or services that we or our competitors offer;
- changes in the structure of healthcare payment systems;
- the initiation, conduct and/or outcome of intellectual property and/or litigation matters;
- changes in financial or other estimates by securities analysts or other reviewers or evaluators of our business;
- conditions or trends in bio-pharmaceutical or other healthcare industries;
- regulatory developments in the United States and other countries;
- perceptions of gene-based therapy;
- changes in the economic performance and/or market valuations of other biotechnology and medical device companies;

- additions or departures of key personnel;
- sales or other transactions involving our common stock;
- changes in our capital structure;
- sales or other transactions by executive officers or directors involving our common stock;
- changes in accounting principles;
- global unrest including geopolitical risks emanating from countries such as Russia and China, terrorist activities, and economic and other external factors; and
- catastrophic weather and/or global disease pandemics, including COVID-19.

The stock market in general has recently experienced relatively large price and volume fluctuations, particularly in response to the COVID-19 pandemic. In particular, the market prices of securities of smaller biotechnology and medical device companies have experienced dramatic fluctuations that often have been unrelated or disproportionate to the operating results of these companies. Continued market fluctuations could result in extreme volatility in the price of our common stock, which could cause a decline in the value of our common stock. In addition, price volatility may increase if the trading volume of our common stock remains limited or declines.

We have broad discretion in the use of our cash, cash equivalents, and investments, and may not use them effectively.

Our management has broad discretion in the application of our cash, cash equivalents, and investments, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Furthermore, our operating expenses have significantly increased due to development and manufacturing activities for our COVID-19 vaccine program, and we may not deploy our expanded capital base effectively. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse impact on our business, cause the price of our common stock to decline, and delay the development of our investigational medicines. Pending their use, we may invest our cash, cash equivalents, and investments in a manner that does not produce income or that loses value.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock.

Our amended and restated certificate of incorporation contains provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- the authority of our board of directors to issue shares of undesignated preferred stock and to determine the rights, preferences and privileges of these shares, without stockholder approval;
- all stockholder actions must be effected at a duly called meeting of stockholders and not by written consent; and
- the elimination of cumulative voting.

In addition, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These and other provisions in our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors, including to delay or impede a merger, tender offer or proxy contest involving our company. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

We have never paid cash dividends on our common stock and we do not anticipate paying dividends in the foreseeable future.

We have paid no cash dividends on our common stock to date, and we currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, the terms of any future debt or credit facility may preclude or limit our ability to pay any dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of potential gain for the foreseeable future.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the revised Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage point change (by value) in the ownership of its equity by certain significant shareholders over a rolling three year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income and taxes may be limited. We may have experienced such ownership changes in the past, and we may experience ownership changes in the future as a result of shifts in our share ownership, some of which would be outside our control. If our ability to use our net operating losses and other tax attributes is limited by ownership changes, we may be unable to utilize a material portion of our net operating losses and other tax attributes to offset our future taxable income. In addition, there is also a risk that due to changes

in laws and regulations, including changes proposed or implemented by the current U.S. presidential administration, such as alternative minimum taxes or suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities.

General Risk Factors

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our electroporation equipment, product candidates or future development programs;
- expenses related to corporate transactions, including ones not fully completed;
- addition or termination of clinical trials or funding support;
- any intellectual property infringement lawsuit in which we may become involved;
- any legal claims that may be asserted against us or any of our officers;
- regulatory developments affecting our electroporation equipment and product candidates or those of our competitors;
- debt service obligations;
- changes in the fair value of our investments, including investments in affiliated entities;
- our execution of any collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements; and
- if any of our products receives regulatory approval, the levels of underlying demand for our products.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our results of operations and liquidity needs could be materially affected by market fluctuations and general economic conditions.

Our results of operations could be materially affected by economic conditions generally, both in the United States and elsewhere around the world. Concerns over inflation, energy costs, geopolitical issues, global pathogen outbreaks or pandemics, including COVID-19, and the availability and cost of credit have in the past and may continue to contribute to increased volatility and diminished expectations for the economy and the markets going forward. Market upheavals may have an adverse effect on us. In the event of a market downturn, our results of operations could be adversely affected. Our future cost of equity or debt capital and access to the capital markets could be adversely affected, and our stock price could decline. There may be disruption or delay in the performance of our third-party contractors and suppliers. If our contractors, suppliers and partners are unable to satisfy their contractual commitments, our business could suffer. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits, and we may experience losses on these deposits.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that equity research analysts publish about us and our business, and we have limited research coverage by equity research analysts. Equity research analysts may elect not to initiate or continue to provide research coverage of our common stock, and such lack of research coverage may adversely affect the market price of our common stock. Even if we have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our stock could decrease, which in turn could cause our stock price or trading volume to decline.

The issuance of additional stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other stockholders.

Our certificate of incorporation authorizes us to issue up to 600,000,000 shares of common stock and up to 10,000,000 shares of preferred stock with such rights and preferences as may be determined by our board of directors. Subject to compliance with applicable rules and regulations, we may issue our shares of common stock or securities convertible into our common stock from time to time in connection with a financing, acquisition, investment, our stock incentive plans or otherwise.

Any such issuance could result in substantial dilution to our existing stockholders and cause the trading price of our common stock to decline.

We incur significant costs and demands upon management as a result of being a public company.

As a public company listed in the United States, we incur significant legal, accounting and other costs that could negatively affect our financial results. In addition, changing laws, regulations and standards relating to corporate governance and public disclosure, including regulations implemented by the SEC and stock exchanges, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. We intend to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, on committees of our board of directors or as members of senior management.

Changes in tax laws could adversely affect our business and financial condition.

The tax regimes to which we are subject or under which we operate are unsettled and may be subject to significant change. In December 2017, tax legislation commonly known as the Tax Cuts and Jobs Act was enacted, which significantly revised the Internal Revenue Code of 1986, as amended, or the Code. The Tax Cuts and Jobs Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35 percent to a flat rate of 21 percent, limitation of the tax deduction for interest expense to 30 percent of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80 percent of current-year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits (including reducing the business tax credit for certain clinical testing expenses incurred in the testing of certain drugs for rare diseases or conditions). Notwithstanding the reduction in the corporate income tax rate, the overall impact of the federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the federal tax law. The issuance of additional regulatory or accounting guidance related to the Tax Act, or changes proposed or implemented by the current U.S. presidential administration or otherwise, could materially affect our tax obligations and effective tax rate.

The increasing use of social media platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our research, development candidates, investigational medicines, and the diseases our development candidates and investigational medicines are being developed to treat. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business, resulting in potential regulatory actions against us. For example, participants may use social media channels to comment on their experience in an ongoing blinded clinical trial or to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend our business or the public’s legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our development candidates and investigational medicines. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face regulatory actions, or incur other harm to our business.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We own no real property and have no plans to acquire any real property in the future.

San Diego Leases

In April 2013, we entered into a lease, or the First San Diego Lease, for office space in San Diego, California. The term of the First San Diego Lease commenced on December 1, 2013. The initial term of the First San Diego Lease is ten years, with an

option to extend the term by five years, subject to specified conditions. In June 2015, we amended the First San Diego Lease to increase the total leased space to 31,207 square feet and occupy the entire building. The commencement of the amended First San Diego Lease was in January 2016. As of December 31, 2021, rent payments under the First San Diego Lease include base rent with an annual increase of approximately 3 percent, and additional monthly fees to cover our share of certain facility expenses, including utilities, property taxes, insurance and maintenance. We had an option to terminate the First San Diego Lease on December 1, 2019, which we did not exercise.

In October 2016, we entered into an office lease, or the Second San Diego Lease, for a second property in San Diego, California. The total space under the Second San Diego Lease is approximately 51,000 square feet. We are using the facility for office, manufacturing and research and development purposes. The term of the Second San Diego Lease commenced on June 1, 2017. The initial term of the Second San Diego Lease is ten years, with a right to terminate on November 30, 2023, subject to specified conditions.

The base rent adjusts periodically throughout the term of the Second San Diego Lease. As of December 31, 2021, rent payments under the Second San Diego Lease include base rent with an annual increase of approximately 3 percent, and additional monthly fees to cover our share of certain facility expenses, including utilities, property taxes, insurance and maintenance. In addition, we have paid a security deposit of $95,000.

Plymouth Meeting Lease

In March 2014, we entered into a lease, or the Plymouth Meeting Lease, for our corporate headquarters in Plymouth Meeting, Pennsylvania. We occupied the space in June 2014. The initial term of the Plymouth Meeting Lease was 11.5 years, with a right to extend the term by five years, subject to specified conditions. We use the space for office purposes.

The base rent adjusts periodically throughout the term of the Plymouth Meeting Lease. As of December 31, 2021, rent payments under the Plymouth Meeting Lease include base rent with an annual increase of approximately 2 percent, and additional monthly fees to cover our share of certain facility expenses, including utilities, property taxes, insurance and maintenance. In addition, we have paid a security deposit of $49,000. In July 2015, we amended the Plymouth Meeting Lease to increase the total leased space to 27,583 square feet.

In June 2017, we entered into another amendment to the Plymouth Meeting Lease to increase the total leased space to 57,361 square feet and extend the lease term through December 31, 2029. In connection with this amendment, we paid the landlord an additional security deposit of $75,000.

In the fourth quarter of 2019, we entered into two agreements to sublease a total of approximately 13,500 square feet in our Plymouth Meeting headquarters through periods between December 31, 2022 and March 31, 2025.

We believe our current and future planned facilities will be adequate to meet our operating needs for the foreseeable future. Should we need additional space, we believe we will be able to secure additional space at commercially reasonable rates.

ITEM 3. LEGAL PROCEEDINGS

Securities Litigation

On March 12, 2020, a purported shareholder class action complaint, McDermid v. Inovio Pharmaceuticals, Inc. and J. Joseph Kim, was filed in the United States District Court for the Eastern District of Pennsylvania, naming us and J. Joseph Kim, our Chief Executive Officer, as defendants. The lawsuit alleges that we made materially false and misleading statements regarding our development of a vaccine for COVID-19 in our public disclosures in violation of certain federal securities laws. The plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including reasonable attorneys' fees. On June 18, 2020, the court appointed Manuel Williams to serve as lead plaintiff. On August 3, 2020, Mr. Williams filed a consolidated complaint, naming us and three of our officers as defendants. On September 21, 2020, Mr. Williams and another purported stockholder, Andrew Zenoff filed a first amended complaint, naming us and three of our officers as defendants. Defendants filed a motion to dismiss plaintiff's first amended complaint on November 5, 2020. On February 16, 2021, the court issued an order granting in part, and denying in part, Defendants' motion to dismiss. The court granted Defendants' motion to dismiss, and dismissed with prejudice, the claims premised on the April 30 and June 30, 2020 statements. The court denied Defendants' motion to dismiss as to the remaining statements. On March 9, 2021, Defendants filed their answer to the complaint. The case is currently in discovery. On July 29, 2021, Plaintiffs moved to certify the class action. That motion is fully briefed and remains pending. On February 17, 2022, the court granted Plaintiffs' motion for leave to amend their complaint, and further ordered that the amended complaint is deemed filed as of February 17. Defendants intend to move to dismiss the new allegations in the amended complaint.

On April 20, 2020, a purported shareholder derivative complaint, Behesti v. Kim, et al., was filed in the United States District Court for the Eastern District of Pennsylvania, naming eight current and former directors as defendants. The lawsuit asserts state and federal claims and is based on the same alleged misstatements as the shareholder class action complaint. The lawsuit accuses our board of directors of failing to exercise reasonable and prudent supervision over our management, policies,

practices, and internal controls. The plaintiff seeks unspecified monetary damages on behalf of us as well as governance reforms. On June 5, 2020, the court stayed the Beheshti action pending resolution of a forthcoming motion to dismiss the McDermid securities class action or until any party provides notice that they no longer consent to the stay. On June 12 and June 15, 2020, two additional shareholder derivative complaints were filed in the United States District Court for the Eastern District of Pennsylvania, captioned Isman v. Benito, et al. and Devarakonda et al. v Kim, et. al. The complaints assert substantially similar claims as the Beheshti action and name our current directors as defendants. The Devarakonda complaint also names one of our former directors as a defendant. On July 21, 2020, the court consolidated the three derivative cases under the caption In re Inovio Pharmaceuticals, Inc. Derivative Litigation. The consolidated action is stayed.

On July 7, 2020, a fourth shareholder derivative complaint, Fettig v. Kim et al., was filed in the United States District Court for the Eastern District of Pennsylvania, naming eight current and former directors as defendants. The complaint asserts substantially similar claims as those in the consolidated derivative action. On August 27, 2020, the Fettig action was consolidated with the other derivative cases, which remain stayed as explained above.

We intend to defend these actions vigorously.

VGXI Litigation

On June 3, 2020, we filed a complaint in the Court of Common Pleas of Montgomery County, Pennsylvania against VGXI, Inc. and GeneOne Life Science, Inc., or GeneOne, and together with VGXI, Inc. collectively referred to as VGXI, alleging that VGXI had materially breached our supply agreement with them. The complaint seeks declaratory judgments, specific performance of the agreement, injunctive relief, an accounting, damages, attorneys' fees, interest, costs and other relief from VGXI. On June 3, 2020, we filed a petition for preliminary injunction, which was denied on June 25, 2020. On June 26, 2020, we filed notice of appeal of the denial of the petition with the Pennsylvania Superior Court.

On July 7, 2020, VGXI filed an answer, new matter and counterclaims against us, alleging that we had breached the supply agreement, as well as misappropriation of trade secrets and unjust enrichment. The counterclaims seek injunctive relief, damages, attorneys' fees, interest, costs and other relief from us. Also, on July 7, 2020, VGXI filed a third-party complaint against Ology Bioservices, Inc., a contract manufacturing organization that we had engaged to provide services similar to those that were being provided by VGXI. On July 27, 2020, we filed an answer to VGXI's counterclaims, disputing the allegations and the claims raised in VGXI's filing. On October 1, 2020, we filed a notice of discontinuance of appeal with the Pennsylvania Superior Court. A trial date for the litigation has not been set.

We intend to aggressively prosecute the claims set forth in our complaint against VGXI and to vigorously defend ourselves against VGXI's counterclaims.

GeneOne Litigation

On December 7, 2020, GeneOne filed a complaint in the Court of Common Pleas of Montgomery County, Pennsylvania against us, alleging that we had breached the CELLECTRA Device License Agreement, or the Agreement, between us and GeneOne. We terminated the Agreement on October 9, 2020. The complaint asserts claims for breach of contract, declaratory judgment, unfair competition, and unjust enrichment. The complaint seeks injunctive relief, an accounting, damages, disgorgement of profits, attorneys' fees, interest, and other relief from us. On January 29, 2021, we filed preliminary objections to the complaint. On August 23, 2021, the Court overruled our preliminary objections to the complaint. On September 13, 2021, we filed an answer to the complaint, new matter, and counterclaims. The Company's counterclaims allege that GeneOne breached the Agreement, and assert claims for breach of contract and declaratory judgment. The counterclaims seek damages, interest, expenses, attorney's fees, and costs. On October 18, 2021, GeneOne filed its answer to our counterclaims and new matter. On November 8, 2021, we filed our answer to GeneOne's new matter. A trial date for this litigation has not been set.

We intend to aggressively prosecute the claims set forth in our counterclaims against GeneOne and to vigorously defend ourselves against the claims in GeneOne's complaint.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock, par value $0.001 per share, began trading on the Nasdaq Global Select Market on September 15, 2014 under the symbol "INO," having previously traded on the NYSE MKT exchange.

As of February 11, 2022, we had approximately 100 common stockholders of record. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

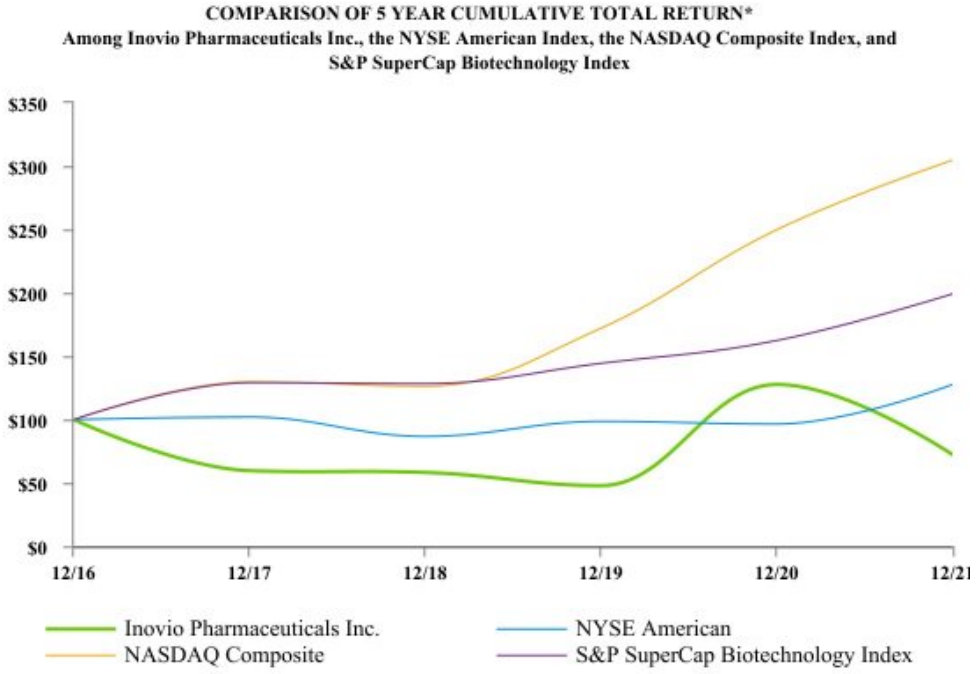
The closing price per share of our common stock on February 11, 2022 was $3.32, as reported on the Nasdaq Global Select Market.

Dividends

The payment of any dividends on our common stock is within the discretion of our board of directors. We have never paid cash dividends on our common stock and the board of directors does not expect to declare cash dividends on the common stock in the foreseeable future.

Performance Graph

The graph below compares the performance of our common stock with the performance of the NYSE American Index, the S&P SuperCap Biotechnology index and the Nasdaq Composite Index for the five years ended December 31, 2021. The graph assumes a $100 investment on December 31, 2016 in our common stock and in each index, with the reinvestment of all dividends, if any.



*$100 invested on 12/31/16 in stock or index, including reinvestment of dividends.
Fiscal year ended December 31.

	12/16	12/17	12/18	12/19	12/20	12/21
Inovio Pharmaceuticals, Inc.	100.00	59.51	57.64	47.55	127.52	71.90
NYSE American	100.00	101.61	86.60	97.92	95.85	127.23
Nasdaq Composite	100.00	129.64	125.96	172.17	249.51	304.85
S&P SuperCap Biotechnology Index	100.00	128.50	127.87	144.12	161.82	198.92

The stock price performance included in this graph is not necessarily indicative of future stock price performance. The performance graph is furnished solely to accompany this Form 10-K annual report and shall not be deemed to be incorporated by reference by means of any general statement incorporating by reference this Form 10-K into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that we specifically incorporate such information by reference, and shall not otherwise be deemed filed under such acts.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Parties

None.

ITEM 6. RESERVED

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This report contains forward-looking statements, as defined in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements relate to future events or our future financial performance. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential" or "continue," the negative of such terms or other comparable terminology. These statements are only predictions. Actual events or results may differ materially.

Although we believe that the expectations reflected in the forward-looking statements are reasonable based on our current expectations and projections, we cannot guarantee future results, levels of activity, performance or achievements. Moreover, neither we, nor any other person, assume responsibility for the accuracy and completeness of the forward-looking statements. We are under no obligation to update any of the forward-looking statements after the filing of this Annual Report to conform such statements to actual results or to changes in our expectations.

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes and other financial information appearing elsewhere in this Annual Report. Readers are also urged to carefully review and consider the various disclosures made by us which attempt to advise interested parties of the factors which affect our business, including without limitation the disclosures made in Item 1A of Part I of this Annual Report under the Caption "Risk Factors."

Risk factors that could cause actual results to differ from those contained in the forward-looking statements include but are not limited to: our history of losses; our lack of products that have received regulatory approval; uncertainties inherent in clinical trials and product development programs, including but not limited to the fact that pre-clinical and clinical results may not be indicative of results achievable in other trials or for other indications, that the studies or trials may not be successful or achieve desired results, that preclinical studies and clinical trials may not commence, have sufficient enrollment or be completed in the time periods anticipated, that results from one study may not necessarily be reflected or supported by the results of other similar studies, that results from an animal study may not be indicative of results achievable in human studies, that clinical testing is expensive and can take many years to complete, that the outcome of any clinical trial is uncertain and failure can occur at any time during the clinical trial process, and that our electroporation technology and DNA vaccines may fail to show the desired safety and efficacy traits in clinical trials; the availability of funding; the ability to manufacture vaccine candidates; the availability or potential availability of alternative therapies or treatments for the conditions targeted by us or our collaborators, including alternatives that may be more efficacious or cost-effective than any therapy or treatment that we and our collaborators hope to develop; our ability to receive development, regulatory and commercialization event-based payments under our collaborative agreements; whether our proprietary rights are enforceable or defensible or infringe or allegedly infringe on rights of others or can withstand claims of invalidity; and the impact of government healthcare laws and proposals.

Overview

We are a biotechnology company focused on bringing to market precisely designed DNA medicines and vaccines to help protect people from infectious diseases, including COVID-19, and to help treat people with cancer, and conditions associated with human papillomavirus ("HPV"). We have shown in clinical trials that our DNA vaccine candidates can be delivered into cells in the body via a proprietary smart device allowing the nucleic-acid delivered gene products to activate functional T cell and antibody responses against targeted pathogens and cancers.

Our DNA medicines pipeline is comprised of three types of product candidates: prophylactic DNA vaccines, therapeutic DNA immunotherapies, and DNA encoded monoclonal and bispecific antibodies ("dMAbs" and "dBTAs"), all of which utilize the two components of our integrated platform, SynCon® and CELLECTRA®.

Our proprietary SynCon® technology creates optimized plasmids, which are circular strands of DNA that instruct a cell to produce proteins or antigens to help the person's immune system respond with antibodies and immune cells which recognize and then help block viruses and destroy cancerous or pre-cancerous cells.

Our patented CELLECTRA nucleic-acid delivered gene products smart delivery devices facilitate uptake of our DNA medicines into the cell, which has been a key limitation of historical DNA-based technology approaches. Human clinical trial data from more than 15,000 CELLECTRA® smart device administrations across more than 5,000 participants to date have shown a tolerable safety profile.

Our corporate strategy is to develop, seek regulatory approval for and commercialize our novel DNA medicines to address unmet global health needs. We continue to advance and clinically validate an array of DNA medicine candidates that target infectious diseases, such as COVID-19, as well as HPV-associated diseases and cancer.

Our partners and collaborators include ApolloBio Corporation, AstraZeneca, Advaccine Biopharmaceuticals Suzhou Co, The Bill & Melinda Gates Foundation (Gates), Coalition for Epidemic Preparedness Innovations ("CEPI"), Defense Advanced Research Projects Agency ("DARPA"), The U.S. Department of Defense ("DoD"), HIV Vaccines Trial Network, the U.S. Defense Threat Reduction Agency's Medical CBRN Defense Consortium ("MCDC"), International Vaccine Institute ("IVI"), Kaneka Eurogentec, National Cancer Institute, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Ology Bioservices, the Parker Institute for Cancer Immunotherapy, Plumbline Life Sciences, Regeneron Pharmaceuticals, Richter-Helm BioLogics, Thermo Fisher Scientific, the University of Pennsylvania, the Walter Reed Army Institute of Research, and The Wistar Institute.

We or our collaborators are currently evaluating the feasibility of, conducting or planning clinical studies of our DNA medicines for COVID-19, which includes both homologous and heterologous boosting approaches; Middle East Respiratory Syndrome, or MERS; Lassa fever; Ebola; as well as HPV-associated precancers, including cervical, vulvar, and anal dysplasia; HPV-associated cancers, including head & neck, cervical, anal, penile, vulvar, and vaginal; other HPV-associated disorders, such as recurrent respiratory papillomatosis, or RRP; glioblastoma multiforme, or GBM; and prostate cancer.

All of our product candidates are in the research and development phase. We have not generated any revenues from the sale of any products, and we do not expect to generate any such revenues for at least the next several years. We earn revenue from license fees and milestone revenue and collaborative research and development agreements. Our product candidates will require significant additional research and development efforts, including extensive preclinical and clinical testing. All product candidates that we advance to clinical testing will require regulatory approval prior to commercial use, and will require significant costs for commercialization. We may not be successful in our research and development efforts, and we may never generate sufficient product revenue to be profitable.

As of December 31, 2021, we had an accumulated deficit of $1.2 billion. We expect to continue to incur substantial operating losses in the future due to our commitment to our research and development programs, the funding of preclinical studies, clinical trials and regulatory activities and the costs of general and administrative activities.

Impacts of COVID-19 on Our Business

Operationally, we have experienced some disruptions as a result of the COVID-19 pandemic. Our clinical trial operations have been adversely affected, including our ability to initiate and conduct our planned trials on our expected timelines and our ability to recruit and retain participants in our trials. Our data collection timelines have also been impacted, as an increasing number of trial participants are either not able or do not feel safe going into healthcare facilities, which is necessary for the collection and completion of data samples. As a result, it is taking longer than anticipated to complete the data collection process.

The COVID-19 pandemic has caused supply chain disruptions and supply shortages globally. As a result, we have experienced delays and disruptions in obtaining clinical supplies, manufacturing supplies and components, and have had to secure new vendors for certain supplies and components at higher prices. Some manufacturing supplies and components remain in limited supply with uncertain delivery dates.

In 2020, a number of governmental orders and other public health guidance measures were implemented across much of the United States, including in the locations of our offices, laboratories, clinical trial sites and third parties on whom we rely. We have implemented a work from home policy allowing employees who can work from home to do so, while those needing to work in laboratory facilities work in shifts to reduce the number of people gathered together at one time. We have also implemented a mask-wearing mandate for all on-site activities. Non-essential business travel has been suspended, and online and teleconference technology is used to meet virtually rather than in person. We have taken measures to secure our research and development project activities, while work in laboratories has been organized to reduce risk of COVID-19 transmission.

Our liquidity has also not been negatively impacted to date by the pandemic. During the years ended December 31, 2021 and 2020, we raised $47.7 million and $454.5 million, respectively, in net proceeds from the sale of shares of our common stock through "at-the-market" equity offering programs and in January 2021 we closed an underwritten public offering with net proceeds to us of $162.1 million, which further enhanced our liquidity and capital resources. As of December 31, 2021, our cash and cash equivalents and short-term investments were $401.3 million, compared to $411.6 million as of December 31, 2020.

We are continuing to closely monitor the impact of the COVID-19 pandemic on our employees, collaborators and service providers. The extent to which the pandemic will impact our business and operations will depend on future developments, including travel restrictions to, from and within the United States and other countries, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease, including mass vaccination efforts, that are highly uncertain. For additional information on the potential effects of the COVID-19 pandemic on our business, financial condition and results of operations, see the "Risk Factors" section above in Part I, Item 1A of this Form 10-K.

Critical Accounting Policies and Estimates

The SEC defines critical accounting policies as those that are, in management's view, important to the portrayal of our financial condition and results of operations and require management's judgment. Our discussion and analysis of our financial condition and results of operations are based on our audited consolidated financial statements, which have been prepared in accordance with U.S. GAAP. Our significant accounting policies are outlined in Note 2 to the Consolidated Financial Statements included in this Form 10-K.

The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue and expenses. We base our estimates on experience and on various assumptions that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from those estimates. We believe the following accounting policies to be critical to the judgements and estimates used in the preparation of our consolidated financial statements:

Collaboration Agreements and Revenue Recognition

We assess whether our collaboration agreements are subject to Accounting Standards Codification ("ASC") Topic 808: Collaborative Arrangements ("Topic 808") based on whether they involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of Topic 808 and we conclude that our collaboration partner is not a customer, we present such payments as a reduction of research and development expense. If payments from our collaboration partner to us represent consideration from a customer, then we account for those payments within the scope of Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers ("Topic 606").

We enter into collaborative arrangements with partners that typically include payment of one or more of the following: (i) license fees; (ii) product supply services; (iii) milestone payments related to the achievement of developmental, regulatory, or commercial goals; and (iv) royalties on net sales of licensed products. At contract inception, we assess the goods or services agreed upon within each contract and assess whether each good or service is distinct and determine those that are performance obligations. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

As part of the accounting for these arrangements, we must develop estimates and assumptions that require judgment of management to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligation. The standalone selling price may include items such as forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success. We evaluate each performance obligation to determine if it can be satisfied at a point in time or over time. In addition, variable consideration must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price. Differences in the allocation of the transaction price between delivered and undelivered performance obligations can impact the timing of revenue recognition but do not change the total revenue recognized under any agreement.

For collaboration arrangements that include license fees, we recognize revenues from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

For collaboration arrangements that include milestone payments (variable consideration), we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. This assessment is based on our past experience with our collaboration partner, market insight and partner communication. Milestone payments that are not within our or our collaboration partner's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. At the end of each subsequent reporting period, we re-evaluate the probability of achieving such milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration or other revenues and earnings in the period of adjustment and could be material.

For collaboration arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties relate, we recognize revenue in the period the underlying sales occur. To date, we have not recognized any royalty revenue resulting from any of our collaborative arrangements.

Research and Development Expenses - Clinical Trial Accruals

Our activities have largely consisted of research and development efforts related to developing electroporation delivery technologies, DNA vaccines, DNA immunotherapies and dMABs. For clinical trial expenses, judgements used in estimating accruals rely on estimates of total costs incurred based on participant enrollment, completion of studies and other events. Accrued clinical trial costs are subject to revisions as trials progress. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to research and development expense; however a modification in the protocol of a clinical trial or cancellation of a trial could result in a charge to our results of operations.

Recent Accounting Pronouncements

Information regarding recent accounting pronouncements is contained in Note 2 to the consolidated financial statements, included elsewhere in this report.

Results of Operations

The consolidated financial data for the years ended December 31, 2021, 2020 and 2019 is presented in the following table and the results of these periods are used in the discussion thereafter.

	Year Ended December 31,			Increase/(Decrease) 2021 vs. 2020		Increase/(Decrease) 2020 vs. 2019	
	2021	2020	2019	$	%	$	%
Revenues:							
Revenue under collaborative research and development arrangements, including from affiliated entities	$ 1,147,570	$ 6,624,316	$ 3,872,594	$ (5,476,746)	(83)%	$ 2,751,722	71 %
Other revenue, including from affiliated entities	627,188	786,904	239,336	(159,716)	(20)	547,568	229
Total revenues	1,774,758	7,411,220	4,111,930	(5,636,462)	(76)	3,299,290	80
Operating expenses:							
Research and development	249,240,324	94,245,436	88,017,319	154,994,888	164	6,228,117	7
General and administrative	53,752,353	37,247,828	27,203,156	16,504,525	44	10,044,672	37
Total operating expenses	302,992,677	131,493,264	115,220,475	171,499,413	130	16,272,789	14
Loss from operations	(301,217,919)	(124,082,044)	(111,108,545)	(177,135,875)	(143)	(12,973,499)	(12)
Interest income	3,363,080	3,311,846	2,605,981	51,234	2	705,865	27
Interest expense	(1,936,447)	(8,702,450)	(7,948,539)	6,766,003	(78)	(753,911)	9
Change in fair value of derivative liability	—	(75,670,977)	(1,763,652)	75,670,977	*	(73,907,325)	*
Gain (loss) on investment in affiliated entity	(553,570)	36,556,658	(3,090,557)	(37,110,228)	*	39,647,215	*
Net unrealized gain (loss) on available-for-sale equity securities	(3,222,838)	1,695,497	—	(4,918,335)	*	1,695,497	*
Other income (expense), net	343,371	(704,896)	496,200	1,048,267	*	(1,201,096)	*
Gain on deconsolidation of Geneos	—	4,121,075	—	(4,121,075)	*	4,121,075	*
Loss on extinguishment of convertible bonds	—	(8,177,043)	—	8,177,043	*	(8,177,043)	*
Gain on extinguishment of convertible senior notes	—	8,762,030	—	(8,762,030)	*	8,762,030	*
Net loss before income tax benefit	(303,224,323)	(162,890,304)	(120,809,112)	(140,334,019)	(86)	(42,081,192)	(35)
Income tax benefit	—	—	257,335	—	*	(257,335)	*
Share in net loss of Geneos	(434,387)	(4,584,610)	—	4,150,223	*	(4,584,610)	*
Net loss	(303,658,710)	(167,474,914)	(120,551,777)	(136,183,796)	81	(46,923,137)	39
Net loss attributable to non-controlling interest	—	1,063,757	1,192,558	(1,063,757)	(100)	(128,801)	(11)
Net loss attributed to Inovio Pharmaceuticals, Inc.	$ (303,658,710)	$ (166,411,157)	$ (119,359,219)	$ (137,247,553)	(82)%	$ (47,051,938)	(39)%

*Not meaningful

Comparison of Years Ended December 31, 2021 and 2020

Revenue

Revenue primarily consisted of revenues under collaborative research and development arrangements, including arrangements with affiliated entities for the years ended December 31, 2021 and 2020. Our year over year total revenue decreased $5.6 million, or 76%. The decrease in revenue was primarily due to revenue earned from Advaccine in connection with upfront and milestone payments, and milestone revenue earned from our affiliated entity Plumbline Life Sciences, Inc. ("PLS"), for the year ended December 31, 2020 that did not occur for the year ended December 31, 2021.

Research and Development Expenses

The $155.0 million increase in research and development expenses for the year ended December 31, 2021 as compared to 2020 was primarily due to increases of:

- $39.5 million in drug manufacturing, outside services and clinical study expenses related to INO-4800;
- $35.0 million in expenses related to manufacturing capacity access fees;
- $21.9 million related to the acquisition and installation of manufacturing equipment related to INO-4800;
- $13.6 million in engineering services and expensed equipment and inventory related to our CELLECTRA® 3PSP device array automation project;
- $12.8 million in expensed materials purchased in preparation for the manufacturing of INO-4800; and
- $12.1 million in employee and contractor compensation.

These increases were primarily offset by an increase in contra-research and development expense recorded from grant agreements of $6.2 million, among other variances.

Contributions received from current grant agreements and recorded as contra-research and development expense were $53.7 million and $47.5 million for the years ended December 31, 2021 and 2020, respectively. The increase year over year was primarily due to increases of $5.9 million, $3.6 million and $2.4 million earned from the DoD OTA Agreement, CEPI Lassa and MERS grant and reimbursements from Advaccine, respectively, partially offset by decreases of $3.2 million and $3.2 million, earned from CEPI and Gates, respectively, related to INO-4800 and device development activities, among other variances.

General and Administrative Expenses

The $16.5 million increase in general and administrative expenses for the year ended December 31, 2021 as compared to 2020 was primarily due to increases of:

- $5.3 million in employee and consultant stock-based compensation;
- $3.9 million in employee compensation;
- $2.7 million in insurance expenses; and
- $2.2 million in legal expenses.

The increase was also due to less contra-general and administrative expense recorded related to gain on foreign exchange of $2.8 million, among other variances.

Employee stock-based compensation cost is measured at the grant date, based on the fair value of the award, and is recognized as expense over the employee's requisite service period. Total employee stock-based compensation cost for the years ended December 31, 2021 and 2020 was $25.0 million and $14.5 million, of which $13.4 million and $8.0 million was included in research and development expenses and $11.6 million and $6.5 million was included in general and administrative expenses, respectively. The increase for 2021 compared to 2020 was primarily due to an increase in options granted and a higher weighted average grant date fair value for the awards granted in the first quarter of 2021 and grants vesting during the period.

Interest Income

The $51,000 increase in interest income for the year ended December 31, 2021 as compared to 2020 was primarily due to more interest earned on our higher balance of short-term investment holdings.

Interest Expense

The $6.8 million decrease in interest expense for the year ended December 31, 2021 as compared to 2020 was primarily due to less interest expense recorded from our convertible senior notes, or the Notes, due to the partial conversions of the Notes

into shares of our common stock in the third and fourth quarters of 2020 and the full conversion of the December 2019 Bonds into shares of our common stock in March 2021, as well as no interest expense recorded on our August 2019 Bonds due to their full conversion into shares of our common stock in August 2020.

Gain (Loss) on Investment in Affiliated Entity

The gain (loss) on investment in affiliated entity for the year ended December 31, 2021 was $(554,000) resulting from the change in the fair market value of our investment in PLS, and for the year ended December 31, 2020 was $36.6 million, resulting from the change in the fair market value of our investments in GeneOne and PLS. During the third quarter of 2020, we sold our full equity interest in GeneOne. We record our investment in PLS at its market value based on the closing price of the shares on the Korea New Exchange Market at each balance sheet date, with changes in fair value reflected in the consolidated statements of operations.

Net Unrealized Gain (Loss) on Available-for-Sale Equity Securities

The net unrealized gain (loss) on available-for-sale equity securities for the years ended December 31, 2021 and 2020 was $(3.2) million and $1.7 million, respectively, resulted from a change in the fair market value of the investments.

Share in Net Loss of Geneos

The share in net loss of Geneos represents our share of Geneos' losses during the period after deconsolidation in June 2020.

Income Taxes

Since inception, we have incurred operating losses and accordingly have not recorded a provision for U.S. income taxes for any of the periods presented. Utilization of net operating losses and tax credits are subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended, or IRC. As of December 31, 2021, we had net operating loss carry forwards for U.S. federal, California and Pennsylvania income tax purposes of $864.5 million, $146.5 million and $89.0 million, respectively, net of the net operating losses that will expire due to IRC Section 382 limitations. We also had U.S. federal and state research and development tax credits of $35.1 million and $4.4 million, respectively, net of the federal research and development credits that will expire due to IRC Section 383 limitations. The net operating losses and credits began to expire during 2021.

Comparison of Years Ended December 31, 2020 and 2019

For a comparison of the years ended December 31, 2020 and 2019, you may refer to Part II, Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the SEC on March 1, 2021.

Liquidity and Capital Resources

Historically, our primary uses of cash have been to finance research and development activities including clinical trial activities in the oncology, DNA vaccines and other immunotherapy areas of our business. Since inception, we have satisfied our cash requirements principally from proceeds from the sale of equity securities, indebtedness and grants and government contracts.

Working Capital and Liquidity

As of December 31, 2021, we had cash and short-term investments of $401.3 million and working capital of $382.7 million, as compared to $411.6 million and $429.5 million as of December 31, 2020, respectively.

Cash Flows

Operating Activities

Net cash used in operating activities was $215.7 million and $178.0 million for the years ended December 31, 2021 and 2020, respectively. The variance was primarily due to increased research and development expenses offset by the timing and changes in working capital balances.

Investing Activities

Net cash used in investing activities was $175.3 million and $58.8 million for the years ended December 31, 2021 and 2020, respectively. The variance was primarily the result of timing differences in short-term investment purchases, sales and maturities, offset by the proceeds from the sale of our investment in GeneOne in 2020 of $40.1 million. Our capital expenditures were $1.2 million and $1.5 million, respectively, and we do not expect our capital expenditure requirements to increase materially.

Financing Activities

Net cash provided by financing activities was $211.5 million and $465.3 million for the years ended December 31, 2021 and 2020, respectively. The decrease was primarily due to less proceeds from the sale of common stock under ATM sales agreements in 2021 compared to 2020, offset by the net proceeds from the January 2021 underwritten public offering.

Issuances of Common Stock

On November 9, 2021, we entered into an ATM Equity Offering℠ Sales Agreement (the "Sales Agreement") with outside sales agents (collectively, the "Sales Agents") under which we may offer and sell, from time to time at our sole discretion, shares of our common stock with aggregate gross proceeds of up to $300.0 million, through the Sales Agents.

Subject to the terms and conditions of the Sales Agreement, the Sales Agents may sell the common stock by any method permitted by law deemed to be an "at the market offering". The Sales Agents will use commercially reasonable efforts to sell the common stock from time to time, based upon instructions from us, including any price, time or size limits or other customary parameters or conditions we may impose. We will pay the Sales Agents a commission of up to three percent (3.0%) of the gross sales proceeds of any common stock sold through the Sales Agents under the Sales Agreement, and we have provided the Sales Agents with certain indemnification rights. During the year ended December 31, 2021, we sold 6,955,341 shares of common stock under the Sales Agreement for aggregate net proceeds of $47.7 million.

On January 25, 2021, we closed an underwritten public offering of 20,355,000 shares of our common stock at a public offering price of $8.50 per share. The net proceeds, after deducting the underwriters' discounts and commissions and other estimated offering expenses payable by us, were $162.1 million.

In May 2018, we entered into an At-the-Market Equity Offering Sales Agreement, or the 2018 Sales Agreement, with an outside placement agent, or the Placement Agent, to sell shares of our common stock with aggregate gross proceeds of up to $100.0 million, from time to time, through an "at-the-market" equity offering program under which the Placement Agent would act as sales agent. In the first quarter of 2020, we entered into amendments to the 2018 Sales Agreement to increase the amount of our common stock that could be sold through the Placement Agent under the 2018 Sales Agreement to an aggregate offering price of up to $250.0 million. During the three months ended March 31, 2020, we sold 43,148,952 shares of common stock under the 2018 Sales Agreement for aggregate net proceeds of $208.2 million. Following these sales, there was no remaining capacity under the 2018 Sales Agreement.

On April 3, 2020, we entered into a sales agreement, or the 2020 Sales Agreement, with the same Placement Agent to sell shares of our common stock. On that same day, we filed a prospectus supplement for the offer and sale of our common stock pursuant to the 2020 Sales Agreement for aggregate gross proceeds of up to $150.0 million. On May 12, 2020 we filed an additional prospectus supplement for the offer and sale of our common stock pursuant to the 2020 Sales Agreement for an additional $100.0 million of gross proceeds, bringing the maximum gross proceeds of sales under the 2020 Sales Agreement to $250.0 million. Through December 31, 2020, we sold 22,915,934 shares of common stock under the 2020 Sales Agreement for aggregate net proceeds of $246.2 million. On November 8, 2021, we terminated the 2020 Sales Agreement.

During the year ended December 31, 2021, stock options to purchase 1,310,263 shares of common stock were exercised for aggregate net proceeds of $6.7 million, which proceeds were offset by tax payments made related to net share settlement of RSU awards of $4.6 million. During the year ended December 31, 2020, stock options to purchase 2,178,252 shares of common stock were exercised for aggregate net proceeds of $12.3 million, which proceeds were offset by tax payments made related to net share settlement of RSU awards of $4.0 million. During the year ended December 31, 2019, stock options to purchase 42,969 shares of common stock were exercised for aggregate net proceeds of $113,000, which proceeds were offset by tax payments made related to net share settlement of RSU awards of $893,000.

As of December 31, 2021, we had an accumulated deficit of $1.2 billion and we expect to continue to operate at a loss for some time. The amount of the accumulated deficit will continue to increase, as it will be expensive to continue research and development efforts. These activities will require additional financing. If these activities are successful and if we receive approval from the FDA to market our product candidates, then we will need to raise additional funding to market and sell the approved products and equipment. We cannot predict the outcome of the above matters at this time. We are evaluating potential collaborations as an additional way to fund operations. We believe that our current cash and short-term investments are sufficient to meet our planned working capital requirements for at least the next twelve months from the date of this report.

Contractual Obligations

As of December 31, 2021, future minimum payments due under our contractual obligations are set forth in the table below. We expect to be able to satisfy these obligations, both in the short-term and in the longer-term, with cash on hand and proceeds from sales of our common stock under the Sales Agreement.

	Payments Due by Period				
	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
Convertible senior notes (1)	$ 19,082,000	$ 1,067,000	$ 1,067,000	$ 16,948,000	$ —
Operating lease obligations (2)	$ 24,175,000	$ 4,085,000	$ 7,139,000	$ 6,202,000	$ 6,749,000
Manufacturing commitments (3)	$ 47,427,000	$ 47,427,000	$ —	$ —	$ —

(1) Amounts represent remaining contractual amounts due under our Notes, including interest based on the fixed rate of 6.5% per year. Although these Notes mature in March 2024, they may be converted into shares of our common stock prior to maturity if certain conditions are met. We may also redeem the Notes prior to their maturity if certain conditions are met. Any redemption prior to maturity would result in repayments of the principal amounts sooner than the scheduled repayments as indicated in the table. See Note 9, "Convertible Debt" in the Consolidated Financial Statements section of this report for further discussion.

(2) We have entered into operating leases for our facilities, which expire from 2023 to 2029, and operating leases for office equipment, which expire in 2024. In the fourth quarter of 2019, we entered into two subleases for a portion of our Plymouth Meeting corporate headquarters facility through December 31, 2022 and March 31, 2025. As of December 31, 2021, we expect to receive aggregate future minimum lease payments totaling $814,000 (non-discounted) over the duration of the sublease agreements, which expected payments are not included in the table above.

(3) We have entered into agreements with contract manufacturers for INO-4800 that contain minimum purchase requirements by us in 2022.

In the normal course of business, we are a party to a variety of agreements pursuant to which we may be obligated to indemnify the other party. It is not possible to predict the maximum potential amount of future payments under these types of agreements due to the conditional nature of our obligations and the unique facts and circumstances involved in each particular agreement. Historically, payments made by us under these types of agreements have not had a material effect on our business, consolidated results of operations or financial condition.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risk

Market risk represents the risk of loss that may impact our consolidated financial position, results of operations or cash flows due to adverse changes in financial and commodity market prices and rates. We are exposed to market risk primarily in the area of changes in United States interest rates and conditions in the credit markets, and the recent fluctuations in interest rates and availability of funding in the credit markets primarily impact the performance of our investments. We do not have any material foreign currency or other derivative financial instruments. Under our current policies, we do not use interest rate derivative instruments to manage exposure to interest rate changes. We attempt to increase the safety and preservation of our invested principal funds by limiting default risk, market risk and reinvestment risk. We mitigate default risk by investing in investment grade securities. Due to the short-term maturities of our cash equivalents and the low risk profile of our investments at December 31, 2021, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

The interest rate on our indebtedness is fixed and not subject to fluctuations in interest rates.

Fair Value Measurements

The investment in affiliated entity at December 31, 2021 represents our ownership interest in the Korean-based company PLS. We report this investment at fair value on the consolidated balance sheet using the closing price of PLS shares of common stock as reported on the date of determination on the Korea New Exchange Market.

Foreign Currency Risk

We have operated primarily in the United States and most transactions during the year ended December 31, 2021 were made in United States dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations, with the exception of certain cash and cash equivalents held in South Korea that are denominated in South Korean Won and the valuation of our equity investment in PLS, which is denominated in South Korean Won and then translated into United States dollars. We do not have any foreign currency hedging instruments in place.

Certain transactions are denominated primarily in foreign currencies, including South Korean Won, Euros, British Pounds and Canadian Dollars. These transactions give rise to monetary assets and liabilities that are denominated in currencies other than the U.S. dollar. The value of these monetary assets and liabilities are subject to changes in currency exchange rates from

the time the transactions are originated until settlement in cash. As a result, our financial results could be affected by factors such as changes in foreign currency exchange rates or weak economic conditions in foreign markets where we conduct business.

We do not use derivative financial instruments for speculative purposes and do not engage in exchange rate hedging or hold or issue foreign exchange contracts for trading purposes.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is incorporated by reference to our Consolidated Financial Statements and the Report of Independent Registered Public Accounting Firm beginning at page F-1 of this report.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures, which are designed to ensure that information required to be disclosed in the reports we file or submit under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer, or CEO, and Chief Financial Officer, or CFO, as appropriate to allow timely decisions regarding required disclosures.

In designing and evaluating our disclosure controls and procedures, management recognizes that disclosure controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the disclosure controls and procedures are met. Additionally, in designing disclosure controls and procedures, our management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible disclosure controls and procedures. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a control system, misstatements due to error or fraud may occur and not be detected.

Based on an evaluation carried out as of the end of the period covered by this Annual Report, under the supervision and with the participation of our management, including our CEO and CFO, our CEO and CFO have concluded that, as of the end of such period, our disclosure controls and procedures (as defined in Rule 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934) were effective as of December 31, 2021 at the reasonable assurance level.

Internal Control Over Financial Reporting

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934. Our internal control over financial reporting is a process designed under the supervision of our Chief Executive Officer and Chief Financial Officer to provide reasonable assurance regarding the reliability of financial reporting and the preparation of our financial statements for external purposes in accordance with United States generally accepted accounting principles.

As of December 31, 2021, management, with the participation of the Chief Executive Officer and Chief Financial Officer, assessed the effectiveness of our internal control over financial reporting based on the criteria for effective internal control over financial reporting established in "Internal Control—Integrated Framework," issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on the assessment, management determined that we maintained effective internal control over financial reporting as of December 31, 2021.

Changes in Internal Control over Financial Reporting

There have not been any changes in our internal control over financial reporting that occurred during the fourth quarter of our fiscal year ended December 31, 2021, that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Attestation Report of Independent Registered Public Accounting Firm

The independent registered public accounting firm that audited the consolidated financial statements that are included in this Annual Report on Form 10-K has issued an audit report on the effectiveness of our internal control over financial reporting as of December 31, 2021. The report appears below.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Inovio Pharmaceuticals, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Inovio Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission 2013 framework (the COSO criteria). In our opinion, Inovio Pharmaceuticals, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2021, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2021 and related notes and our report dated March 1, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for designing, implementing, and maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process effected by those charged with governance, management, and other personnel, designed to provide reasonable assurance regarding the preparation of reliable financial statements in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and those charged with governance; and (3) provide reasonable assurance regarding prevention, or timely detection and correction of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent, or detect and correct, misstatements. Also, projections of any assessment of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

San Diego, California
March 1, 2022

ITEM 9B. OTHER INFORMATION

On February 24, 2022, our Board of Directors adopted resolutions (the "Resolutions") ratifying pursuant to Section 204 of the Delaware General Corporation Law (the "Ratification") the grant to employees of certain options to purchase common stock and restricted stock units (collectively, the "Grants"). The Board has determined that the Grants were defective corporate acts because they did not fully comply with the requirements of Section 157(c) of the Delaware General Corporation Law. A copy of the Resolutions adopted by the Board setting forth the information with respect to the Ratification required under Section 204 of the Delaware General Corporation Law is attached hereto as Exhibit 99.1. Any claim that the defective corporate acts (including all options and restricted stock units and putative common stock issued upon the exercise of such options or the settlement of such restricted stock unit awards) identified in the Resolutions are void or voidable due to the failure of authorization, or any claim that the Court of Chancery of the State of Delaware should declare in its discretion that the Ratification not be effective or be effective only on certain conditions, must be brought within 120 days from the date of the filing of this Annual Report. For additional detail of the relevant statutory provisions refer to Sections 157, 204 and 205 of the Delaware General Corporation Law.

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item 10 is hereby incorporated by reference from our definitive proxy statement, to be filed pursuant to Regulation 14A within 120 days after the end of our 2021 fiscal year, under the captions "Election of Directors" and "Executive Officers and Other Information."

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item 11 is hereby incorporated by reference from our definitive proxy statement, to be filed pursuant to Regulation 14A within 120 days after the end of our 2021 fiscal year, under the captions "Compensation Discussion and Analysis," "Executive Compensation," "Compensation of Directors" and "Director Compensation Table."

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this Item 12 is hereby incorporated by reference from our definitive proxy statement, to be filed pursuant to Regulation 14A within 120 days after the end of our 2021 fiscal year, under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information."

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Director independence and other information required by this Item 13 is hereby incorporated by reference from our definitive proxy statement, to be filed pursuant to Regulation 14A within 120 days after the end of our 2021 fiscal year, under the captions "Certain Relationships and Related Party Transactions" and "Election of Directors."

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item 14 is hereby incorporated by reference from our definitive proxy statement, to be filed pursuant to Regulation 14A within 120 days after the end of our 2021 fiscal year, under the caption "Ratification of Appointment of Registered Public Accounting Firm."

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Financial Statements

   Consolidated financial statements required to be filed hereunder are indexed on Page F-1 hereof.

2. Financial Statement Schedules

   Schedules not listed herein have been omitted because the information required to be set forth therein is not applicable or is included in the Financial Statements or notes thereto.

3. Exhibits

   The following exhibits are filed as part of this annual report on Form 10-K:

Exhibit Number	Description of Document
3.1	Certificate of Incorporation with all amendments (incorporated by reference to Exhibit 3.1 of the registrant's Form S-3 registration statement, filed on July 23, 2014).
3.2	Amended and Restated Bylaws of Inovio Pharmaceuticals, Inc. dated August 10, 2011 (incorporated by reference to Exhibit 3.2 to the registrant's Form 8-K current report filed on August 12, 2011).
4.1	Indenture, dated as of February 19, 2019, by and between the registrant and U.S. Bank National Association, as trustee (incorporated by reference to Exhibit 4.1 to the registrant's current report on Form 8-K filed with the SEC on February 20, 2019).
4.2	Form of Note representing the registrant's 6.50% Convertible Senior Notes due 2024 (included as Exhibit A to the Indenture filed as Exhibit 4.1).
4.3	Description of the Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended (incorporated by reference to Exhibit 4.9 to the registrant's annual report on Form 10-K filed with the SEC on March 12, 2020).
10.1†	R&D Alliance Agreement dated December 19, 2005 by and between Ganial Immunotherapeutics, Inc. and VGX Pharmaceuticals, Inc., as amended by Novation and Amendment Agreement by and between VGX Pharmaceuticals, Inc., Ganial Immunotherapeutics, Inc., and Onconox (incorporated by reference to Exhibit 10.31 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.2†	R&D Collaboration and License Agreement dated December 18, 2006 by and between VGX International, Inc. and VGX Pharmaceuticals, Inc., as amended by First Amendment dated October 31, 2007 and as amended by Second Amendment dated August 4, 2008 (incorporated by reference to Exhibit 10.39 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.3†	Patent License Agreement dated April 27, 2007 by and between The Trustees of the University of Pennsylvania and VGX Pharmaceuticals, Inc., as amended by First Amendment dated June 12, 2008 (incorporated by reference to Exhibit 10.50 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.4†	License Agreement dated May 9, 2007 by and between Baylor University and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.34 as filed with the registrant's registration statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.5	ATM Equity Offering℠ Sales Agreement dated November 9, 2021 by and among Inovio Pharmaceuticals, Inc., BofA Securities, Inc., RBC Capital Markets, LLC and Oppenheimer & Co. Inc. (incorporated by reference to Exhibit 10.1 as filed with the registrants Form 10-Q quarterly report for the quarter ended September 30, 2021 filed on November 9, 2021).
10.6†	License and Collaboration Agreement dated March 24, 2010 between Inovio Pharmaceuticals, Inc. and VGX International, Inc. (incorporated by reference to Exhibit 10.2 as filed with the registrant's Form 10-Q quarterly report for the quarter ended March 31, 2010 filed on May 17, 2010).

10.7†	Collaborative Development and License Agreement dated October 7, 2011 between VGX International, Inc. and Inovio Pharmaceuticals, Inc., as amended by First Amendment dated August 21, 2013, and Second Amendment dated October 7, 2013 (incorporated by reference to Exhibit 10.1 as filed with the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2011 filed on November 7, 2011).
10.8	Collaborative Research Agreement dated March 14, 2016 by and between The Wistar Institute of Anatomy and Biology, a Commonwealth of Pennsylvania nonprofit corporation, and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 as filed with the registrant's Form 10-Q quarterly report for the quarter ended March 31, 2016 filed on May 9, 2016).
10.9	Collaborative Research Agreement dated March 14, 2016 by and between The Wistar Institute of Anatomy and Biology, a Commonwealth of Pennsylvania nonprofit corporation, and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.2 as filed with the registrant's Form 10-Q quarterly report for the quarter ended March 31, 2016 filed on May 9, 2016).
10.10†	Amended and Restated License and Collaboration Agreement, dated December 29, 2017, by and between Inovio Pharmaceuticals, Inc. and Beijing Apollo Saturn Biological Technology Limited (incorporated by reference to Exhibit 10.12 as filed with the registrant's Form 10-K annual report for the year ended December 31, 2017 filed on March 14, 2018).
10.11††	Other Transaction Authority For Prototype Agreement dated June 22, 2020 between Inovio Pharmaceuticals, Inc. and Natick Contracting Division (incorporated by reference to Exhibit 10.1 as filed with the registrant's Form 10-Q quarterly report for the quarter ended June 30, 2020 filed on August 10, 2020).
10.12††	Award Agreement dated June 18, 2020 between Inovio Pharmaceuticals, Inc. and Natick Contracting Division (incorporated by reference to Exhibit 10.2 as filed with the registrant's Form 10-Q quarterly report for the quarter ended June 30, 2020 filed on August 10, 2020).
10.13††	Amended and Restated Collaboration and License Agreement dated June 7, 2021 between Inovio Pharmaceuticals, Inc. and Advaccine Biopharmaceuticals Suzhou Co., Ltd. (incorporated by reference to Exhibit 10.1 as filed with the registrants Form 10-Q quarterly report for the quarter ended June 30, 2021 filed on August 9, 2021).
10.14	Lease dated April 9, 2013 by and between BMR-Wateridge LP and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to registrant's quarterly report for the quarter ended March 31, 2013, filed on May 10, 2013).
10.15	Lease Agreement dated as of March 5, 2014 between Brandywine Operating Partnership L.P. and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.36 as filed with the registrant's Form 10-K annual report for the year ended December 31, 2014 filed on March 17, 2014).
10.16	Office Lease Agreement dated October 10, 2016 by and between 6759 Mesa Ridge Road Holdings, LLC and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 as filed with the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2016 filed on November 9, 2016).
10.17	Sublease dated June 21, 2017 between Accolade, Inc. and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.2 as filed with the registrant's Form 10-Q quarterly report for the quarter ended June 30, 2017 filed on August 8, 2017).
10.18	Second Amendment to the Lease Agreement dated June 22, 2017 between Brandywine Operating Partnership, L.P. and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 as filed with the registrant's Form 10-Q quarterly report for the quarter ended June 30, 2017 filed on August 8, 2017).
10.19+	Employment Agreement dated March 31, 2008 by and between J. Joseph Kim, Ph.D. and VGX Pharmaceuticals, Inc., as amended by First Amendment of Employment Agreement dated March 31, 2008 (incorporated by reference to Exhibit 10.43 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.20+	First Amendment to Employment Agreement dated as of December 31, 2012 between Inovio Pharmaceuticals, Inc. and J. Joseph Kim, PhD. (incorporated by reference to Exhibit 10.41 of the registrant's Form 10-K annual report for the year ended December 31, 2012 filed on March 18, 2013).

10.21+	Employment Agreement dated as of December 27, 2010 between Inovio Pharmaceuticals, Inc. and Peter Kies (incorporated by reference to Exhibit 10.5 to the registrant's Form 10-K report for the year ended December 31, 2010 filed on March 16, 2011).
10.22+	First Amendment to Employment Agreement dated as of December 31, 2012 between Inovio Pharmaceuticals, Inc. and Peter Kies (incorporated by reference to Exhibit 10.42 of the registrant's Form 10-K annual report for the year ended December 31, 2012 filed on March 18, 2013).
10.23+	Second Amendment to Employment Agreement dated November 7, 2014 by and between Inovio Pharmaceuticals, Inc. and Peter Kies (incorporated by reference to Exhibit 10.2 of the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2014 filed on November 10, 2014).
10.24+	Employment Agreement dated March 8, 2019 between Inovio Pharmaceuticals, Inc. and Jacqueline E. Shea (incorporated by reference to Exhibit 10.26 of the registrant's Form 10-K annual report for the year ended December 31, 2019 filed on March 12, 2020).
10.25+	Employment Agreement dated as of March 4, 2019 between Inovio Pharmaceuticals, Inc. and Laurent M. Humeau (incorporated by reference to Exhibit 10.27 of the registrant's Form 10-K annual report for the year ended December 31, 2019 filed on March 12, 2020).
10.26+	Form of Indemnification Agreement for Directors and Officers of Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 to the registrant's Form 10-Q quarterly report for the quarterly period ended June 30, 2009, filed on August 19, 2009).
10.27+	Amended and Restated 2007 Omnibus Incentive Plan, as amended (incorporated by reference to Exhibit 10.12 to the registrant's Form 10-K report for the year ended December 31, 2015 filed on March 14, 2016).
10.28+	Form of Incentive and Non-Qualified Stock Option Grants under the 2007 Omnibus Stock Incentive Plan (incorporated by reference to Exhibit 4.4 to the registrant's Registration Statement on Form S-8 filed on May 14, 2007).
10.29+	Inovio Pharmaceuticals, Inc. 2016 Omnibus Incentive Plan, as amended to date (incorporated by reference to Exhibit 10.1 to the registrant's Form 8-K filed on May 10, 2019).
10.30+	Form of Incentive Stock Option Agreement under 2016 Omnibus Incentive Plan (incorporated by reference to Exhibit 10.55 as filed with the registrant's Form 10-K annual report for the year ended December 31, 2016 filed on March 15, 2017.)
10.31+	Form of Nonqualified Stock Option Agreement under 2016 Omnibus Incentive Plan (incorporated by reference to Exhibit 10.56 as filed with the registrant's Form 10-K annual report for the year ended December 31, 2016 filed on March 15, 2017.)
10.32+	Form of Restricted Stock Units Award Agreement under 2016 Omnibus Incentive Plan (incorporated by reference to Exhibit 10.54 as filed with the registrant's Form 10-K annual report for the year ended December 31, 2016 filed on March 15, 2017.)
21.1	Subsidiaries of the registrant (filed herewith).
23.1	Consent of Independent Registered Public Accounting Firm (filed herewith).
24.1	Power of Attorney (included on signature page).
31.1	Certification of the Principal Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).
31.2	Certification of the Principal Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 (filed herewith).

32.1^	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (furnished herewith).
99.1	Resolutions adopted by the Board of Directors Ratifying Option and Restricted Stock Unit Grants (filed herewith)
101.INS	XBRL Instance Document (the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document).
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

+ Designates management contract, compensatory plan or arrangement.

† Confidential treatment has been granted for certain portions omitted from this exhibit (indicated by asterisks) pursuant to Rule 24b-2 under the Securities Exchange Act of 1934, as amended. The confidential portions of this exhibit have been separately filed with the Securities and Exchange Commission.

†† Certain confidential portions of this exhibit (indicated by asterisks) were omitted because the identified confidential portions are not material and are of the type that the registrant treats as private or confidential.

^ These certifications are being furnished solely to accompany this Annual Report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any filing of the registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

ITEM 16. FORM 10-K SUMMARY

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on March 1, 2022.

Inovio Pharmaceuticals, Inc.

By: /s/ J. JOSEPH KIM

J. Joseph Kim
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints J. Joseph Kim and Peter Kies, and each of them severally, his or her true and lawful attorney-in-fact with power of substitution and resubstitution to sign in his or her name, place and stead, in any and all capacities, to do any and all things and execute any and all instruments that such attorney may deem necessary or advisable under the Securities Exchange Act of 1934 and any rules, regulations and requirements of the United States Securities and Exchange Commission in connection with the Annual Report on Form 10-K and any and all amendments hereto, as fully for all intents and purposes as he or she might or could do in person, and hereby ratifies and confirms all said attorneys-in-fact and agents, each acting alone, and his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ J. JOSEPH KIM **J. Joseph Kim**	President, Chief Executive Officer and Director (Principal Executive Officer)	March 1, 2022
/s/ SIMON X. BENITO **Simon X. Benito**	Chairman of the Board of Directors	March 1, 2022
/s/ PETER KIES **Peter Kies**	Chief Financial Officer (Principal Accounting Officer and Principal Financial Officer)	March 1, 2022
/s/ ROGER DANSEY **Roger Dansey**	Director	March 1, 2022
/s/ ANN MILLER **Ann Miller**	Director	March 1, 2022
/s/ JAY SHEPARD **Jay Shepard**	Director	March 1, 2022
/s/ DAVID WEINER **David Weiner**	Director	March 1, 2022
/s/ WENDY YARNO **Wendy Yarno**	Director	March 1, 2022
/s/ LOTA ZOTH **Lota Zoth**	Director	March 1, 2022

INOVIO PHARMACEUTICALS, INC.

Index to Consolidated Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Inovio Pharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Inovio Pharmaceuticals, Inc. (the "Company") as of December 31, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 1, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the US federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures include examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Accrual of Clinical Trial Expenses

Description of the Matter	During 2021, the Company incurred $249.2 million for research and development expenses and as of December 31, 2021 accrued $10.3 million for clinical study costs. A substantial portion of the Company' ongoing research and development activities are conducted by third-party service providers, including clinical research organizations ("CROs"). External costs to be paid to CROs are accrued and expensed based upon actual work completed in accordance with signed agreements. Auditing management's accounting for accrued clinical study costs is especially challenging because the evaluation is dependent upon a high-volume of data and input exchanged between clinical personnel and third-party service providers, such as the number of sites activated, the number of patients enrolled, and t number of patient visits, which is tracked in spreadsheets and other end user computing programs.
How We Addressed the Matter in our Audit	We obtained an understanding, evaluated the design and tested the operating effectiveness of controls ov the accounting for accrued clinical trial expenses. For example, we tested controls over management's assessment and measurement of estimated accrued clinical study costs, including patient enrollment and total cost incurred to date from third-parties. To test the completeness of the Company's accrued clinical trial expenses, we obtained from third-partie confirmation of patient enrollment and direct service cost to date for significant clinical trials. We attend internal clinical trial and project status meetings with accounting personnel and the clinical project mana to understand the status of significant clinical trial activities. To assess the appropriate measurement of accrued clinical trial expenses, we inspected key terms, timelines of completion, activities and costs for a sample of vendor contracts, including amendments, and compared these to management's analyses used tracking the progress of service agreements. We also tested a sample of subsequent payments by agreein the invoice to the original accrual and the invoice payments to bank statements.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2002.

San Diego, California
March 1, 2022

Inovio Pharmaceuticals, Inc.

CONSOLIDATED BALANCE SHEETS

	December 31,	
	2021	**2020**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 71,143,778	$ 250,728,118
Short-term investments	330,170,940	160,914,935
Accounts receivable	5,466,850	18,559,967
Accounts receivable from affiliated entities	2,565,194	503,782
Prepaid expenses and other current assets	38,836,991	40,357,456
Prepaid expenses and other current assets from affiliated entities	261,192	106,432
Total current assets	448,444,945	471,170,690
Fixed assets, net	17,453,206	11,348,144
Investments in affiliated entity	3,906,796	4,460,366
Investment in Geneos	—	434,387
Intangible assets, net	2,626,355	3,146,770
Goodwill	10,513,371	10,513,371
Operating lease right-of-use assets	11,571,026	12,741,296
Other assets	1,425,794	25,957,448
Total assets	$ 495,941,493	$ 539,772,472
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	$ 47,644,530	$ 21,203,808
Accounts payable and accrued expenses due to affiliated entities	548,032	642,969
Accrued clinical trial expenses	10,326,266	9,950,345
Deferred revenue	21,628	46,628
Operating lease liability	2,603,956	2,329,394
Grant funding liability	4,559,721	7,474,310
Grant funding liability from affiliated entities	37,500	58,500
Total current liabilities	65,741,633	41,705,954
Deferred revenue, net of current portion	64,361	79,214
Convertible senior notes	14,959,647	14,139,988
Convertible bonds	—	4,515,834
Operating lease liability, net of current portion	15,459,559	18,063,515
Deferred tax liabilities	32,046	32,046
Grant funding liability from affiliated entity, net of current portion	—	37,500
Other liabilities	14,826	57,663
Total liabilities	96,272,072	78,631,714
Commitments and contingencies		
Inovio Pharmaceuticals, Inc. stockholders' equity:		
Preferred stock—par value $0.001; Authorized shares: 10,000,000, issued and outstanding shares: 9 at December 31, 2021 and 2020	—	—
Common stock—par value $0.001; Authorized shares: 600,000,000 at December 31, 2021 and 2020, issued and outstanding: 217,382,887 at December 31, 2021 and 186,851,493 at December 31, 2020	217,382	186,851
Additional paid-in capital	1,609,589,797	1,367,406,869
Accumulated deficit	(1,209,855,522)	(906,196,812)
Accumulated other comprehensive income (loss)	(282,236)	(256,150)
Total Inovio Pharmaceuticals, Inc. stockholders' equity	399,669,421	461,140,758
Total liabilities and stockholders' equity	$ 495,941,493	$ 539,772,472

The accompanying notes are an integral part of these consolidated financial statements.

Inovio Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF OPERATIONS

	For the Year ended December 31,		
	2021	**2020**	**2019**
Revenues:			
Revenue under collaborative research and development arrangements	$ 902,260	$ 5,170,586	$ 3,636,945
Revenue under collaborative research and development arrangements from affiliated entities	245,310	1,453,730	235,649
Other revenue	627,188	786,904	237,536
Other revenue from affiliated entities	—	—	1,800
Total revenues	1,774,758	7,411,220	4,111,930
Operating expenses:			
Research and development	249,240,324	94,245,436	88,017,319
General and administrative	53,752,353	37,247,828	27,203,156
Total operating expenses	302,992,677	131,493,264	115,220,475
Loss from operations	(301,217,919)	(124,082,044)	(111,108,545)
Other income (expense):			
Interest income	3,363,080	3,311,846	2,605,981
Interest expense	(1,936,447)	(8,702,450)	(7,948,539)
Change in fair value of derivative liability	—	(75,670,977)	(1,763,652)
Gain (loss) on investment in affiliated entities	(553,570)	36,556,658	(3,090,557)
Net unrealized gain (loss) on available-for-sale equity securities	(3,222,838)	1,695,497	—
Other income (expense), net	343,371	(704,896)	496,200
Gain on deconsolidation of Geneos	—	4,121,075	—
Loss on extinguishment of convertible bonds	—	(8,177,043)	—
Gain on extinguishment of convertible senior notes	—	8,762,030	—
Net loss before income tax benefit	(303,224,323)	(162,890,304)	(120,809,112)
Income tax benefit	—	—	257,335
Share in net loss of Geneos	(434,387)	(4,584,610)	—
Net loss	(303,658,710)	(167,474,914)	(120,551,777)
Net loss attributable to non-controlling interest	—	1,063,757	1,192,558
Net loss attributable to Inovio Pharmaceuticals, Inc.	$ (303,658,710)	$ (166,411,157)	$ (119,359,219)
Net loss per share attributable to Inovio Pharmaceuticals, Inc. stockholders			
Basic and diluted	$ (1.45)	$ (1.07)	$ (1.21)
Weighted average number of common shares outstanding			
Basic and diluted	208,829,801	155,126,857	98,717,999

The accompanying notes are an integral part of these consolidated financial statements.

Inovio Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

	For the Year ended December 31,		
	2021	**2020**	**2019**
Net loss	$ (303,658,710)	$ (167,474,914)	$ (120,551,777)
Other comprehensive income (loss):			
Foreign currency translation	(30,134)	27,205	—
Unrealized gain (loss) on short-term investments, net of tax	4,048	(755,963)	1,001,475
Comprehensive loss	$ (303,684,796)	$ (168,203,672)	$ (119,550,302)
Comprehensive loss attributable to non-controlling interest	—	1,063,757	1,192,558
Comprehensive loss attributable to Inovio Pharmaceuticals, Inc.	$ (303,684,796)	$ (167,139,915)	$ (118,357,744)

The accompanying notes are an integral part of these consolidated financial statements.

Inovio Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

	Preferred stock		Common stock		Additional paid-in capital	Accumulated deficit	Accumulated other comprehensive income (loss)	Non-controlling interest	Total stockholders' equity
	Number of shares	Amount	Number of shares	Amount					
Balance at December 31, 2018	23	—	97,225,810	$ 97,226	$ 707,794,215	$ (620,426,436)	$ (528,867)	$ 96,269	$ 87,032,407
Issuance of common stock for cash, net of capital raising related expenses	—	—	3,340,678	3,340	9,085,669	—	—	—	9,089,009
Exercise of stock options for cash and vesting of RSUs, net of tax payments	—	—	794,546	795	(781,200)	—	—	—	(780,405)
Equity component of issuance of convertible notes	—	—	—	—	15,752,698	—	—	—	15,752,698
Stock-based compensation	—	—	—	—	10,795,403	—	—	105,917	10,901,320
Acquisition of non-controlling interest in Geneos, net	—	—	—	—	—	—	—	2,960,131	2,960,131
Net loss attributable to common stockholders	—	—	—	—	—	(119,359,219)	—	(1,192,558)	(120,551,777)
Unrealized gain on short-term investments, net of tax	—	—	—	—	—	—	1,001,475	—	1,001,475
Balance at December 31, 2019	23	—	101,361,034	$ 101,361	$ 742,646,785	$ (739,785,655)	$ 472,608	$ 1,969,759	$ 5,404,858
Issuance of common stock for cash, net of capital raising related expenses	—	—	66,064,886	66,065	454,420,335	—	—	—	454,486,400
Conversion of preferred stock to common stock	(14)	—	5,147	5	(5)	—	—	—	—
Conversion of senior notes to common stock	—	—	11,535,660	11,536	43,682,850	—	—	—	43,694,386
Conversion of August 2019 Bonds to common stock	—	—	4,962,364	4,961	102,666,349	—	—	—	102,671,310
Exercise of stock options for cash and vesting of RSUs, net of tax payments	—	—	2,922,402	2,923	8,238,701	—	—	—	8,241,624
Stock-based compensation	—	—	—	—	15,655,585	—	—	(8,062)	15,647,523
Acquisition of non-controlling interest in Geneos, net	—	—	—	—	—	—	—	2,379,969	2,379,969
Deconsolidation of Geneos	—	—	—	—	—	—	—	(3,181,640)	(3,181,640)
Net loss attributable to common stockholders	—	—	—	—	—	(166,411,157)	—	(1,063,757)	(167,474,914)
Dissolution of majority-owned subsidiary VGX Animal Health, Inc.	—	—	—	—	96,269	—	—	(96,269)	—
Unrealized loss on short-term investments, net of tax	—	—	—	—	—	—	(755,963)	—	(755,963)
Foreign currency translation	—	—	—	—	—	—	27,205	—	27,205
Balance at December 31, 2020	9	—	186,851,493	$ 186,851	$ 1,367,406,869	$ (906,196,812)	$ (256,150)	$ —	$ 461,140,758
Issuance of common stock for cash, net of capital raising related expenses	—	—	27,310,341	27,310	209,414,100	—	—	—	209,441,410
Conversion of December 2019 Bonds to common stock	—	—	1,009,450	1,009	4,376,883	—	—	—	4,377,892
Exercise of stock options for cash and vesting of RSUs, net of tax payments	—	—	2,211,603	2,212	2,055,181	—	—	—	2,057,393
Stock-based compensation	—	—	—	—	26,336,764	—	—	—	26,336,764
Net loss attributable to common stockholders	—	—	—	—	—	(303,658,710)	—	—	(303,658,710)
Unrealized gain on short-term investments, net of tax	—	—	—	—	—	—	4,048	—	4,048
Foreign currency translation	—	—	—	—	—	—	(30,134)	—	(30,134)
Balance at December 31, 2021	9	—	217,382,887	$ 217,382	$ 1,609,589,797	$ (1,209,855,522)	$ (282,236)	$ —	$ 399,669,421

The accompanying notes are an integral part of these consolidated financial statements.

Inovio Pharmaceuticals, Inc.

CONSOLIDATED STATEMENTS OF CASH FLOWS

	For the Year ended December 31,		
	2021	**2020**	**2019**
Cash flows from operating activities:			
Net loss	$ (303,658,710)	$ (167,474,914)	$ (120,551,777)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	3,040,096	3,038,996	3,598,388
Amortization of intangible assets	520,415	547,081	1,066,294
Amortization of operating lease right-of-use assets	1,170,270	1,041,713	851,760
Change in fair value of derivative liability	—	75,670,977	1,763,652
Stock-based compensation	26,336,764	15,647,523	10,901,320
Non-cash interest expense	858,644	4,077,686	5,230,954
Amortization of premiums on investments	1,633,286	—	1,962
Deferred taxes	—	—	5,397
Loss (gain) on short-term investments	5,397	588,270	(476,368)
Settlement of receivable with shares of common stock from affiliated entity (PLS)	—	(1,713,770)	—
Gain on deconsolidation of Geneos	—	(4,121,075)	—
Loss on disposal of fixed assets	—	26,913	5,889
Loss (gain) on equity investment in affiliated entities	553,570	(36,556,658)	3,090,557
Share of net loss in Geneos	434,387	4,584,610	—
Loss on extinguishment of convertible August 2019 bonds	—	8,177,043	—
Gain on extinguishment of convertible senior notes	—	(8,762,030)	—
Net unrealized loss (gain) on available-for-sale equity securities	3,222,838	(1,695,497)	—
Tax benefit from other unrealized gains on short-term investments	—	—	(266,215)
Unrealized transaction (gain) loss on foreign-currency denominated debt	(176,927)	15,902	471,172
Changes in operating assets and liabilities:			
Accounts receivable	13,093,117	(17,859,894)	2,616,288
Accounts receivable from affiliated entities	(2,061,412)	844,423	(593,461)
Prepaid expenses and other current assets	(6,188,872)	(38,849,572)	(178,008)
Prepaid expenses and other current assets from affiliated entities	(154,760)	374,107	70,665
Other assets	24,531,654	(23,285,424)	(2,026)
Accounts payable and accrued expenses	26,235,907	3,115,828	(4,337,829)
Accrued clinical trial expenses	375,921	5,962,381	(1,622,037)
Accounts payable and accrued expenses due to affiliated entities	(94,937)	135,650	(248,063)
Deferred revenue	(39,853)	(68,078)	(180,450)
Deferred revenue from affiliated entities	—	5,725	(1,800)
Operating lease right-of-use assets and liabilities, net	(2,329,394)	(2,091,855)	(1,733,599)
Grant funding liability	(2,914,589)	1,409,098	1,899,364
Grant funding liability from affiliated entities	(58,500)	(784,925)	816,342
Other liabilities	(42,837)	20,720	(48,507)
Net cash used in operating activities	(215,708,525)	(177,979,046)	(97,850,136)
Cash flows from investing activities:			
Purchases of investments	(348,953,236)	(156,216,677)	(100,950,301)
Proceeds from sale of or maturity of investments	174,839,758	62,991,023	92,893,232
Purchases of capital assets	(1,231,006)	(1,520,665)	(987,926)
Proceeds from sale of investment of GeneOne	—	40,125,418	—
Decrease in cash resulting from the deconsolidation of Geneos	—	(2,774,851)	—
Investment in Geneos	—	(1,399,999)	—
Net cash used in investing activities	(175,344,484)	(58,795,751)	(9,044,995)
Cash flows from financing activities:			
Proceeds from issuances of convertible senior notes and convertible bonds	—	—	97,443,617
Costs related to issuances of convertible senior notes and convertible bonds	—	—	(3,314,757)
Proceeds from issuance of common stock, net of issuance costs	209,441,410	454,486,400	9,089,010
Proceeds from stock option exercises, net of tax payments	6,668,741	12,269,801	112,522
Taxes paid related to net share settlement of equity awards, net of proceeds from option exercises	(4,611,348)	(4,028,177)	(892,928)
Acquisition of non-controlling interest	—	2,379,969	2,960,131
Proceeds from Geneos issuance of note payable	—	171,620	—
Net cash provided by financing activities	211,498,803	465,279,613	105,397,595
Effect of exchange rate changes on cash and cash equivalents	(30,134)	27,205	—
Increase (decrease) in cash and cash equivalents	(179,584,340)	228,532,021	(1,497,536)
Cash and cash equivalents, beginning of period	250,728,118	22,196,097	23,693,633
Cash and cash equivalents, end of period	$ 71,143,778	$ 250,728,118	$ 22,196,097
Supplemental disclosure:			
Amounts accrued for purchases of property and equipment	$ 204,815	$ 136,711	$ —
Interest paid	$ 1,077,803	$ 4,624,764	$ 2,717,585
Change in prepaid expenses and other current assets included in fixed assets	$ 7,709,337	$ —	$ —
Equity component of issuance of convertible notes	$ —	$ —	$ 15,752,698
Right-of-use assets obtained in exchange for lease obligations	$ —	$ —	$ 14,634,769

The accompanying notes are an integral part of these consolidated financial statements.

Inovio Pharmaceuticals, Inc.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. The Company

Inovio Pharmaceuticals, Inc. (the "Company" or "INOVIO"), is a biotechnology company focused on bringing to market precisely designed DNA medicines and vaccines to help protect people from infectious diseases, including COVID-19, and to help treat people with cancer, and conditions associated with human papillomavirus ("HPV"). INOVIO has shown in clinical trials that its DNA vaccine candidates can be delivered into cells in the body via a proprietary smart device allowing the nucleic-acid delivered gene products to activate functional T cell and antibody responses against targeted pathogens and cancers.

The Company's DNA medicines pipeline is comprised of three types of product candidates: prophylactic DNA vaccines, therapeutic DNA immunotherapies, and DNA encoded monoclonal and bispecific antibodies ("dMAbs" and "dBTAs"), all of which utilize the two components of INOVIO's integrated platform, SynCon® and CELLECTRA®.

The Company's proprietary SynCon® technology creates optimized plasmids, which are circular strands of DNA that instruct a cell to produce proteins or antigens to help the person's immune system respond with antibodies and immune cells which recognize and then help block viruses and destroy cancerous or pre-cancerous cells.

INOVIO's patented CELLECTRA® smart delivery devices facilitate uptake of its DNA medicines into the cell, which has been a key limitation of historical DNA-based technology approaches. Human clinical trial data from more than 15,000 CELLECTRA® smart device administrations across more than 5,000 participants to date have shown a tolerable safety profile.

INOVIO's corporate strategy is to develop, seek regulatory approval for and commercialize its novel DNA medicines to address unmet global health needs. The Company continues to advance and clinically validate an array of DNA medicine candidates that target infectious diseases, such as COVID-19, as well as HPV-associated diseases and cancer.

The Company's partners and collaborators include ApolloBio Corporation, AstraZeneca, Beijing Advaccine, The Bill & Melinda Gates Foundation (Gates), Coalition for Epidemic Preparedness Innovations ("CEPI"), The U.S. Department of Defense ("DoD"), Defense Advanced Research Projects Agency ("DARPA"), HIV Vaccines Trial Network, the U.S. Defense Threat Reduction Agency's Medical CBRN Defense Consortium ("MCDC"), International Vaccine Institute ("IVI"), Kaneka Eurogentec, National Cancer Institute, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Ology Bioservices, the Parker Institute for Cancer Immunotherapy, Plumbline Life Sciences, Regeneron Pharmaceuticals, Inc., Richter-Helm BioLogics, Thermo Fisher Scientific, the University of Pennsylvania, the Walter Reed Army Institute of Research and The Wistar Institute.

The Company and its collaborators are currently evaluating the feasibility of, conducting or planning clinical studies of DNA medicines for COVID-19, which includes both homologous and heterologous boosting approaches; Middle East Respiratory Syndrome, or MERS; Lassa fever; Ebola; as well as HPV-associated precancers, including cervical, vulvar, and anal dysplasia; HPV-associated cancers, including head & neck, cervical, anal, penile, vulvar, and vaginal; other HPV-associated disorders, such as recurrent respiratory papillomatosis, or RRP; glioblastoma multiforme, or GBM; and prostate cancer.

INOVIO was incorporated in Delaware in June 2001 and has its principal executive offices in Plymouth Meeting, Pennsylvania.

2. Summary of Significant Accounting Policies

Basis of Presentation and Liquidity

The Company incurred a net loss attributable to common stockholders of $303.7 million for the year ended December 31, 2021. The Company had working capital of $382.7 million and an accumulated deficit of $1.2 billion as of December 31, 2021. The Company has incurred losses in each year since its inception and expects to continue to incur significant expenses and operating losses for the foreseeable future in connection with the research and preclinical and clinical development of its product candidates. The Company's cash, cash equivalents and short-term investments of $401.3 million as of December 31, 2021, are sufficient to support the Company's operations for a period of at least 12 months from the date it is issuing these financial statements.

In order to continue to fund future research and development activities, the Company will need to seek additional capital. This may occur through strategic alliance and licensing arrangements, grant agreements and/or future public or private debt or equity financings including At-the-Market Equity Offering Sales Agreements ("Sales Agreements"). The Company has a history of conducting debt and equity financings, including the receipt of net proceeds of $162.1 million from a January 2021 underwritten public offering, net proceeds of $47.7 million under a Sales Agreement during the year ended December 31, 2021,

net proceeds of $454.5 million under Sales Agreements during the year ended December 31, 2020, and net proceeds of $9.1 million under a Sales Agreement during the year ended December 31, 2019. The Company also received net proceeds of $75.7 million from a private placement of 6.50% convertible senior notes due 2024 (the “Notes”), net proceeds of $14.5 million from the private placement of 18 billion Korean Won (KRW) (approximately USD $15.0 million based on the exchange rate on the date of issuance) aggregate principal amount of its 1.0% convertible bonds due August 2024 (the "August 2019 Bonds"), and net proceeds of $4.0 million from the private placement of 4.7 billion KRW (approximately USD $4.1 million based on the exchange rate on the date of issuance) aggregate principal amount of its 1.0% convertible bonds due December 2024 (the "December 2019 Bonds" and, together with the August 2019 Bonds, the “Bonds”) during the year ended December 31, 2019. However, sufficient funding may not be available in the future, or if available, may be on terms that significantly dilute or otherwise adversely affect the rights of existing stockholders. If adequate funds are not available, the Company may need to delay, reduce the scope of or put on hold one or more of its clinical and/or preclinical programs.

The Company’s ability to continue its operations is dependent upon its ability to obtain additional capital in the future and achieve profitable operations. The Company expects to continue to rely on outside sources of financing to meet its capital needs and the Company may never achieve positive cash flow. These consolidated financial statements do not include any adjustments to the specific amounts and classifications of assets and liabilities, which might be necessary should Inovio be unable to continue as a going concern. The Company's consolidated financial statements as of and for the year ended December 31, 2021 have been prepared on a going concern basis, which contemplates the realization of assets and the settlement of liabilities and commitments in the normal course of business for the foreseeable future. The Company has evaluated subsequent events after the balance sheet date through the date it issued these consolidated financial statements.

The Company is and, from time to time, may in the future be subject to various legal proceedings and claims arising in the ordinary course of business. The Company assesses contingencies to determine the degree of probability and range of possible loss for potential accrual in its consolidated financial statements. An estimated loss contingency is accrued in the consolidated financial statements if it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. Legal proceedings, including litigation, government investigations and enforcement actions, could result in material costs, occupy significant management resources and entail civil and criminal penalties, even if the Company ultimately prevails. Any of the foregoing consequences could result in serious harm to the Company’s business, results of operations and financial condition.

Risks and Uncertainties

The global pandemic resulting from COVID-19, caused by a novel strain of coronavirus, SARS-CoV-2, has caused national and global economic and financial market disruptions. The impact of this pandemic has been and will likely continue to be extensive in many aspects of society, which has resulted in and will continue to cause significant disruptions to the global economy, as well as businesses and capital markets around the world.

The Company continues to closely monitor the impact of the COVID-19 pandemic on its employees, collaborators and service providers. The extent to which the pandemic will continue to impact the Company's business and operations will depend on future developments, including travel restrictions to, from and within the United States and other countries, and the effectiveness of actions taken in the United States and other countries to contain and treat the disease, including mass vaccination efforts, that are highly uncertain as of the date the Company is issuing these financial statements.

Consolidation

In June 2020, the Company formed a wholly-owned subsidiary, Inovio Asia LLC, under the laws of South Korea, through which the Company intends to advance its corporate development projects and other functions in South Korea and other Asian countries.

The consolidated financial statements include the accounts of Inovio Pharmaceuticals, Inc. and its subsidiary. As of December 31, 2021 the Company consolidated its wholly-owned subsidiary Inovio Asia LLC. On December 31, 2020, former wholly-owned subsidiaries Genetronics, Inc. and VGX Pharmaceuticals Inc. and former majority -owned subsidiary VGX Animal Health, Inc. were merged into Inovio Pharmaceuticals, Inc. All intercompany accounts and transactions have been eliminated upon consolidation. As of June 1, 2020, the Company deconsolidated its former subsidiary Geneos Therapeutics, Inc. ("Geneos"), as the Company no longer held a controlling financial interest. Refer to Footnote 16 for further discussion of Geneos.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business as one segment operating primarily within the United States.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosures of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash and short-term investments. The Company limits its exposure to credit loss by placing its cash and investments with high credit quality financial institutions. Additionally, the Company has established guidelines regarding diversification of its investments and their maturities which are designed to maintain principal and maximize liquidity.

The Company has contracts with certain of its customers that have represented more than 10% of the Company's total revenues, as discussed in Note 3.

Fair Value of Financial Instruments

The guidance regarding fair value measurements establishes a three-tier fair value hierarchy which prioritizes the inputs used in measuring fair value. These tiers include: Level 1, defined as observable inputs such as quoted prices in active markets that are accessible at the measurement date; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions.

The Company’s financial instruments include cash equivalents, short-term investments, investments in affiliated entities, accounts receivable, prepaid expenses and other assets, accounts payable and accrued expenses, and convertible senior notes. The carrying amounts of cash equivalents, accounts receivable, prepaid expenses and other assets, accounts payable and accrued expenses approximate the related fair values due to the short-term maturities of these instruments. Short-term investments are recorded at fair value on a recurring basis, based on current market valuations. The Company carries convertible senior notes at face value less unamortized debt discount and issuance costs on its consolidated balance sheet, and it presents the fair value of such convertible notes and bonds for disclosure purposes only.

Cash and Cash Equivalents

Cash equivalents are considered by the Company to be highly liquid investments purchased with original maturities of three months or less from the date of purchase. Cash and cash equivalents included certain money market accounts and U.S. treasury securities at December 31, 2021 and 2020.

Short-term Investments

The Company defines investments as income-yielding securities that can be readily converted into cash or equity investments classified as available-for-sale. Investments included mutual funds, U.S. treasury securities, commercial paper, certificates of deposit, U.S. agency mortgage-backed securities and an equity investment in the Company’s affiliated entity, PLS, at December 31, 2021 and 2020.

Short-term investments are recorded at fair value, based on current market valuations. Unrealized gains and losses on the Company's short-term debt investments are excluded from earnings and reported as a separate component of other comprehensive loss until realized. Realized gains and losses and unrealized gains and losses on available-for-sale equity securities are included in non-operating other income (expense) on the consolidated statements of operations and are derived using the specific identification method for determining the cost of the securities sold.

Accounts Receivable

Accounts receivable are recorded at invoiced amounts and do not bear interest. The Company performs ongoing credit evaluations of its customers’ financial condition. Credit is extended to customers as deemed necessary and generally does not require collateral. Management believes that the risk of loss is significantly reduced due to the quality and financial position of the Company's customers. No allowance for doubtful accounts was deemed necessary at December 31, 2021 and 2020.

Fixed Assets

Property and equipment are stated at cost and depreciated using the straight-line method over the estimated useful life of the assets, generally three to five years. Leasehold improvements are amortized over the shorter of the remaining term of the related leases or the estimated economic useful lives of the improvements. Repairs and maintenance are expensed as incurred.

Long-Lived Assets

All long-lived assets are reviewed for impairment in value when changes in circumstances dictate, based upon undiscounted future operating cash flows, and appropriate losses are recognized and reflected in current earnings, to the extent the carrying amount of an asset exceeds its estimated fair value determined by the use of appraisals, discounted cash flow

analyses or comparable fair values of similar assets. The Company has not recognized any losses on long-lived assets through December 31, 2021.

Valuation of Intangible Assets and Goodwill

Intangible assets are amortized over their estimated useful lives ranging from two to 18 years. Acquired intangible assets are continuously being developed for the future economic viability contemplated at the time of acquisition. The Company is concurrently conducting preclinical studies and clinical trials using the acquired intangibles and has entered into licensing agreements for the use of these acquired intangibles.

License costs are recorded based on the fair value of consideration paid and are amortized using the straight-line method over the shorter of the expected useful life of the underlying patents or the term of the related license agreement to the extent the license has an alternative future use. As of December 31, 2021 and 2020, the Company's intangible assets resulting from the acquisition of Inovio AS and Bioject Medical Technologies, Inc. ("Bioject"), and additional intangibles including license costs, net of accumulated amortization, totaled $2.6 million and $3.1 million, respectively.

The determination of the value of intangible assets requires management to make estimates and assumptions that affect the Company's consolidated financial statements. The Company assesses potential impairments to intangible assets when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. The Company's judgments regarding the existence of impairment indicators and future cash flows related to intangible assets are based on operational performance of its acquired businesses, market conditions and other factors. If impairment is indicated, the Company will reduce the carrying value of the intangible asset to fair value. While current and historical operating and cash flow losses are potential indicators of impairment, the Company believes the future cash flows to be received from its intangible assets will exceed the intangible assets' carrying value, and accordingly, the Company has not recognized any impairment losses through December 31, 2021.

Goodwill represents the excess of acquisition cost over the fair value of the net assets of acquired businesses. Goodwill is reviewed for impairment at least annually at November 30, or more frequently if an event occurs indicating the potential for impairment. During its goodwill impairment review, the Company may assess qualitative factors to determine whether it is likely that the fair value of its reporting unit is less than its carrying amount, including goodwill. The qualitative factors include, but are not limited to, macroeconomic conditions, industry and market considerations, and the overall financial performance of the Company. If, after assessing the totality of these qualitative factors, the Company determines that it is not likely that the fair value of its reporting unit is less than its carrying amount, then no additional assessment is deemed necessary. Otherwise, the Company will proceed to perform the impairment test in which the fair value of the reporting unit is compared with its carrying amount, and an impairment charge will be recorded for the amount by which the carrying amount exceeds the reporting unit's fair value, if any. The Company performed its annual assessment for goodwill impairment as of November 30, 2021, identifying no impairment.

Although there are inherent uncertainties in this assessment process, the estimates and assumptions the Company is using are consistent with its internal planning. If these estimates or their related assumptions change in the future, the Company may be required to record an impairment charge on all or a portion of its goodwill and intangible assets. Furthermore, the Company cannot predict the occurrence of future impairment triggering events nor the impact such events might have on its reported asset values. Future events could cause the Company to conclude that impairment indicators exist and that goodwill or other intangible assets associated with its acquired businesses are impaired. Any resulting impairment loss could have an adverse impact on the Company's results of operations. See Note 8 for further discussion of the Company's goodwill and intangible assets.

Income Taxes

The Company recognizes deferred tax assets and liabilities for temporary differences between the financial reporting basis and the tax basis of the Company's assets and liabilities along with net operating loss and tax credit carry forwards. The Company records a valuation allowance against its deferred tax assets to reduce the net carrying value to an amount that it believes is more likely than not to be realized. When the Company establishes or reduces the valuation allowance against its deferred tax assets, its provision for income taxes will increase or decrease, respectively, in the period such determination is made.

Valuation allowances against the Company's deferred tax assets were $237.2 million and $159.7 million at December 31, 2021 and 2020, respectively. Changes in the valuation allowances, when they are recognized in the provision for income taxes, are included as a component of the estimated annual effective tax rate.

Collaboration Agreements

The Company assesses whether its collaboration agreements are subject to ASC Topic 808: Collaborative Arrangements ("Topic 808") based on whether they involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within

the scope of Topic 808 and the Company concludes that its collaboration partner is not a customer, the Company presents such payments as a reduction of research and development expense. If payments from the collaboration partner to the Company represent consideration from a customer, then the Company accounts for those payments within the scope of Accounting Standards Update ("ASU") 2014-09, *Revenue from Contracts with Customers* ("Topic 606").

Revenue Recognition

The Company recognizes revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which it expects to be entitled in exchange for those goods or services. To determine revenue recognition for contracts with customers, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies its performance obligations. At contract inception, the Company assesses the goods or services agreed upon within each contract and assess whether each good or service is distinct and determine those that are performance obligations. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements

The Company enters into collaborative arrangements with partners that typically include payment of one or more of the following: (i) license fees; (ii) product supply services; (iii) milestone payments related to the achievement of developmental, regulatory, or commercial goals; and (iv) royalties on net sales of licensed products. Where a portion of non-refundable, upfront fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as deferred revenue and recognized as revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, the Company must develop estimates and assumptions that require judgment of management to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligation. The standalone selling price may include items such as forecasted revenues, development timelines, discount rates and probabilities of technical and regulatory success. The Company evaluates each performance obligation to determine if it can be satisfied at a point in time or over time. In addition, variable consideration must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

License Fees

If a license to intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company will recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Product Supply Services

Arrangements that include a promise for future supply of drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations. The Company evaluates whether it is the principal or agent in the arrangement. The Company had determined that it is the principal in the current arrangements as the Company controls the product supply before it is transferred to the customer.

Milestone Payments

At the inception of each arrangement that includes milestone payments (variable consideration), the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's or its collaboration partner's control, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achieving such milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration or other revenues and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its collaborative arrangements.

Grants

The Company accounts for various grant agreements under the contributions guidance under Subtopic 958-605, *Not-for-Profit Entities-Revenue Recognition*, which is outside the scope of Topic 606, as the government agencies granting the Company funds are not receiving reciprocal value for their contributions. All contributions received from current grant agreements are recorded as a contra-expense as opposed to revenue on the consolidated statement of operations.

Derivative Liabilities

The Company evaluates its debt and equity issuances to determine if those contracts or embedded components of those contracts qualify as derivatives requiring separate recognition in the Company's financial statements. The result of this accounting treatment is that the fair value of the embedded derivative is revalued at each balance sheet date and recorded as a liability, and the change in fair value during the reporting period is recorded in other income (expense) in the consolidated statements of operations. In circumstances where the embedded conversion option in a convertible instrument is required to be bifurcated and there are also other embedded derivative instruments in the convertible instrument that are required to be bifurcated, the bifurcated derivative instruments are accounted for as a single, compound derivative instrument. The classification of derivative instruments, including whether such instruments should be recorded as liabilities or as equity, is reassessed at the end of each reporting period. Derivative instrument liabilities are classified in the balance sheet as current or non-current based on whether or not net-cash settlement of the derivative instrument is expected within twelve months of the balance sheet date.

Foreign Currency Transactions

The functional and presentation currency of the Company is the U.S. dollar. Transactions denominated in a currency other than the functional currency are recorded on the initial recognition at the exchange rate at the date of the transaction. After initial recognition, monetary assets and liabilities denominated in foreign currency are translated at the end of each reporting period into the functional currency at the exchange rate at that date. The cumulative translation adjustment is included in the accumulated other comprehensive income (loss) within the statement of stockholders' equity. Exchange differences are included in general and administrative expenses in the consolidated statement of operations. Non-monetary assets and liabilities measured at cost are remeasured at the exchange rate at the date of the transaction.

Variable Interest Entities (VIE)

The Company evaluates its ownership, contractual and other interests in entities that are not wholly-owned to determine if these entities are VIEs, and, if so, whether the Company is the primary beneficiary of the VIE. In determining whether the Company is the primary beneficiary of a VIE and therefore required to consolidate the VIE, the Company applies a qualitative approach that determines whether it has both (1) the power to direct the activities of the VIE that most significantly impact the VIE’s economic performance and (2) the obligation to absorb losses of, or the rights to receive benefits from, the VIE that could potentially be significant to that VIE. The Company will continuously perform this assessment, as changes to existing relationships or future transactions may result in the consolidation or deconsolidation of a VIE.

Equity Investments

Under ASC Topic 321, *Investments - Equity Securities,* the Company must measure equity investments (except those accounted for under the equity method, those that result in consolidation of the investee and certain other investments) at fair value and recognize any changes in fair value in the consolidated statement of operations. The Company can elect a measurement alternative for equity investments that do not have readily determinable fair values and do not qualify for the practical expedient in ASC Topic 820, *Fair Value Measurement,* to estimate fair value using the net asset value per share (or its equivalent). The Company's equity investments that do not have readily determinable fair values and do not qualify for the net asset value practical expedient for estimating fair value are measured at cost, less any impairments, plus or minus changes resulting from observable price changes in orderly transactions for identifiable or similar investments of the same issuer.

Research and Development Expenses

The Company’s activities have largely consisted of research and development efforts related to developing electroporation delivery technologies, DNA vaccines, DNA immunotherapies and dMABs. Research and development expenses consist of expenses incurred in performing research and development activities including salaries and benefits, facilities and other overhead expenses, clinical trials, contract services and other outside expenses. Research and development expenses are charged to operations as they are incurred. These expenses result from the Company's independent research and development efforts as well as efforts associated with collaborations and licensing arrangements. The Company reviews and

accrues clinical trial expense based on work performed, which relies on estimates of total costs incurred based on participant enrollment, completion of studies and other events. Accrued clinical trial costs are subject to revisions as trials progress. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to research and development expense; however, a modification in the protocol of a clinical trial or cancellation of a trial could result in a charge to the Company's results of operations.

Advance payments for goods or services to be rendered in the future for use in research and development activities are deferred and included in prepaid expenses and other assets. The deferred amounts are expensed as the related goods are delivered or the services are performed.

Net Loss Per Share

Basic net loss per share is computed by dividing the net loss for the year by the weighted average number of common shares outstanding during the year. Diluted net loss per share is calculated in accordance with the treasury stock method for the outstanding stock options and restricted stock units and reflects the potential dilution that would occur if securities or other contracts to issue common stock were exercised or converted to common stock. The dilutive impact of the outstanding Notes and Bonds issued by the Company (discussed in Note 9) has been considered using the "if-converted" method. The calculation of diluted net loss per share requires that, to the extent the average market price of the underlying shares for the reporting period exceeds the exercise price of the options or other securities and the presumed exercise of such securities are dilutive to net loss per share for the period, an adjustment to net loss used in the calculation is required to remove the change in fair value of such securities from the numerator for the period. Likewise, an adjustment to the denominator is required to reflect the related dilutive shares, if any. For the years ended December 31, 2021, 2020 and 2019, basic and diluted net loss per share are the same, as the assumed exercise or settlement of stock options, restricted stock units and the potentially dilutive shares issuable upon conversion of the Notes and Bonds are antidilutive.

The following table summarizes potential shares of common stock that were excluded from diluted net loss per share calculation because of their anti-dilutive effect:

	Year Ended December 31,		
	2021	2020	2019
Options to purchase common stock	10,488,993	8,906,624	9,265,390
Service-based restricted stock units	2,448,868	2,558,052	2,069,936
Performance-based restricted stock units	663,353	663,353	—
Convertible preferred stock	3,309	3,309	8,456
Convertible notes	3,049,980	3,049,980	14,585,653
August 2019 Bonds	—	—	3,799,071
December 2019 Bonds	—	1,009,450	1,009,450
Total	16,654,503	16,190,768	30,737,956

Leases

For its long-term operating leases, the Company recognized an operating lease right-of-use asset and an operating lease liability on its consolidated balance sheets. The lease liability is determined as the present value of future lease payments using an estimated rate of interest that the Company would pay to borrow equivalent funds on a collateralized basis at the lease commencement date. The right-of-use asset is based on the liability adjusted for any prepaid or deferred rent. The Company determines the lease term at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise.

Fixed rent expense for the Company's operating leases is recognized on a straight-line basis over the term of the lease and is included in operating expenses on the consolidated statements of operations. Variable lease payments including lease operating expenses are recorded as incurred.

Stock-Based Compensation

The Company incurs stock-based compensation expense related to restricted stock units ("RSUs") and stock options. The fair value of restricted stock is determined by the closing price of the Company's common stock reported on the Nasdaq Global Select Market on the date of grant. The Company estimates the fair value of stock options granted using the Black-Scholes option pricing model. The Black-Scholes option pricing model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of subjective assumptions, including the expected stock price volatility and expected option life. The Company amortizes the fair value of the awards on a straight-line basis over the requisite vesting period of the awards. Expected volatility is based on historical volatility. The expected life of options granted is based on historical expected life. The risk-free interest rate is based

on the U.S. Treasury yield in effect at the time of grant. The dividend yield is based on the fact that no dividends have been paid historically and none are currently expected to be paid in the foreseeable future. The Company recognizes forfeitures as they occur.

The weighted average assumptions used in the Black-Scholes model for option grants to employees and directors are presented below:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	0.91%	0.63%	2.42%
Expected volatility	93%	78%	70%
Expected life in years	6	6	6
Dividend yield	—	—	—

The Company adopted ASU 2018-07 on January 1, 2019, which generally aligned the accounting for stock-based compensation for non-employees with that of employees. The fair value of the stock options granted to non-employees was estimated using the Black-Scholes pricing model.

The weighted average assumptions used in the Black-Scholes model for option grants to non-employees are presented below:

	Year Ended December 31,		
	2021	2020	2019
Risk-free interest rate	1.45%	0.82%	2.45%
Expected volatility	87%	76%	88%
Expected life in years	10	10	10
Dividend yield	—	—	—

Recent Accounting Pronouncements - Pending Adoption

The recent accounting pronouncements below may have a significant effect on the Company's financial statements. Recent accounting pronouncements that are not anticipated to have an impact on or are unrelated to the Company's financial condition, results of operations, or related disclosures are not discussed.

ASU No. 2020-06. In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity* ("ASU 2020-06"), which simplifies the guidance on an issuer's accounting for convertible instruments and contracts in its own equity. ASU 2020-06 is effective for public entities for fiscal years beginning after December 15, 2021, and interim periods within those fiscal years. Effective January 1, 2022, the Company will adopt ASU 2020-06. The Company is finalizing its analysis of certain assumptions that will be utilized at the transition and expects the effect of adopting ASU 2020-06 will result in an increase to retained earnings, a decrease to additional paid-in capital, and an increase to the convertible senior notes. The Company expects that interest expense recognized in future periods will be reduced as a result of accounting for the convertible debt instrument as a single liability measured at its amortized cost.

3. Revenue Recognition and Concentration of Credit Risk

During the years ended December 31, 2021, 2020 and 2019, the Company recognized revenue from various license and other agreements. The following table indicates the percentage of total revenues in excess of 10% with any single customer:

Customer	2021 Revenue	% of Total Revenue	2020 Revenue	% of Total Revenue	2019 Revenue	% of Total Revenue
AstraZeneca	$ 41,659	2 %	$ 170,587	2 %	$ 3,194,877	78 %
Advaccine	—	—	5,000,000	68	—	—
Plumbline Life Sciences, Inc. (affiliated entity)	245,310	14	1,370,396	18	—	—
Department of Defense	754,853	43	—	—	—	—
All other, including affiliated entities	732,936	41	870,237	12	917,053	22
Total revenue	$ 1,774,758	100 %	$ 7,411,220	100 %	$ 4,111,930	100 %

Of the total revenue recognized during the year ended December 31, 2021, $46,000 was in deferred revenue as of December 31, 2020. During the year ended December 31, 2020, the Company recognized revenue of $127,000 that was included in deferred revenue at December 31, 2019. Performance obligations are generally satisfied within 12 months of the initial contract date.

As of December 31, 2021, $3.6 million, or 65%, and $1.9 million, or 34%, of the Company's accounts receivable was attributable to the DoD and the CEPI MERS grant, respectively. As of December 31, 2020, $11.4 million, or 62%, and $7.1 million, or 38%, of the Company's accounts receivable was attributable to the DoD and Advaccine, respectively. There is minimal credit risk with these customers based upon collection history, their size and financial condition. Accordingly, the Company does not consider it necessary to record a reserve for uncollectible accounts receivable.

4. Collaborative Agreements

Advaccine Biopharmaceuticals Suzhou Co., Ltd.

On December 31, 2020, the Company entered into a Collaboration and License Agreement with Advaccine Biopharmaceuticals Suzhou Co., Ltd. (“Advaccine”), which was amended and restated on June 7, 2021 (as amended and restated, the “Advaccine Agreement”). Under the terms of the Advaccine Agreement, the Company granted to Advaccine the exclusive right to develop, manufacture and commercialize the Company’s vaccine candidate INO-4800 within the territories of China, Taiwan, Hong Kong and Macau (referred to collectively as “Greater China”) and 33 additional countries in Asia. Advaccine does not have the right to grant sublicenses, other than to affiliated entities, without the Company’s express prior written consent. As part of the collaboration, Advaccine also granted to the Company a non-exclusive license to certain DNA vaccine manufacturing processes.

The June 2021 amendment relates to the collaboration between the Company and Advaccine to jointly conduct the global Phase 3 segment of the Company’s ongoing Phase 2/3 trial of INO-4800 and expand the existing collaboration to include the planned global Phase 3 trial. The parties will jointly participate in the trial and will equally share the global development costs for the trial, including the Company’s manufacturing costs to supply INO-4800. In certain instances, the Company will have the right to convert the exclusive license to a non-exclusive license in the licensed territories, other than Greater China, unless Advaccine agrees to pay the Company its full share of development costs in excess of a specified maximum. Notwithstanding the foregoing, Advaccine will be fully responsible for conducting the trial in Greater China, including its costs and expenses incurred. The Company will be fully responsible for its costs and expenses, if any, incurred solely as a result of its activities in connection with the performance of the trial in the United States. The parties may continue to conduct clinical trials of INO-4800 outside of the territories covered by the Advaccine Agreement.

In the event that a global purchasing entity desires to enter into a purchase agreement for INO-4800 in both parties’ territories, the parties will enter into good faith negotiations for an arrangement to supply INO-4800 to such entity. In addition, the Company is permitted to enter into an agreement with a global purchasing entity to authorize the entity to conduct a portion of the global Phase 3 trial in the licensed territory outside of Greater China.

Under the Advaccine Agreement, Advaccine made an upfront payment to the Company of $3.0 million in January 2021. In addition to the upfront payment, the Company is entitled to receive up to an aggregate of $206.0 million upon the achievement of specified milestones related to the development, regulatory approval and commercialization of INO-4800, including the achievement of specified net sales thresholds for INO-4800 in Greater China and the additional covered territories, if approved. As of December 31, 2020 the Company had earned a $2.0 million milestone payment based on the enrollment of the first participant in the Phase 2 clinical trial for the product in the Advaccine territory. The Company will also be entitled to receive a royalty equal to a high single-digit percentage of annual net sales in each region within the licensed territory, subject to reduction in the event of competition from biosimilar products in a particular region and in other specified circumstances. Advaccine’s obligation to pay royalties will continue, on a licensed product-by-licensed product basis and region-by-region basis, for ten years after the first commercial sale in a particular region within Greater China or, if later, until the expiration of the last-to-expire patent covering a given licensed product in a given region.

Beginning in the first calendar year following the first commercial sale of INO-4800 in the licensed territory outside of Greater China, Advaccine will pay the Company an annual maintenance fee of $1.5 million for a period of five years, which fee will be creditable against any royalties payable by Advaccine with respect to sales outside of Greater China.

Under the Advaccine Agreement, the Company will supply Advaccine's clinical requirements of INO-4800 and devices, although Advaccine may manufacture INO-4800 for its clinical use and may procure alternate suppliers. Advaccine is responsible for the manufacture and supply of INO-4800 itself or through a contract manufacturer for commercial use. Upon Advaccine's reasonable request, the parties may negotiate a separate clinical and/or commercial supply agreement.

The Advaccine Agreement will continue in force on a region-by-region basis until Advaccine has no remaining royalty obligations in such region. Either party may terminate the Advaccine Agreement (i) in the event the other party shall have materially breached its obligations thereunder and such default shall have continued for a specified period after written notice thereof or (ii) upon the bankruptcy or insolvency of the other party. In addition, the Company may terminate the agreement, upon prior written notice, if Advaccine (i) ceases all development or commercialization activities for at least nine months, subject to certain exceptions, or (ii) challenges the validity, enforceability or scope of any of the patents licensed by the Company to Advaccine under the Advaccine Agreement, subject to certain conditions. Advaccine may terminate the Advaccine Agreement at any time for convenience upon nine months' written notice to the Company, if such notice is provided before the first commercial sale of INO-4800 in the licensed territory, or 18 months' written notice thereafter; provided that the Company may accelerate the effectiveness of such termination to the extent permitted by law.

The Company evaluated the terms of the Advaccine Agreement under ASC Topics 606 and 808 at inception and determined that the contract was with a customer and therefore should be accounted for under ASC Topic 606. The license to INO-4800 in the territories was identified as the only distinct performance obligation on a standalone basis as of the inception of the Advaccine Agreement. The Company concluded that the license was distinct from potential future manufacturing and supply obligations. The Company further determined that the transaction price under the Advaccine Agreement consisted of the $3.0 million upfront payment received in January 2021 plus the initial $2.0 million milestone payment which was achieved upon contract signing. The future potential milestone amounts were not included in the transaction price, as they were all determined to be fully constrained. As part of the evaluation of the development and regulatory milestones constraint, the Company determined that the achievement of such milestones is contingent upon success in future clinical trials and regulatory approvals, each of which is uncertain. Future potential milestone amounts may be recognized as revenue under the Advaccine Agreement, as well as under other collaborative research and development arrangements, if unconstrained. Reimbursable program costs will be recognized proportionately with the performance of the underlying services or delivery of drug supply and are excluded from the transaction price.

Under Topic 606, the entire transaction price of $5.0 million was allocated to the license performance obligation. The Company determined that as of December 31, 2020, the transfer of technology has occurred for the use and benefit of the license and accordingly, the performance obligation was fully satisfied. The Company accordingly recognized $5.0 million in revenue under collaborative research and development arrangements on the consolidated statement of operations during the year ended December 31, 2020. As of December 31, 2020, the Company had an accounts receivable balance of $7.1 million from Advaccine. There has been no additional revenue earned under this collaboration agreement with Advaccine for the year ended December 31, 2021.

In connection with the June 2021 amendment, the Company determined that the Global Phase 3 trial component of the agreement is a collaboration and not a contract with a customer and therefore concluded to account for the June 2021 amendment under ASC Topic 808. Reimbursements from Advaccine will be recognized as contra-research development expense on the condensed consolidated statement of operations once earned and collectibility is assured. During the year ended December 31, 2021, the Company received funding of $4.5 million from Advaccine that was recorded as contra-research and development expense.

ApolloBio Corporation

On December 29, 2017, the Company entered into an Amended and Restated License and Collaboration Agreement (the "ApolloBio Agreement"), with ApolloBio Corporation ("ApolloBio"), with an effective date of March 20, 2018. Under the terms of the ApolloBio Agreement, the Company granted to ApolloBio the exclusive right to develop and commercialize VGX-3100, its DNA immunotherapy product candidate designed to treat pre-cancers caused by HPV, within the agreed upon territories.

Under the ApolloBio Agreement, the Company received proceeds of $19.4 million in March 2018, which comprised the upfront payment of $23.0 million less $2.2 million in foreign income taxes and $1.4 million in certain foreign non-income taxes. The foreign income taxes were recorded as a provision for income taxes and the foreign non-income taxes were recorded as a general and administrative expense, on the consolidated statement of operations. The Company also incurred advisory fees of $960,000 in connection with receiving the upfront payment from ApolloBio. These fees were determined to be incremental costs of obtaining the contract. The Company applied the practical expedient that permits a company to expense incremental

costs to obtain a contract when the expected amortization period is one year or less and recorded the fees in general and administrative expense during the quarter ended March 31, 2018. No additional advisory fees are due related to the ApolloBio Agreement.

In addition to the upfront payment, the Company is entitled to receive up to an aggregate of $20.0 million, less required income, withholding or other taxes, upon the achievement of specified milestones related to the regulatory approval of VGX-3100 in accordance with the ApolloBio Agreement. In the event that VGX-3100 is approved for marketing, the Company will be entitled to receive royalty payments based on a tiered percentage of annual net sales, with such percentage being in the low- to mid-teens, subject to reduction in the event of generic competition in a particular territory. ApolloBio's obligation to pay royalties will continue for 10 years after the first commercial sale in a particular territory or, if later, until the expiration of the last-to-expire patent covering the licensed products in the specified territory.

The ApolloBio Agreement will continue in force until ApolloBio has no remaining royalty obligations. Either party may terminate the ApolloBio Agreement in the event the other party shall materially breach or default in the performance of its material obligations thereunder and such default continues for a specified period after written notice thereof. In addition, ApolloBio may terminate the ApolloBio Agreement at any time beginning one year after the effective date for any reason upon 90 days written notice to the Company.

The Company evaluated the terms of the ApolloBio Agreement under ASC Topic 606, and the license to VGX-3100 in the territories was identified as the only distinct performance obligation on a standalone basis as of the inception of the agreement. The Company concluded that the license was distinct from potential future manufacturing and supply obligations. The Company further determined that the transaction price under the agreement consisted of the $23.0 million upfront payment. The future potential milestone amounts were not included in the transaction price, as they were all determined to be fully constrained. As part of the evaluation of the development and regulatory milestones constraint, the Company determined that the achievement of such milestones is contingent upon success in future clinical trials and regulatory approvals, each of which is uncertain at this time. Future potential milestone amounts may be recognized as revenue under the ApolloBio Agreement, as well as under other collaborative research and development arrangements, if unconstrained. Reimbursable program costs will be recognized proportionately with the performance of the underlying services or delivery of drug supply and are excluded from the transaction price. As of December 31, 2021 there have been no significant reimbursable program costs under the ApolloBio Agreement.

Under Topic 606, the entire transaction price of $23.0 million was allocated to the license performance obligation. The Company determined that during the quarter ended June 30, 2018, the transfer of technology occurred and accordingly, the performance obligation was fully satisfied.

AstraZeneca

On August 7, 2015, the Company entered into a license and collaboration agreement with MedImmune, the global biologics research and development arm of AstraZeneca ("AstraZeneca"). Under the agreement, AstraZeneca acquired exclusive rights to the Company's INO-3112 immunotherapy, renamed as MEDI0457, which targets cancers caused by human papillomavirus (HPV) types 16 and 18, with the ability to sublicense those license rights. AstraZeneca made an upfront payment of $27.5 million to the Company in September 2015. AstraZeneca was obligated to make potential future development and regulatory event-based payments to the Company and potential future commercial event-based payments, in each case upon the achievement of specified milestones related to MEDI0457 set forth in the license and collaboration agreement. AstraZeneca was funding all development costs associated with MEDI0457 immunotherapy. The Company was entitled to receive up to mid-single to double-digit tiered royalties on MEDI0457 product sales. Under the agreement, AstraZeneca could also request the Company to provide certain clinical manufacturing at an agreed upon price. The Company determined these options did not represent material rights at the inception of the agreement.

As of December 31, 2017, the Company had recognized all of the $27.5 million upfront payment as revenue, as all identified material performance obligations had been met with respect to that payment. In both December 2018 and March 2019, the Company recognized as revenue $2.0 million in milestone payments from AstraZeneca triggered by AstraZeneca's initiation of the Phase 2 portion of ongoing clinical trials in the second and third major indication, respectively, under the agreement.

On October 28, 2021, AstraZeneca provided notice to the Company to terminate the INO-3112 / MEDI0457 development program under the agreement. As a result of the termination, the agreement has been terminated in its entirety and the Company has no further obligations under the collaboration.

Coalition for Epidemic Preparedness Innovations

On April 11, 2018, the Company entered into agreements with CEPI, pursuant to which the Company intends to develop vaccine candidates against Lassa fever and MERS. The goal of the collaboration between the Company and CEPI is to conduct research and development so that investigational stockpiles will be ready for clinical efficacy trial testing during potential

disease outbreaks. The agreements with CEPI contemplate preclinical studies, as well as Phase 1 and Phase 2 clinical trials, occurring over multiple years. As part of the arrangement between the parties, CEPI has agreed to fund up to an aggregate of $56 million of costs over a five-year period for preclinical studies, as well as planned Phase 1 and Phase 2 clinical trials, to be conducted by the Company and collaborators, with funding from CEPI based on the achievement of identified milestones. During the years ended December 31, 2021 and 2020, the Company received funding of $10.0 million and $6.4 million, respectively, related to these grants and recorded those payments as contra-research and development expense. As of December 31, 2021, the Company had an accounts receivable balance of $1.9 million and recorded $23,000 as deferred grant funding on the consolidated balance sheet related to these CEPI grants.

In January 2020, CEPI awarded the Company a grant of up to $9.0 million to support preclinical and clinical development of INO-4800 through Phase 1 human testing in the United States. In April 2020, CEPI awarded the Company a grant of $6.9 million to work with the International Vaccine Institute ("IVI") and the Korea National Institute of Health ("KNIH") to conduct clinical trials of INO-4800 in South Korea, a grant of $5.0 million to accelerate development of the Company's next-generation intradermal electroporation device, known as CELLECTRA® 3PSP, for the intradermal delivery of INO-4800, and a grant of $1.3 million to support large-scale manufacturing of INO-4800. During the years ended December 31, 2021 and 2020, the Company received funding of $6.9 million and $10.0 million, respectively, from CEPI related to these grants for INO-4800 and recorded such amounts as contra-research and development expense. As of December 31, 2021 the Company had $1.8 million recorded as deferred grant funding on the consolidated balance sheet related to the CEPI grants related to INO-4800.

Bill & Melinda Gates Foundation

In October 2018, the Bill & Melinda Gates Foundation (“Gates”) awarded and funded the Company a grant of $2.2 million to advance the development of dMAbs to address issues in infectious disease prevention and therapy. This technology has high relevance for the control of influenza and HIV. This next-generation approach to the delivery of monoclonal antibodies would make the technology accessible to low and middle-income countries. In August 2019, Gates funded an additional $1.1 million for the project. During the years ended December 31, 2021 and 2020, the Company recorded $182,000 and $463,000, respectively, as contra-research and development expense related to the Gates dMAb grant. As of December 31, 2021, the Company had $384,000 recorded as deferred grant funding on the consolidated balance sheet related to the grant.

In March 2020, Gates awarded and funded the Company a grant of $5.0 million to accelerate the development of the CELLECTRA® 3PSP device for the intradermal delivery of INO-4800. During the years ended December 31, 2021 and 2020, the Company recorded $893,000 and $4.1 million, respectively, as contra-research and development expense related to this Gates grant.

Department of Defense (DoD)

In June 2020, the Company entered into an Other Transaction Authority for Prototype Agreement (the “OTA Agreement”) with the DoD to fund the Company’s efforts in developing the CELLECTRA® 3PSP device and associated arrays to be used for delivery of INO-4800 against COVID-19. Under the OTA Agreement, the Company intends to develop the CELLECTRA® 3PSP device and arrays for use in the U.S. military population and the U.S. population as a whole, subject to approval of the device by the U.S. Food and Drug Administration (the “FDA”). The OTA Agreement is also expected to support large-scale manufacturing of the CELLECTRA® 3PSP device, as well as large-scale DNA plasmid production for manufacture and supply of a specified number of doses of INO-4800 in support of FDA approval of the device. The total amount of funding being made available to the Company under the OTA Agreement is $54.5 million. The Company has determined that the OTA Agreement should be considered under Subtopic 958-605, *Not-for-Profit Entities-Revenue Recognition*, which is outside the scope of Topic 606, as the government agency granting the Company funds is not receiving reciprocal value for their contributions. The Company will record contra-research development expense on the consolidated statement of operations in the same period that the underlying expenses are incurred.

Additionally, in June 2020, the Company was awarded a fixed-price contract (the “Procurement Contract”) from the DoD for the purchase of the Company’s intradermal CELLECTRA® 2000 device and accessories. The CELLECTRA® 2000 devices will be used to inject INO-4800 in the Company’s later-stage clinical trials. The total purchase price under the Procurement Contract is expected to be approximately $10.7 million. As of December 31, 2021, the Company determined that the Procurement Contract falls under the scope of ASC Topic 606 as the contract is with a customer and the Company is able to satisfy its obligations under the arrangement as the Phase 3 clinical trials of INO-4800 are underway. Performance obligations under the Procurement Contract consist of the delivery of a specified number of CELLECTRA® 2000 devices and accessories. The total transaction price was allocated to the individual performance obligations based on the determined standalone selling price for the devices and accessories. The Company will recognize revenue on the consolidated statement of operations upon shipment of the purchased devices and accessories. During the year ended December 31, 2021, the Company recorded revenue of $755,000 from the Procurement Contract. This revenue was recognized at a 100% margin as the sale was for products whose related inventory had previously been written down to zero.

During the years ended December 31, 2021 and 2020, the Company recorded $27.1 million and $21.2 million, respectively, as contra-research and development expense related to the OTA agreement. As of December 31, 2021, the Company had an accounts receivable balance of $3.6 million on the consolidated balance sheet from the DoD. As of December 31, 2021, the Company had $2.3 million recorded as deferred grant funding on the consolidated balance sheet related to the Procurement Contract.

In April 2021, the Company announced that the DoD had notified the Company that it will discontinue funding for the Phase 3 segment of the Company's clinical trial of INO-4800 in the United States, while continuing funding under the OTA Agreement and Procurement Contract.

5. Short-term Investments and Fair Value Measurements

The following is a summary of available-for-sale securities as of December 31, 2021 and 2020:

		As of December 31, 2021			
	Contractual Maturity (in years)	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Mutual funds	---	$ 192,966,772	$ 87,069	$ (1,614,411)	$ 191,439,430
U.S. treasury securities	Less than 1	94,193,441	—	(9,921)	94,183,520
Commercial paper	Less than 1	39,967,853	—	—	39,967,853
Certificates of deposit	Less than 1	2,976,210	15,618	(338)	2,991,490
U.S. agency mortgage-backed securities	*	1,608,137	4,508	(23,998)	1,588,647
		$ 331,712,413	$ 107,195	$ (1,648,668)	$ 330,170,940

		As of December 31, 2020			
	Contractual Maturity (in years)	Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Mutual funds	---	$ 153,177,675	$ 2,339,639	$ (644,140)	$ 154,873,174
Certificates of deposit	Less than 1	3,000,000	26,260	(10,000)	3,016,260
U.S. agency mortgage-backed securities	*	3,062,256	—	(36,755)	3,025,501
		$ 159,239,931	$ 2,365,899	$ (690,895)	$ 160,914,935

*No single maturity date.

During the years ended December 31, 2021 and 2020, the Company recorded gross realized gain on investments of $394,000 and $744,000, respectively, and gross realized loss on investments of $399,000 and $1.3 million, respectively. During the years ended December 31, 2021 and 2020, the Company recorded net unrealized (loss) gain on available-for-sale equity securities of $(3.2) million and $1.7 million, respectively. No material balances were reclassified out of accumulated other comprehensive income (loss) for the years ended December 31, 2021, 2020 and 2019. Interest and dividends on investments classified as available-for-sale are included in interest income in the consolidated statements of operations. As of December 31, 2021, the Company had 24 available-for-sale securities in a gross unrealized loss position, of which six with an aggregate total unrealized loss of $766,000 were in such position for longer than 12 months.

The Company periodically reviews its portfolio of available-for-sale debt securities to determine if any investment is impaired due to credit loss or other potential valuation concerns. For the debt securities where the fair value of the investment is less than the amortized cost basis, the Company has assessed at the individual security level for various quantitative factors including, but not limited to, the nature of the investments, changes in credit ratings, interest rate fluctuations, industry analyst reports, and the severity of impairment. Unrealized losses on available-for-sale debt securities as of December 31, 2021 were primarily due to changes in interest rates, and not due to increased credit risks associated with specific securities. The Company does not intend to sell these investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost basis, which may be at maturity. Based on the credit quality of the available-for-sale debt securities that are in an unrealized loss position, and the Company’s estimates of future cash flows to be collected from those securities, the Company believes the unrealized losses are not credit losses. Accordingly, at December 31, 2021, the Company has not recorded an allowance for credit losses related to its available-for-sale debt securities.

The following table presents the Company's assets that were measured at fair value on a recurring basis, determined using the following inputs as of December 31, 2021:

	Fair Value Measurements at December 31, 2021			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Unobservable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Short-term investments				
Mutual funds	$ 191,439,430	$ 191,439,430	$ —	$ —
U.S. treasury securities	94,183,520	94,183,520	—	—
Commercial paper	39,967,853	—	39,967,853	—
Certificates of deposit	2,991,490	—	2,991,490	—
U.S. agency mortgage-backed securities	1,588,647	—	1,588,647	—
Total short-term investments	330,170,940	285,622,950	44,547,990	—
Investment in affiliated entity	3,906,796	3,906,796	—	—
Total assets measured at fair value	$ 334,077,736	$ 289,529,746	$ 44,547,990	$ —

The following table presents the Company's assets that were measured at fair value on a recurring basis, determined using the following inputs as of December 31, 2020:

	Fair Value Measurements at December 31, 2020			
	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Unobservable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash and cash equivalents				
U.S. treasury securities	$ 59,996,800	$ 59,996,800	$ —	$ —
Short-term investments				
Mutual funds	154,873,174	154,873,174	—	—
Certificates of deposit	3,016,260	—	3,016,260	—
U.S. agency mortgage-backed securities	3,025,501	—	3,025,501	—
Total short-term investments	160,914,935	154,873,174	6,041,761	—
Investments in affiliated entity	4,460,366	4,460,366	—	—
Total assets measured at fair value	$ 225,372,101	$ 219,330,340	$ 6,041,761	$ —

Level 1 assets at December 31, 2021 and 2020 consisted of mutual funds and U.S. treasury securities held by the Company that are valued at quoted market prices, as well as the Company's investment in its affiliated entity, PLS. The Company accounts for its investment in 597,808 common shares of PLS based on the closing price of the shares on the Korea New Exchange Market on the applicable balance sheet date. Unrealized gains and losses on the Company's equity securities are reported in the consolidated statement of operations as unrealized gain (loss) on available-for-sale equity securities or as a gain (loss) on investment in affiliated entity.

Level 2 assets at December 31, 2021 consisted of commercial paper, certificates of deposit and U.S. agency mortgage-backed securities held by the Company that are initially valued at the transaction price and subsequently valued, at the end of each reporting period, typically utilizing market observable data. Level 2 assets at December 31, 2020 consisted of certificates of deposit and U.S. agency mortgage-backed securities. The Company obtains the fair value of its Level 2 assets from a

professional pricing service, which may use quoted market prices for identical or comparable instruments, or inputs other than quoted prices that are observable either directly or indirectly. The professional pricing service gathers quoted market prices and observable inputs from a variety of industry data providers. The valuation techniques used to measure the fair value of the Company's Level 2 financial instruments were derived from non-binding market consensus prices that are corroborated by observable market data, quoted market prices for similar instruments, or pricing models such as discounted cash flow techniques. The Company validates the quoted market prices provided by the primary pricing service by comparing the service's assessment of the fair values of the Company's investment portfolio balance against the fair values of the Company's investment portfolio balance obtained from an independent source.

There were no Level 3 assets held as of December 31, 2021 and 2020.

6. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets at December 31, 2021 and 2020 consisted of the following:

	2021	2020
Prepaid manufacturing expenses (a)	$ 27,474,159	$ 35,661,947
Other prepaid expenses	11,362,832	4,695,509
	$ 38,836,991	$ 40,357,456

(a) Includes prepaid manufacturing expenses related to deposits made to reserve capacity for the manufacture of INO-4800. The Company deposited a total of $50.0 million to reserve manufacturing capacity, of which $30.0 million was paid in 2020 and the remainder paid in the first quarter of 2021. Of these deposits, $35.0 million was included in research and development expenses in December 2021.

7. Fixed Assets

Fixed assets at December 31, 2021 and 2020 consisted of the following:

	Cost	Accumulated Depreciation and Amortization	Net Book Value
As of December 31, 2021			
Leasehold improvements	$ 15,803,108	$ (8,258,608)	$ 7,544,500
Laboratory equipment	12,392,916	(4,279,816)	8,113,100
Office furniture and fixtures	2,827,476	(2,599,643)	227,833
Computer equipment and other	5,374,084	(3,806,311)	1,567,773
	$ 36,397,584	$ (18,944,378)	$ 17,453,206
As of December 31, 2020			
Leasehold improvements	$ 15,179,447	$ (6,549,418)	$ 8,630,029
Laboratory equipment	4,788,678	(3,727,508)	1,061,170
Office furniture and fixtures	2,828,675	(2,296,942)	531,733
Computer equipment and other	4,544,915	(3,419,703)	1,125,212
	$ 27,341,715	$ (15,993,571)	$ 11,348,144

Depreciation expense for the years ended December 31, 2021, 2020 and 2019 was $3.0 million, $3.0 million and $3.6 million, respectively. The Company determined that the carrying value of these long-lived assets was not impaired during the periods presented. During the year ended December 31, 2021 the Company disposed of fixed assets with a net book value of $89,000 and accumulated depreciation of $89,000.

8. Goodwill and Intangible Assets

The following sets forth goodwill and intangible assets by major asset class:

	Weighted Average Useful Life (Yrs)	December 31, 2021 Gross	December 31, 2021 Accumulated Amortization	December 31, 2021 Net Book Value	December 31, 2020 Gross	December 31, 2020 Accumulated Amortization	December 31, 2020 Net Book Value
Indefinite lived:							
Goodwill		$ 10,513,371	$ —	$ 10,513,371	$ 10,513,371	$ —	$ 10,513,371
Definite lived:							
Licenses	10	1,323,761	(1,305,600)	18,161	1,323,761	(1,276,852)	46,909
Bioject (a)	12	5,100,000	(2,735,556)	2,364,444	5,100,000	(2,468,889)	2,631,111
Other (b)	18	4,050,000	(3,806,250)	243,750	4,050,000	(3,581,250)	468,750
Total intangible assets	11	10,473,761	(7,847,406)	2,626,355	10,473,761	(7,326,991)	3,146,770
Total goodwill and intangible assets		$ 20,987,132	$ (7,847,406)	$ 13,139,726	$ 20,987,132	$ (7,326,991)	$ 13,660,141

(a) Bioject intangible assets represent the estimated fair value of developed technology and intellectual property which were recorded from an asset acquisition.

(b) Other intangible assets represent the estimated fair value of acquired intellectual property.

Aggregate amortization expense on intangible assets was $520,000, $547,000 and $1.1 million for the years ended December 31, 2021, 2020 and 2019, respectively. Amortization expense related to intangible assets at December 31, 2021 is expected to be incurred as follows:

Year ending December 31,	
2022	$ 493,000
2023	276,000
2024	253,000
2025	253,000
2026	253,000
Thereafter	1,098,000
	$ 2,626,000

There were no impairment or impairment indicators present and no losses were recorded during the years ended December 31, 2021, 2020 and 2019, respectively.

9. Convertible Debt

Convertible Senior Notes

On February 19, 2019 and March 1, 2019, the Company completed a private placement of $78.5 million aggregate principal amount of its 6.50% convertible senior notes due 2024 (the "Notes"). The Notes were sold in a private offering to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933, as amended. Net proceeds from the offering were $75.7 million.

The Notes are senior unsecured obligations of the Company and accrue interest payable in cash semi-annually in arrears on March 1 and September 1 of each year, beginning on September 1, 2019, at a rate of 6.50% per annum. The Notes will mature on March 1, 2024, unless earlier converted, redeemed or repurchased. Prior to the close of business on the business day immediately preceding November 1, 2023, the Notes will be convertible at the option of the holders only upon the satisfaction of certain circumstances. Thereafter, the Notes will be convertible at the option of the holders at any time until the close of business on the scheduled trading day immediately before the maturity date. Upon conversion, the Company will pay or deliver, as the case may be, cash, shares of its common stock or a combination of cash and shares of its common stock, at its election. The initial conversion rate was 185.8045 shares per $1,000 principal amount of Notes (equivalent to an initial conversion price of approximately $5.38 per share), subject to adjustment upon the occurrence of specified events.

The Company may redeem all, or any portion, of the Notes for cash if the last reported sale price per share of the Company's common stock exceeds 130% of the conversion price on (i) each of at least 20 trading days (whether or not consecutive) during the 30 consecutive trading days ending on, and including, the trading day immediately before the Company sends the related redemption notice; and (ii) the trading day immediately before the date the Company sends such redemption notice. The redemption price will be equal to 100% of the principal amount of the Notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

The Company evaluated the accounting for the issuance of the Notes and concluded that the embedded conversion features meet the requirements for a derivative scope exception for instruments that are both indexed to an entity's own stock and classified in stockholders' equity in its consolidated balance sheet, and that the cash conversion guidance applies. Therefore, the Notes issuance proceeds of $78.5 million are allocated first to the liability component based on the fair value of non-convertible debt with otherwise identical residual terms with the residual proceeds allocated to equity for the conversion features. The Company determined that the fair value of the non-convertible debt upon issuance of the Notes was $62.2 million and recorded this amount as a liability and the offsetting amount as a debt discount as a reduction to the carrying value of the Notes on the closing date. The debt issuance costs associated with the Notes of $2.8 million are allocated to the liability and equity component in the same proportion as the issuance proceeds.

The Company determined that all other features of the Notes were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements.

The Company determined that the expected life of the Notes was equal to the period through November 1, 2023 as this represents the point at which the Notes are initially subject to repurchase by the Company at the option of the holders. Accordingly, the total debt discount of $18.6 million, inclusive of the fair value of the embedded conversion feature derivative at issuance, is being amortized using the effective interest method through November 1, 2023. The effective interest rate of the liability component is 13.1%.

During the year ended December 31, 2020, the Company received notices for the conversion of $62.1 million of principal amount of the Notes, which were settled into an aggregate of 11,535,660 shares of the Company's common stock. The fair value of the Notes at the date of conversion was $43.7 million compared to the carrying value of $52.5 million, resulting in a $8.8 million gain on extinguishment of debt. This gain was recorded in the consolidated statement of operations. To measure the fair value of the converted Notes as of the conversion dates, the Company engaged a third-party valuation expert and utilized a binomial lattice model.

The balance of the Notes at December 31, 2021 is as follows:

Principal amount	$	78,500,000
Principal amount converted into common shares		(62,085,000)
Unamortized debt discount on the liability component		(1,591,909)
Unamortized debt issuance cost		(219,101)
Accrued interest		355,657
Net carrying amount	$	14,959,647

For the years ended December 31, 2021 and 2020, the Company recognized $1.9 million and $6.9 million, respectively, of interest expense related to the Notes, of which $1.1 million and $4.1 million, respectively, related to the contractual interest coupon.

As of December 31, 2021, future minimum payments due under the Notes, representing contractual amounts due, including interest based on the fixed rate of 6.5% per annum, are as follows:

2022	$	1,067,000
2023		1,067,000
2024		16,948,000
Total	$	19,082,000

August 2019 Convertible Bonds

On August 1, 2019, the Company closed a private placement of the August 2019 Bonds with an aggregate principal amount of 18 billion Korean Won (KRW) (approximately USD $15.0 million based on the exchange rate on the date of issuance) issued to institutional investors led by Korea Investment Partners (KIP), a global venture capital and private equity firm based in Seoul, Korea. Net proceeds from the offering were $14.5 million.

The August 2019 Bonds, which were unsecured obligations of the Company, were issued on August 1, 2019 and accrued interest at a coupon rate of 1.00% per annum, payable quarterly. The August 2019 Bonds were scheduled to mature on July 31, 2024, unless earlier converted or repurchased. On August 3, 2020, the August 2019 Bonds were converted in full into an aggregate of 4,962,364 shares of the Company's common stock, leaving no further August 2019 Bonds outstanding. The initial conversion rate was 211.0595 shares per KRW1,000,000 in principal amount (equivalent to an initial conversion price of approximately USD $4.00 per share based on the exchange rate as of July 30, 2019), subject to adjustment upon the occurrence of specified events. The conversion rate was reset on January 2, 2020 and was subject to reset quarterly thereafter if the current market price was lower than the conversion price then in effect. The conversion rate as of the date of conversion on August 1, 2020 was 275.69 shares per KRW1,000,000 in principal amount (equivalent to a conversion price of approximately USD $3.14 per share).

The Company evaluated the accounting for the issuance of the August 2019 Bonds and concluded that the embedded conversion feature was considered a derivative requiring bifurcation from the August 2019 Bonds as it did not meet the equity scope exception due to the fact that it was denominated in a currency other than the Company's functional currency. The fair value of the conversion feature at August 1, 2019 was $7.1 million, which was recorded as a reduction to the carrying value of the debt. This debt discount was being amortized to interest expense over the term of the debt using the effective interest method. The conversion option was accounted for as a derivative liability, which was revalued each reporting period with the resulting change in fair value reflected in other income (expense), net, in the consolidated statements of operations.

The Company determined that all other features of the August 2019 Bonds were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements.

At their issuance, the Company determined that the expected life of the August 2019 Bonds was through August 1, 2022 as this represented the point at which the August 2019 Bonds were initially subject to repurchase by the Company at the option of the holders. Accordingly, the total debt discount of $7.3 million, inclusive of the fair value of the embedded conversion feature derivative at issuance, was being amortized using the effective interest method through August 1, 2022. For the year ended December 31, 2020, the Company recognized $1.6 million of interest expense related to the August 2019 Bonds, of which $87,000 related to the contractual interest coupon.

Immediately prior to the August 2020 conversion in full of the August 2019 Bonds, the derivative liability associated with the August 2019 Bonds was revalued at $84.5 million. The change in fair value of the derivative liability was an increase of $75.7 million, which was recorded on the consolidated statement of operations for the year ended December 31, 2020. To measure the fair value of the derivative liability as of the conversion date, the Company engaged a third-party valuation expert.

Upon conversion, a loss on extinguishment of $8.2 million was recorded on the consolidated statement of operations for the year ended December 31, 2020. This loss represents the difference between (a) the calculated fair value of the derivative liability immediately prior to its derecognition plus the carrying amount of the debt component including any unamortized debt discount and issuance costs and (b) the fair value of the 4,692,364 shares of the Company's common stock issued upon conversion.

December 2019 Convertible Bonds

On December 26, 2019, the Company closed a private placement of convertible promissory notes (the “December 2019 Bonds”) with an aggregate principal amount of 4.7 billion KRW (approximately USD $4.1 million based on the exchange rate on the date of issuance) issued to a Korea-based institutional investor. Net proceeds from the offering were $4.0 million.

The December 2019 Bonds, which were unsecured obligations of the Company, were issued on December 31, 2019 and accrue interest at a coupon rate of 1.00% per annum, payable quarterly. The December 2019 Bonds were scheduled to mature on December 31, 2024, unless earlier converted or repurchased. On March 17, 2021, the December 2019 Bonds were converted in full into an aggregate of 1,009,450 shares of the Company's common stock, leaving no further December 2019 Bonds outstanding. The initial conversion rate was 214.7766 shares per KRW1,000,000 principal amount of Bonds (equivalent to an initial conversion price of approximately USD $4.00 per share based on the exchange rate as of December 19, 2019), subject to adjustment upon the occurrence of certain events. As of the conversion date of March 17, 2021, the conversion rate had not been reset from the initial conversion rate.

The Company evaluated the accounting for the issuance of the December 2019 Bonds and concluded that the embedded conversion feature did not require bifurcation from the December 2019 Bonds. Although the embedded conversion feature met the definition of a derivative, it qualified for the equity scope exception for instruments that are both indexed to an entity’s own stock and classified in stockholders’ equity in its consolidated balance sheet. The December 2019 Bonds were denominated in a foreign currency other than the Company’s functional currency, which would typically violate the settlement provision criteria when analyzing whether the conversion option is indexed to an entity’s own stock. However, per the terms of the agreement, the functional currency rate required to be used in a conversion scenario was fixed as of the date preceding the date of issuance of the Bonds. Therefore, the fluctuation in functional currency did not impact the settlement of the conversion option. Further,

as there was no cash conversion feature or beneficial conversion feature on the date of issuance, and the Bonds were not issued at a substantial premium, all of the proceeds were recorded as a liability.

The Company determined that all other features of the December 2019 Bonds were clearly and closely associated with a debt host and did not require bifurcation as a derivative liability, or the fair value of the feature was immaterial to the Company's consolidated financial statements.

At their issuance, the Company determined that the expected life of the December 2019 Bonds was through December 31, 2022 as this represented the point at which the December 2019 Bonds were initially subject to repurchase by the Company at the option of the holders. The effective interest rate of the December 2019 Bonds is 6.2%. For the years ended December 31, 2021 and 2020, the Company recognized $50,000 and $253,000, respectively, of interest expense related to the December 2019 Bonds, of which $9,000 and $40,000, respectively, related to the contractual interest coupon.

As of December 31, 2021, all outstanding December 2019 Bonds were converted into 1,009,450 shares of the Company's common stock. Upon conversion, the $4.4 million carrying value of the December 2019 Bonds was reclassified to stockholders' equity.

10. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses at December 31, 2021 and 2020 consisted of the following:

	2021	2020
Trade accounts payable	$ 24,213,673	$ 825,516
Accrued compensation	16,112,912	13,127,257
Accrued subcontract costs	11,602	247,796
Other accrued expenses	7,306,343	7,003,239
	$ 47,644,530	$ 21,203,808

11. Stockholders' Equity

Preferred Stock

			Shares Outstanding as of December 31,	
	Shares Authorized	Shares Issued	2021	2020
Series C Preferred Stock, par $0.001	1,091	1,091	9	9

In June 2020, 14 shares of the Company's Series C preferred stock were converted into an aggregate of 5,147 shares of the Company's common stock.

The holder of a share or shares of Series C preferred stock has the right at any time, at such holder's option, to convert all or any lesser portion of such holder's shares of the preferred stock into fully paid and non-assessable shares of common stock. As of December 31, 2021, the conversion value was $27.20 per share, such that the outstanding shares of Series C preferred stock were convertible into an aggregate of 3,309 shares of common stock.

Common Stock

On November 9, 2021, the Company entered into an ATM Equity Offering℠ Sales Agreement (the "2021 Sales Agreement") with outside sales agents (collectively, the "Sales Agents") for the offer and sale of its common stock for an aggregate offering price of up to $300.0 million. The 2021 Sales Agreement provides that the Sales Agents will be entitled to compensation in an amount equal to up to 3.0% of the gross sales proceeds of any common stock sold through the Sales Agents under the 2021 Sales Agreement. For the year ended December 31, 2021, the Company sold 6,955,341 shares of its common stock under the 2021 Sales Agreement. The sales were made at a weighted average price of $6.96 per share, resulting in aggregate net proceeds of $47.7 million. As of December 31, 2021 there was $251.6 million of remaining capacity under the 2021 Sales Agreement.

On January 25, 2021, the Company closed an underwritten public offering of 20,355,000 shares of common stock at a public offering price of $8.50 per share. The net proceeds to the Company, after deducting the underwriters' discounts and commissions and other offering expenses, were $162.1 million.

On April 3, 2020, the Company and the Placement Agent entered into a new Sales Agreement (the "2020 Sales Agreement") to sell shares of its common stock. On April 3, 2020 and May 12, 2020, the Company filed prospectus supplements pursuant to the 2020 Sales Agreement for the offer and sale of its Common Stock for aggregate gross proceeds of up to an aggregate of $250.0 million.

During the year ended December 31, 2020, the Company sold a total of 22,919,934 shares of its common stock under the 2020 Sales Agreement. The sales were made at a weighted average price of $10.91 per share resulting in aggregate net proceeds of $246.2 million. As of December 31, 2020, there was no remaining capacity under the 2020 Sales Agreement.

In May 2018, the Company entered into a Sales Agreement with an outside placement agent (the “Placement Agent”) to sell shares of its common stock with aggregate gross proceeds of up to $100.0 million, from time to time, through an “at-the-market” equity offering program under which the Placement Agent will act as sales agent. During the first quarter of 2020, the Company and the Placement Agent entered into amendments to the Sales Agreement (as so amended, the "2018 Sales Agreement") to increase the amount of common stock that could be sold under the 2018 Sales Agreement from $100.0 million to $250.0 million. During the three months ended March 31, 2020, the Company sold 43,148,952 shares of its common stock under the 2018 Sales Agreement. The sales were made at a weighted average price of $4.92 per share, resulting in aggregate net proceeds of $208.2 million. As of March 31, 2020, there was no remaining capacity under the 2018 Sales Agreement.

Stock Options and Restricted Stock Units

The Company has a stock-based incentive plan, the 2016 Omnibus Incentive Plan (as amended to date, the "2016 Incentive Plan"), pursuant to which the Company may grant stock options, restricted stock awards, restricted stock units and other stock-based awards or short-term cash incentive awards to employees, directors and consultants.

The 2016 Incentive Plan was originally approved by the Company's stockholders on May 13, 2016, and an amendment to the plan to increase the number of shares available for issuance was approved by the stockholders on May 8, 2019. As of December 31, 2021, the maximum number of shares of the Company’s common stock available for issuance over the term of the 2016 Incentive Plan was 20,000,000 shares. On the first business day of each calendar year, such maximum number of shares shall be increased by 2,000,000 shares of common stock unless the Board determines, prior to January 1 for any such calendar year, to increase such maximum amount by a fewer number of shares or not to increase the maximum amount at all for such year. On January 1, 2022, the maximum number of shares increased by 2,000,000. At December 31, 2021, the Company had 4,481,745 shares of common stock available for future grant under the 2016 Incentive Plan, 2,448,868 shares underlying outstanding but unvested restricted stock units and options outstanding to purchase 8,060,957 shares of common stock under the 2016 Incentive Plan. The awards granted and available for future grant under the 2016 Incentive Plan generally vest over three years and have a maximum contractual term of ten years. The 2016 Incentive Plan terminates by its terms on March 9, 2026.

The Amended and Restated 2007 Omnibus Incentive Plan (the "2007 Incentive Plan") was adopted on March 31, 2007 and terminated by its terms on March 31, 2017. At December 31, 2021, the Company had options outstanding to purchase 2,428,036 shares of common stock under the 2007 Incentive Plan. The awards granted under the 2007 Incentive Plan generally vest over three years and have a maximum contractual term of ten years.

Total employee and director stock-based compensation expense recognized in the consolidated statements of operations for the years ended December 31, 2021, 2020 and 2019 was $25.0 million, $14.5 million and $9.8 million, respectively, of which $13.4 million, $8.0 million and $5.9 million was included in research and development expenses and $11.6 million, $6.5 million and $3.9 million was included in general and administrative expenses, respectively.

At December 31, 2021 and 2020, there was $16.5 million and $4.4 million, respectively, of total unrecognized compensation expense related to unvested stock options, which is expected to be recognized over a weighted-average period of 2.0 years and 1.4 years, respectively.

At December 31, 2021 and 2020, there was $13.4 million and $10.9 million, respectively, of total unrecognized compensation expense related to unvested restricted stock units, which is expected to be recognized over a weighted-average period of 1.8 years and 1.9 years, respectively.

The fair value of stock options granted to non-employees was estimated using the Black-Scholes pricing model. Total stock-based compensation expense for stock options and restricted stock units granted to non-employees for the years ended December 31, 2021, 2020 and 2019 was $1.4 million, $1.2 million and $970,000, respectively. As of December 31, 2021, options to purchase 632,375 shares of common stock granted to non-employees remained outstanding.

The following table summarizes total stock options outstanding at December 31, 2021:

Exercise Price	Options Outstanding: Shares Underlying Options Outstanding	Options Outstanding: Weighted-Average Remaining Contractual Life (in Years)	Options Outstanding: Weighted Average Exercise Price	Options Exercisable: Shares Underlying Options Exercisable	Options Exercisable: Weighted Average Exercise Price
$1.60-$3.00	272,063	1.8	$ 2.25	262,148	$ 2.24
$3.01-$6.00	2,583,652	6.8	$ 3.80	2,137,202	$ 3.88
$6.01-$9.00	4,148,238	6.4	$ 7.60	2,848,150	$ 7.48
$9.01-$12.00	2,562,668	8.8	$ 10.95	827,259	$ 10.77
$12.01-$15.00	824,184	5.1	$ 13.54	663,646	$ 13.40
$15.01-$25.62	98,188	8.6	$ 20.64	52,227	$ 20.67
	10,488,993	6.9	$ 7.93	6,790,632	$ 7.22

At December 31, 2021, the aggregate intrinsic value of options outstanding was $3.8 million, the aggregate intrinsic value of options exercisable was $3.1 million, and the weighted average remaining contractual term of options exercisable was 5.9 years.

At December 31, 2021, the aggregate intrinsic value of unvested restricted stock units was $12.2 million and the aggregate intrinsic value of restricted stock units which vested during the year ended December 31, 2021 was $12.7 million.

At December 31, 2021, options to purchase 10,488,993 shares of common stock and 2,448,868 restricted stock units were expected to vest.

Stock option activity under the Company's equity incentive plans during the year ended December 31, 2021 was as follows:

	Number of Shares	Weighted-Average Exercise Price
Balance, December 31, 2020	8,906,624	$ 6.78
Granted	3,483,118	10.29
Exercised	(1,310,263)	5.09
Cancelled	(590,486)	10.81
Balance, December 31, 2021	10,488,993	$ 7.93

Restricted stock unit activity under the Company's equity incentive plans during the year ended December 31, 2021 was as follows:

	Number of Shares
Balance, December 31, 2020	2,558,052
Granted	1,392,124
Vested	(1,387,384)
Cancelled	(113,924)
Balance, December 31, 2021	2,448,868

The weighted average exercise price per share was $4.56 for the 7,000 options which expired during the year ended December 31, 2021, $4.44 for the 78,750 options which expired during the year ended December 31, 2020 and $6.27 for the 324,502 options which expired during the year ended December 31, 2019.

The weighted average grant date fair value per share was $7.61, $6.87 and $2.19 for options granted during the years ended December 31, 2021, 2020 and 2019, respectively.

The weighted average grant date fair value was $10.37, $9.12 and $3.09 per share for restricted stock units granted during the years ended December 31, 2021, 2020 and 2019, respectively.

The Company received $6.7 million, $12.3 million and $113,000 in proceeds from the exercise of stock options during the years ended December 31, 2021, 2020 and 2019, respectively. The aggregate intrinsic value of options exercised was $7.0 million, $14.2 million and $25,000 during the years ended December 31, 2021, 2020 and 2019, respectively.

On August 28, 2020, the Company granted 663,353 performance-based RSUs to key employees under the 2016 Incentive Plan. The RSUs will vest in two tranches as follows: 50% of the shares in each tranche will vest upon achievement of the predetermined performance milestones and the remaining 50% of the shares in each tranche will vest upon subsequent completion of a one-year service period. The grant date fair value of the performance-based RSUs was $8.0 million based on the grant date closing price per share of $12.06. As of December 31, 2021, the underlying performance milestones of the RSUs were not probable of achievement, and no stock-based compensation expense was recognized for the performance-based RSUs for the year then ended.

12. Commitments and Contingencies

Leases

The Company leases approximately 82,200 square feet of office, laboratory, and manufacturing space in San Diego, California and 57,360 square feet of office space in Plymouth Meeting, Pennsylvania under various non-cancellable operating lease agreements with remaining lease terms as of December 31, 2021 of 1.9 years to 8.0 years, which represent the non-cancellable periods of the leases. The Company has excluded the extension options from its lease terms in the calculation of future lease payments as they are not reasonably certain to be exercised. The Company's lease payments consist primarily of fixed rental payments for the right to use the underlying leased assets over the lease terms as well as payments for common area maintenance and administrative services. The Company has received customary incentives from its landlords, such as reimbursements for tenant improvements and rent abatement periods, which effectively reduce the total lease payments owed for these leases.

The Company performed an evaluation of its contracts with customers and suppliers in accordance with ASC Topic 842 and determined that, except for the real estate leases described above and various copier leases, none of its other contracts contain a right-of-use asset.

Operating lease right-of-use assets and liabilities on the consolidated balance sheet represents the present value of the remaining lease payments over the remaining lease terms. Payments for additional monthly fees to cover the Company's share of certain facility expenses are not included in operating lease right-of-use assets and liabilities. The Company uses its incremental borrowing rate to calculate the present value of its lease payments, as the implicit rates in the leases are not readily determinable.

As of December 31, 2021, the maturities of the Company's operating lease liabilities were as follows:

Year ending December 31,	
2022	$ 4,085,000
2023	4,089,000
2024	3,050,000
2025	3,063,000
2026	3,139,000
Thereafter	6,749,000
Total remaining lease payments	24,175,000
Less: present value adjustment	(6,111,000)
Total operating lease liabilities	18,064,000
Less: current portion	(2,604,000)
Long-term operating lease liabilities	$ 15,460,000
Weighted-average remaining lease term	6.6 years
Weighted-average discount rate	8.5 %

Lease costs included in operating expenses in the consolidated statements of operations for the years ended December 31, 2021, 2020 and 2019 were $3.4 million, $3.4 million and $3.2 million, respectively. Operating lease costs consisting of the fixed lease payments included in operating lease liabilities are recorded on a straight-line basis over the lease terms. Variable lease costs are recorded as incurred.

In the fourth quarter of 2019, the Company entered into two agreements to sublease a total of approximately 13,500 square feet in its Plymouth Meeting headquarters through periods between December 31, 2022 and March 31, 2025.

In the normal course of business, the Company is a party to a variety of agreements pursuant to which it may be obligated to indemnify the other party. It is not possible to predict the maximum potential amount of future payments under these types of agreements due to the conditional nature of the Company's obligations and the unique facts and circumstances involved in each particular agreement. Historically, payments made by the Company under these types of agreements have not had a material effect on its business, consolidated results of operations or financial condition.

Other Commitments

The Company has existing supply agreements with contract manufacturers to manufacture INO-4800 drug substance. Under the terms of the agreements, the Company is committed to certain minimum purchases in 2022. At December 31, 2021, the Company had a $47.4 million minimum purchase obligation in connection with these agreements.

Legal Proceedings

Securities Litigation

On March 12, 2020, a purported shareholder class action complaint, McDermid v. Inovio Pharmaceuticals, Inc. and J. Joseph Kim, was filed in the United States District Court for the Eastern District of Pennsylvania, naming the Company and J. Joseph Kim, the Company's Chief Executive Officer, as defendants. The lawsuit alleges that the Company made materially false and misleading statements regarding its development of a vaccine for COVID-19 in its public disclosures in violation of certain federal securities laws. The plaintiff seeks unspecified monetary damages on behalf of the putative class and an award of costs and expenses, including reasonable attorneys' fees. On August 3, 2020, the lead plaintiff filed a consolidated complaint, naming the Company and three of its officers as defendants. On September 21, 2020, the lead plaintiff and another purported stockholder filed a first amended complaint, naming the Company and three of its officers as defendants. Defendants filed a motion to dismiss plaintiff's first amended complaint on November 5, 2020. On February 16, 2021, the court issued an order granting in part, and denying in part, the defendants' motion to dismiss. The court granted the defendants' motion to dismiss, and dismissed with prejudice, the claims premised on certain of the Company's statements. The court denied defendants' motion to dismiss as to the remaining statements. On March 9, 2021, the defendants filed their answer to the complaint. The case is currently in discovery. On July 29, 2021, the plaintiffs moved to certify the class action. That motion is fully briefed and remains pending. On February 17, 2022, the court granted Plaintiffs' motion for leave to amend their complaint, and further ordered that the amended complaint is deemed filed as of February 17. Defendants intend to move to dismiss the new allegations in the amended complaint.

On April 20, 2020, a purported shareholder derivative complaint, Behesti v. Kim, et al., was filed in the United States District Court for the Eastern District of Pennsylvania, naming eight current and former directors of the Company as defendants. The lawsuit asserts state and federal claims and is based on the same alleged misstatements as the shareholder class action complaint. The lawsuit accuses the Company's board of directors of failing to exercise reasonable and prudent supervision over the Company's management, policies, practices, and internal controls. The plaintiff seeks unspecified monetary damages on behalf of the Company as well as governance reforms. On June 5, 2020, the court stayed the Beheshti action pending resolution of a forthcoming motion to dismiss the McDermid securities class action or until any party provides notice that they no longer consent to the stay. On June 12, 2020 and June 15, 2020, two additional shareholder derivative complaints were filed in the United States District Court for the Eastern District of Pennsylvania, captioned Isman v. Benito, et al. and Devarakonda et al. v Kim, et. al. The complaints assert substantially similar claims as the Beheshti action and name the Company's current directors as defendants. The Devarakonda complaint also names one of the Company's former directors as a defendant. On July 21, 2020, the court consolidated the three derivative cases under the caption In re Inovio Pharmaceuticals, Inc. Derivative Litigation. The consolidated action is stayed.

On July 7, 2020, a fourth shareholder derivative complaint, Fettig v. Kim et al., was filed in the United States District Court for the Eastern District of Pennsylvania, naming eight current and former directors of the Company as defendants. The complaint asserts substantially similar claims as those in the consolidated derivative action. On August 27, 2020, the Fettig action was consolidated with the other derivative cases, which remain stayed as explained above.

The Company intends to defend these actions vigorously.

VGXI Litigation

On June 3, 2020, the Company filed a complaint in the Court of Common Pleas of Montgomery County, Pennsylvania against VGXI, Inc. and GeneOne Life Science, Inc., or GeneOne, and together with VGXI, Inc. collectively referred to as VGXI, alleging that VGXI had materially breached the Company's supply agreement with them. The complaint seeks declaratory judgments, specific performance of the agreement, injunctive relief, an accounting, damages, attorneys' fees, interest, costs and other relief from VGXI. On June 3, 2020, the Company filed a petition for preliminary injunction, which was

denied on June 25, 2020. On June 26, 2020, the Company filed notice of appeal of the denial of the petition with the Pennsylvania Superior Court.

On July 7, 2020, VGXI filed an answer, new matter and counterclaims against the Company, alleging that the Company had breached the supply agreement, as well as misappropriation of trade secrets and unjust enrichment. The counterclaims seek injunctive relief, damages, attorneys' fees, interest, costs and other relief from the Company. Also, on July 7, 2020, VGXI filed a third-party complaint against Ology Bioservices, Inc., a contract manufacturing organization that the Company had engaged to provide services similar to those that were being provided by VGXI. On July 27, 2020, the Company filed an answer to VGXI's counterclaims, disputing the allegations and the claims raised in VGXI's filing. On October 1, 2020, the Company filed a notice of discontinuance of appeal with the Pennsylvania Superior Court. A trial date for the litigation has not been set.

The Company intends to aggressively prosecute the claims set forth in its complaint against VGXI and to vigorously defend itself against VGXI's counterclaims.

GeneOne Litigation

On December 7, 2020, GeneOne filed a complaint in the Court of Common Pleas of Montgomery County, Pennsylvania against the Company, alleging that the Company had breached the CELLECTRA Device License Agreement, or the Agreement, between the Company and GeneOne. The Company terminated the Agreement on October 9, 2020. The complaint asserts claims for breach of contract, declaratory judgment, unfair competition, and unjust enrichment. The complaint seeks injunctive relief, an accounting, damages, disgorgement of profits, attorneys' fees, interest, and other relief from the Company. On January 29, 2021, the Company filed preliminary objections to the complaint. On August 23, 2021, the court overruled the Company's preliminary objections to the complaint. On September 13, 2021, the Company filed an answer to the complaint, new matter, and counterclaims. The Company's counterclaims allege that GeneOne breached the Agreement and assert claims for breach of contract and declaratory judgment. The counterclaims seek damages, interest, expenses, attorney's fees, and costs. On October 18, 2021, GeneOne filed its answer to the Company's counterclaims and new matter. On November 8, 2021, we filed our answer to GeneOne's new matter. A trial date for this litigation has not been set.

The Company intends to aggressively prosecute the claims set forth in its counterclaims against GeneOne and to vigorously defend itself against the claims in GeneOne's complaint.

Other Matters

From time to time, the Company may be involved in disputes, including litigation, relating to claims arising out of operations in the normal course of our business. Any of these claims could subject the Company to costly legal expenses and, while the Company generally believes that it has adequate insurance to cover many different types of liabilities, its insurance carriers may deny coverage or its policy limits may be inadequate to fully satisfy any damage awards or settlements. If this were to happen, the payment of any such awards could have a material adverse effect on the Company's consolidated results of operations and financial position. Additionally, any such claims, whether or not successful, could damage the Company's reputation and business. Except as described above, the Company is not a party to any legal proceedings, the adverse outcome of which, in management's opinion, individually or in the aggregate, would be reasonably expected to have a material adverse effect on the Company's consolidated results of operations or financial position.

13. Income Taxes

In accordance with the accounting guidance for income taxes, a deferred tax asset or liability is determined based on the difference between the financial statement and tax basis of assets and liabilities as measured by the enacted tax rates which will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax asset will be realized.

The components of pretax loss from operations before equity method investment are as follows:

	Year Ended December 31,		
	2021	2020	2019
U.S. Domestic	$ (302,614,003)	$ (162,664,355)	$ (120,809,112)
Foreign	(610,320)	(225,949)	—
Pretax loss from operations before equity method investment	$ (303,224,323)	$ (162,890,304)	$ (120,809,112)

There was no provision for (benefit from) income taxes for the years ended December 31, 2021 and 2020. There was an income tax benefit of $(257,000) for the year ended December 31, 2019.

The reconciliation of income taxes attributable to continuing operations computed at the statutory tax rates to income tax expense (benefit), using a 21% statutory tax rate for December 31, 2021, 2020 and 2019, is as follows:

	Year Ended December 31,		
	2021	2020	2019
Income (benefit) taxes at statutory rates	$ (63,677,000)	$ (34,207,000)	$ (25,370,000)
State income tax, net of federal benefit	(3,447,000)	—	—
Change in valuation allowance	77,424,000	21,428,000	25,457,000
Nondeductible loss on extinguishment of debt	—	14,450,000	—
Research and development tax credits	(16,523,000)	(2,650,000)	(3,838,000)
Stock-based compensation	483,000	(1,953,000)	1,114,000
Uncertain tax positions	6,509,000	1,068,000	1,537,000
Deconsolidation of subsidiary	—	853,000	—
Expired NOLs and credits	616,000	468,000	616,000
Limited NOLs and credits	(542,000)	(368,000)	(616,000)
Change in tax rates	—	—	12,000
Foreign tax rate differential	(24,000)	(9,000)	—
Other	(819,000)	920,000	831,000
	$ —	$ —	$ (257,000)

The income tax benefit recorded during the year ended December 31, 2019 of $257,000 was principally due to a requirement under ASC Topic 740, *Accounting for Income Taxes*, that a company must consider all sources of income in order to determine the tax benefit resulting from a loss from continuing operations. As a result of the requirement under ASC 740-20-45-7, the pretax income which the Company generated from other comprehensive income was a source of income which resulted in the partial realization of the current year loss from continuing operations.

Significant components of the Company's deferred tax assets and liabilities as of December 31, 2021 and 2020 are shown below:

	As of December 31,	
	2021	2020
Deferred tax assets:		
Capitalized research expense	$ 4,200,000	$ 5,250,000
NOL carryforwards	197,144,000	127,835,000
Research and development and other tax credits	23,005,000	13,242,000
Deferred revenue	987,000	1,628,000
Stock-based compensation	3,599,000	3,256,000
Acquired intangibles	637,000	757,000
Interest expense	83,000	564,000
Investment in affiliated entity	750,000	542,000
Lease liability	3,793,000	4,283,000
Other	5,973,000	6,127,000
	240,171,000	163,484,000
Valuation allowance	(237,205,000)	(159,705,000)
Total deferred tax assets	2,966,000	3,779,000
Deferred tax liabilities:		
Acquired intangibles	(194,000)	(179,000)
Right of use asset	(2,430,000)	(2,676,000)
Note discount	(321,000)	(469,000)
Fixed assets	(53,000)	(487,000)
Net deferred tax liabilities	$ (32,000)	$ (32,000)

As of December 31, 2021, the Company had federal, California and Pennsylvania tax net operating loss (NOL) carryforwards of $864.5 million, $146.5 million and $89.0 million, respectively, net of the net operating losses that will expire due to IRC Section 382 limitations. The aggregate federal net operating losses generated in 2018 and after for the amount of $568.9 million will carryforward indefinitely and be available to offset up to 80% of future taxable income each year. The federal NOL carryforward began to expire in 2021, and the California and Pennsylvania NOL carryforwards will begin and have begun to expire in 2028 and 2021, respectively, unless previously utilized.

The Company also has Korean NOL carryforwards of $806,000 as of December 31, 2021. The Korean NOLs are available to offset up to 60% of future taxable income and will begin to expire in 2030, unless previously utilized.

In addition, as of December 31, 2021, the Company had federal and state research and development (R&D) tax credit carryforwards of $35.1 million and $4.4 million, respectively. The federal tax credit carryforwards will begin to expire in 2029. The California research tax credits do not expire.

Based upon statute, federal and state losses and credits are expected to expire as follows (in millions):

Expiration Date:	Federal NOLs	State NOLs	Foreign NOLs	Federal R&D	State R&D
2022	$ 6.1	$ 0.4	$ —	$ —	$ —
2023	5.3	1.2	—	—	—
2024	16.5	9.1	—	—	—
2025 and thereafter	267.7	224.9	0.8	35.1	—
Indefinite	568.9	—	—	—	4.4
	$ 864.5	$ 235.6	$ 0.8	$ 35.1	$ 4.4

Pursuant to Internal Revenue Code (IRC) Sections 382 and 383, annual use of the Company's NOL and R&D credit carryforwards may be limited in the event that a cumulative change in ownership of more than 50% occurs within a three-year period. The Company has completed an IRC Section 382/383 analysis regarding the limitation of NOL and R&D credit carryforwards as of December 31, 2021. As a result of the analysis, the Company estimates that approximately $9.7 million of tax benefits related to NOL and R&D carryforwards will expire unused. Accordingly, the related NOL and R&D credit carryforwards have been removed from deferred tax assets, accompanied by a corresponding reduction of the valuation allowance. Due to the existence of the valuation allowance, limitations created by current and future ownership changes, if any, related to the Company's operations in the United States will not impact its effective tax rate. Any additional ownership changes may further limit the ability to use the NOL and R&D carryforwards.

The Tax Cuts and Jobs Act of 2017 subjects a U.S. stockholder to tax on Global Intangible Low-Taxed Income (GILTI) earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740, No. 5, Accounting for Global Intangible Low-Taxed Income, states that an entity can make an accounting policy election to recognize deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. The Company has elected to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. For 2021, the Company did not generate any GILTI due to losses earned by its foreign subsidiary.

On March 27, 2020, the CARES Act was enacted in response to the COVID-19 pandemic. The CARES Act, among other things, permits federal NOL carryovers and carrybacks to offset 100% of taxable income for taxable years beginning before 2021. In addition, the CARES Act allows federal NOLs incurred in 2019, 2020, and 2021 to be carried back to each of the five preceding taxable years to generate a refund of previously paid income taxes. Due to the Company's history of net operating losses, the CARES Act is not expected to have a material impact on the Company's financial statements.

The following table summarizes the activity related to the Company's unrecognized tax benefits:

	Year ended December 31,		
	2021	2020	2019
Balance at beginning of the year	$ 12,210,000	$ 11,204,000	$ 9,632,000
Increases related to current year tax positions	6,602,000	1,043,000	1,575,000
Increases (decreases) related to prior year tax positions	7,000	27,000	(3,000)
Other	—	(64,000)	—
Balance at end of the year	$ 18,819,000	$ 12,210,000	$ 11,204,000

The amount of unrecognized tax benefits that, if recognized and realized, would affect the effective tax rate was $17.4 million, $10.9 million and $9.9 million as of December 31, 2021, 2020 and 2019, respectively, subject to valuation allowances. The Company has not recorded any interest and penalties on the unrecognized tax positions as the Company has continued to generate net operating losses after accounting for the unrecognized tax benefits. The Company does not anticipate that the total amount of unrecognized tax benefits will significantly increase or decrease within twelve months of the reporting date.

The Company and its subsidiaries are subject to U.S. federal income tax as well as income tax in multiple state and foreign jurisdictions. With few exceptions, the Company is no longer subject to United States federal income tax examinations for years before 2018 and state and local income tax examinations before 2017. However, to the extent allowed by law, the tax authorities may have the right to examine prior periods where net operating losses were generated and carried forward, and make adjustments up to the amount of the NOL carryforward amount. The Company is subject to examinations for tax years beginning in 2020 in Korea. The Company is not currently under Internal Revenue Service ("IRS"), state, local or foreign tax examination.

14. 401(k) Plan

The Company has adopted a 401(k) Profit Sharing Plan covering substantially all of its employees. The defined contribution plan allows the employees to contribute a percentage of their compensation each year. The Company currently matches 50% of its employees' contributions, up to 6% of their annual compensation. The Company's contributions are recorded as expense in the accompanying consolidated statements of operations and totaled $1.5 million, $1.1 million and $1.2 million for the years ended December 31, 2021, 2020 and 2019, respectively.

15. Related Party Transactions

Plumbline Life Sciences, Inc.

The Company owned 597,808 shares of common stock in Plumbline Life Sciences, Inc. ("PLS") as of December 31, 2021 and 2020, representing a 18.9% and 19.7% ownership interest, respectively. One of the Company's directors, Dr. David B. Weiner, acts as a consultant to PLS.

Revenue recognized from PLS consists of milestone, license and patent fees. For the years ended December 31, 2021 and 2020, the Company recognized revenue from PLS of $245,000 and $1.4 million, respectively. At December 31, 2021 and 2020, the Company had an accounts receivable balance of $25,000 and $67,000, respectively, related to PLS.

The Wistar Institute

The Company's director Dr. David B. Weiner is a director of the Vaccine Center of The Wistar Institute ("Wistar"). Dr. Weiner is also the Executive Vice President of Wistar.

In March 2016, the Company entered into collaborative research agreements with Wistar for preventive and therapeutic DNA-based immunotherapy applications and products developed by Dr. Weiner and Wistar for the treatment of cancers and infectious diseases. Under the terms of the agreement, the Company reimbursed Wistar for all direct and indirect costs incurred in the conduct of the collaborative research, not to exceed $3.1 million during the five-year term of the agreement. In March 2021, upon expiration of the March 2016 agreements, the Company entered into new collaborative research agreements with Wistar with the same terms. The Company will have the exclusive right to in-license new intellectual property developed in this agreement.

In 2021, the Company entered into collaborative research agreements with Wistar in support of the clinical development of INO-4800. Under the terms of these collaborative research agreements, the Company will reimburse Wistar for all direct and indirect costs incurred in the conduct of the collaborative research, not to exceed $1.9 million during the two-year term of the agreements.

In November 2016, the Company received a $6.1 million sub-grant through Wistar to develop a DMAb against the Zika infection, with funding through December 2021.

The Company is also a collaborator with Wistar on an Integrated Preclinical/Clinical AIDS Vaccine Development grant from the NIAID, with funding through February 2022.

In 2020, the Company received a $10.7 million sub-grant through Wistar, which was amended in 2021 to $13.5 million, for the preclinical development and translational studies of dMAbs as countermeasures for COVID-19, with funding through September 2022. The sub-grant also includes an option for an additional $6.0 million in funding through September 2024, of which $3.3 million has been exercised as of December 31, 2021.

Deferred grant funding recognized from Wistar and recorded as contra-research and development expense is related to work performed by the Company on the research sub-contract agreements. For the years ended December 31, 2021 and 2020, the Company recorded $3.0 million and $1.9 million, respectively, as contra-research and development expense from Wistar.

Research and development expenses recorded from Wistar relate primarily to the collaborative research agreements and sub-contract agreements related to Gates and CEPI (see Note 4). Research and development expenses recorded from Wistar for the years ended December 31, 2021 and 2020 were $2.9 million and $2.3 million, respectively. At December 31, 2021 and 2020, the Company had an accounts receivable balance of $2.6 million and $425,000, respectively, and an accounts payable and accrued liability balance of $548,000 and $643,000, respectively, related to Wistar. As of December 31, 2021, the Company had a prepaid expense balance of $261,000 and recorded $37,000 as deferred grant funding on its consolidated balance sheet related to Wistar.

16. Geneos Therapeutics, Inc.

In August 2016, the Company formed Geneos to develop and commercialize neoantigen-based personalized cancer therapies. Geneos was considered a variable interest entity (VIE) for which the Company was the primary beneficiary. In February 2019, Geneos completed the initial closing of a Series A preferred stock financing. The Company invested $1.2 million in the Series A preferred stock financing, which was led by an outside investor. Following this transaction, the Company held 61% of the outstanding equity, on an as-converted to common stock basis, of Geneos and continued to consolidate its investment in Geneos under ASC 810, *Consolidation*.

In January 2020, Geneos completed the second closing of the Series A preferred stock financing, in which the Company invested $800,000. Following this transaction, as of March 31, 2020, the Company held 52% of the outstanding equity, on an as-converted to common stock basis, of Geneos and continued to consolidate its investment in Geneos.

In June 2020, Geneos closed an additional Series A preferred stock financing round, in which the Company invested $800,000. Following this transaction, the Company owned 47% of the outstanding equity of Geneos on an as-converted to common stock basis. This transaction triggered a VIE reconsideration, as the Company no longer held a controlling financial interest. Based on the Company's assessment, Geneos continued to be a VIE as it did not have sufficient equity at risk to finance its activities without additional subordinated financial support. However, the Company was not the primary beneficiary of Geneos, as it did not have the power to direct the activities that most significantly impact Geneos' economic performance. Accordingly, the Company deconsolidated its investment in Geneos as of June 1, 2020, resulting in a gain of $4.1 million, of which $2.4 million related to the remeasurement of the retained noncontrolling interest investment to fair value. The gain has been recorded separately on the Company's consolidated statement of operations. The following table shows the amounts related to the deconsolidation accounting:

Working capital (excluding cash)	$	(59,992)
Note payable		171,620
Fixed assets, net of accumulated depreciation		(16,340)
Carrying value of noncontrolling interest		3,181,640
Fair value of investment in Geneos retained		3,618,998
Gain on deconsolidation of Geneos		(4,121,075)
Decrease in cash resulting from the deconsolidation of Geneos	$	2,774,851

The details of the Company's 47% retained equity investment in Geneos are shown in the table below, with fair values calculated as of June 1, 2020, the date of deconsolidation.

Geneos Share Class	Shares	Price per Share	Fair Value
Common	3,000,000	$ 0.273	$ 819,000
Preferred	2,113,206	$ 1.325	$ 2,799,998
Total	5,113,206		$ 3,618,998

The fair value of Geneos Series A preferred stock was based on the per share price paid by third-party investors in connection with the most recent closing of the Series A preferred stock financing for Geneos on June 1, 2020. The fair value of Geneos common stock was determined by a third-party valuation, as there is no public market for such stock. Geneos's enterprise value, which was estimated using a market approach that derived an implied total equity value from a transaction involving its own securities, was allocated to all classes of equity using the option pricing method. Under the option pricing method, each equity class was modeled as having a call option with a distinct claim on the total value of Geneos. Each option's

exercise price was based on the total value available for each participating security holder. The characteristics of each class of ownership determined the claim on the total value for that class of ownership.

The estimated value allocated to common stock included assumptions related to the fair value of the enterprise, expected volatility, expected term, and risk-free interest rate. Expected volatility was based on historical asset volatilities derived from daily stock price changes of guideline public companies. The estimated expected term was based on a weighted average of the estimated time to Geneos's next financing and successful exit timing assumption. The risk-free interest rate was based on the yield of U.S. Treasury with a comparable term. Geneos's common stock is classified as a Level 3 financial instrument. The assumptions used in the fair value calculation as of June 1, 2020 are presented below:

Expected term (years)	2.92
Volatility	70%
Risk-free interest rate	2.46%
Geneos enterprise value	$4,966,531

The Company applies the equity method to investments in common stock and to other investments in entities that have risk and reward characteristics that are substantially similar to an investment in the investee's common stock. Since the Company's Series A preferred stock investment in Geneos has a substantive liquidation preference, it is not substantially similar to the Company's common stock investment and will therefore be recorded as an equity security under ASC 321.

As of June 1, 2020, the Company accounts for its common stock investment in Geneos, in which the Company lacks control but does have the ability to exercise significant influence over operating and financial policies, using the equity method. Generally, the ability to exercise significant influence is presumed when the investor possesses more than 20% of the voting interests of the investee. This presumption may be overcome based on specific facts and circumstances that demonstrate that the ability to exercise significant influence is restricted. In applying the equity method, the Company records the investment at cost unless the initial recognition is the result of the deconsolidation of a subsidiary, in which case it is recorded at fair value. The Company's proportionate share of net loss of Geneos is recorded in equity in net earnings of Geneos in the Company's consolidated statements of operations. The Company's equity method investments are reviewed for indicators of impairment at each reporting period and are written down to fair value if there is evidence of a loss in value that is other-than-temporary. Any difference between the carrying amount of the Company's investment and the amount of underlying equity in Geneos's net assets is amortized into income or expense accordingly. There were no basis differences identified as of the deconsolidation date that would need to be amortized.

Upon deconsolidation, the Company recorded its Series A preferred stock investment at fair value based on the per share price paid by third party investors in connection with the Series A preferred stock financing on June 1, 2020. The Company has determined that its Series A preferred stock investment in Geneos does not have a readily determinable fair value and has therefore elected the measurement alternative in ASC 321 to subsequently record the investment at cost, less any impairments, plus or minus changes resulting from observable price changes in orderly transactions for identical or similar investments of the same issuer. When fair value becomes determinable, from observable price changes in orderly transactions, the Company's investment will be marked to fair value. There have been no observable price changes or impairments identified since the deconsolidation date.

In November 2020, Geneos completed the closing of a Series A-1 preferred stock financing. The Company invested $1.4 million in the Series A-1 preferred stock financing, which was led by outside investors. The closing date of this transaction was determined to be a VIE reconsideration event; based on the Company's assessment, Geneos continues to be a VIE as it does not have sufficient equity at risk to finance its activities without additional subordinated financial support. The Company continues to not be the primary beneficiary of Geneos, as it does not have the power to direct the activities that most significantly impact Geneos's economic performance and should not consolidate Geneos. Following this transaction, the Company held approximately 36% of the outstanding equity, on an as-converted to common stock basis. Accordingly, the Company continues to account for its common stock investment in Geneos as an equity method investment under ASC 323 and its preferred stock investments as equity securities under ASC 321.

The fair value of Geneos's Series A-1 preferred stock was based on the per share price paid by third-party investors in connection with the closing on November 12, 2020. The Company has concluded that its Series A-1 preferred stock investment is not similar to its prior Series A preferred stock investment due to certain material rights held solely by Series A preferred stockholders. Therefore, the Company will continue to record its Series A preferred stock investment in Geneos at cost, as there have been no observable price changes or impairments identified since the deconsolidation date.

The Company's share of net losses of Geneos for the period from June 1, 2020 through December 31, 2020 was $4.6 million and for the three months ended March 31, 2021 was $1.5 million; however, only $434,000 was recorded, reducing the Company's total investment in Geneos to $0. Of this amount, $819,000 has been allocated to the equity method investment, thereby reducing the balance to $0 as of March 31, 2021. The remaining $4.2 million loss has been allocated to the Company's

Series A and Series A-1 preferred stock investments in Geneos, on a ratable basis, thereby reducing the investment balance to $0 as of March 31, 2021 as shown in the table below:

Investment in Geneos upon deconsolidation	$	3,618,998
Investment in Geneos Series A-1 preferred stock		1,399,999
Share in net loss of Geneos from June 30, 2020 - December 31, 2020		(4,584,610)
Share in net loss of Geneos for the three months ended March 31, 2021		(434,387)
Investment in Geneos as of March 31, 2021	$	—

The Company will not reduce its investment below $0 and will not record its share of further net losses of Geneos as the Company has no obligation to fund Geneos.

In February 2021, Geneos completed a second closing of the Series A-1 preferred stock financing, in which the Company did not participate. Following this transaction, the Company held approximately 35% of the outstanding equity, on an as-converted to common stock basis.

The Company continues to exclusively license its SynCon® immunotherapy and CELLECTRA® technology platform to Geneos to be used in the field of personalized, neoantigen-based therapy for cancer. The license agreement provides for potential royalty payments to the Company in the event that Geneos commercializes any products using the licensed technology. The Company is not obligated to use any of its assets to fund the future operations of Geneos.

Exhibit 21.1

INOVIO PHARMACEUTICALS, INC.
Subsidiaries

Subsidiary Name(1)	Jurisdiction of Organization
Inovio Asia, LLC	South Korea

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-3 No. 333- 236202) of Inovio Pharmaceuticals, Inc.,
2. Registration Statement (Form S-3 No. 333- 237172) of Inovio Pharmaceuticals, Inc.,
3. Registration Statement (Form S-3 No. 333- 252256) of Inovio Pharmaceuticals, Inc.,
4. Registration Statement (Form S-8 No.333-161559) pertaining to Inovio Biomedical Corporation 2007 Omnibus Incentive Plan,
5. Registration Statement (Form S-8 Nos. 333-166906, 333-174353, 333-181532, 333-192318, 333-196325, 333-209155, and 333-216061) pertaining to Inovio Pharmaceuticals, Inc's 2007 Omnibus Incentive Plan,
6. Registration Statement (Form S-8 Nos. 333-216059, 333-223776, 333-230337, and 333-231872) Inovio Pharmaceutical, Inc.'s 2016 Omnibus Incentive Plan, and
7. Registration Statement (Form S-8 No. 333-236201) Inovio Pharmaceutical, Inc.'s 2016 Omnibus Incentive Plan, as amended

of our reports dated March 1, 2022, with respect to the consolidated financial statements and the effectiveness of internal control over financial reporting of Inovio Pharmaceuticals, Inc. included in this Annual Report (Form 10-K) of Inovio Pharmaceuticals, Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

San Diego, California

March 1, 2022

Exhibit 31.1

Certification of CEO Pursuant to
Securities Exchange Act Rules 13a-15(e) and 15d-15(e)
as Adopted Pursuant to
Section 302 of the Sarbanes-Oxley Act of 2002

I, J. Joseph Kim, certify that:

1. I have reviewed this annual report on Form 10-K of Inovio Pharmaceuticals, Inc.

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2022

/s/ J. Joseph Kim

J. Joseph Kim
President, Chief Executive Officer and Director

Exhibit 31.2

Certification of CFO Pursuant to
Securities Exchange Act Rules 13a-15(e) and 15d-15(e)
as Adopted Pursuant to
Section 302 of the Sarbanes-Oxley Act of 2002

I, Peter Kies, certify that:

1. I have reviewed this annual report on Form 10-K of Inovio Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control

Date: March 1, 2022

/s/ PETER KIES

Peter Kies
Chief Financial Officer

Exhibit 32.1

Certification Pursuant to
18 U.S.C. Section 1350,
As Adopted Pursuant to
Section 906 of the Sarbanes-Oxley Act of 2002

In connection with the Annual Report of Inovio Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ending December 31, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned, in the capacities and on the date indicated below, hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to his knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 1, 2022

/s/ J. Joseph Kim

J. Joseph Kim
President, Chief Executive Officer and Director
(Principal Executive Officer)

Date: March 1, 2022

/s/ Peter Kies

Peter Kies
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 99.1

Inovio Pharmaceuticals, Inc.
Resolutions of the Board of Directors
Ratification of Equity Awards Made By CEO

Approved and adopted: February 24, 2022

Ratification of the Grant of Certain Stock Options and Restricted Stock Units

WHEREAS, pursuant to Section 157(c) of the General Corporation Law of the State of Delaware ("***DGCL***"), a board of directors may, by a resolution, authorize an officer of a corporation to do one or both of the following: (i) designate officers and employees of the corporation or of any of its subsidiaries to be recipients of equity incentive awards created by the corporation, and (ii) determine the number of such equity incentive awards to be received by such officers and employees; provided, however, that the resolution so authorizing such officer shall specify the total number of equity incentive awards such officer may so award;

WHEREAS, from January 1, 2004 through February 11, 2022, Inovio Pharmaceuticals, Inc., a Delaware Corporation (the "***Company***"), acting via the President and Chief Executive Officer of the Company (the "***CEO***"), awarded stock option grants and restricted stock unit awards to various employees and consultants on the dates and in the amounts of (i) shares of Company common stock, par value $0.001 or (ii) restricted stock units, as the case may be, listed on ***Exhibit A*** attached hereto (such awards, the "***Grants***"), pursuant to the terms and conditions of each awardee's respective stock option grant agreement, stock option grant notice, and/or restricted stock unit agreement (collectively, the ***"Grant Agreements***") and one of the following: the Amended 2000 Stock Option Plan, the 2007 Amended and Restated Omnibus Incentive Plan or the 2016 Omnibus Incentive Plan, as amended (each, a "***Plan***" and together, the "***Plans***");

WHEREAS, Section 204 of the DGCL defines a "defective corporate act" as any act or transaction purportedly taken on behalf of a corporation that is, and at the time such act was purportedly taken would have been, within the power of a corporation, but is void or voidable due to a failure of authorization;

WHEREAS, pursuant to Section 204 of the DGCL, no defective corporate act shall be void or voidable solely as a result of a failure of authorization, if ratified pursuant to Section 204 of the DGCL;

WHEREAS, the Board of Directors of the Company (the "***Board***") has determined that the Grants were defective corporate acts because they did not fully comply with the requirements of Section 157(c) of the DGCL;

WHEREAS, the Board has determined that it is advisable and in the best interests of the Company and its stockholders to approve and ratify the Grants, in all respects;

WHEREAS, pursuant to Section 204(c) of the DGCL, the Company is not required to submit the ratification to the stockholders for approval; and

WHEREAS, pursuant to Section 204(g) of the DGCL, the Company is required to give prompt notice of the ratification to all holders of valid stock, as of a date within 60 days of the adoption of these resolutions, which notice will be deemed to have been given if disclosed in a document publicly filed by the Company with the Securities and Exchange Commission (the "***SEC***") pursuant to §13, §14, or §15(d) of the Securities Exchange Act of 1934 (such notice, the "***Notice***").

NOW, THEREFORE BE IT RESOLVED, that, each of the Grants is a defective corporate act to be ratified hereby; and be it

FURTHER RESOLVED, that the nature of the failure of proper authorization is that the Grants were not properly authorized in accordance with Section 157 of the DGCL; and be it

FURTHER RESOLVED, that pursuant to Section 204 of the DGCL, the Board hereby authorizes, ratifies and approves the Grants, and the stock options and restricted stock units of the Company granted thereunder are authorized, ratified and approved in all respects, subject to the terms and conditions of each award's respective Grant Agreement and the applicable Plan; and be it

FURTHER RESOLVED, that the appropriate officers of the Company are hereby authorized to file pursuant to §13, §14, or §15(d) of the Securities Exchange Act of 1934 a Notice disclosing the ratification; and be it

General Authority

FURTHER RESOLVED, that the officers of the Company (the "***Authorized Officers***"), be, and each of them hereby is, authorized, empowered and directed, in the name and on behalf of the Company, to take or cause to be taken any and all such further actions, to execute and deliver or cause to be executed and delivered all such other documents, certificates, instruments and agreements, and to make such filings, with the SEC or otherwise, in the name and on behalf of the Company, to incur and pay all such fees and expenses and to engage in such acts as they shall in their judgment determine to be necessary, desirable or advisable in order to carry out fully the intent and purposes of the foregoing resolutions and the execution by the Authorized Officers of any such documents, certificates, instruments or agreements or the payment of any such fees and expenses or the doing by them of any act in connection with the foregoing matters shall conclusively establish their authority therefor and the approval of the documents, certificates, instruments and agreements so executed, the expenses so paid, the filings so made and the actions so taken; and be it

FURTHER RESOLVED, that any and all actions heretofore taken by any officer, representative or director of the Company in connection with any matter referred to or contemplated in any of the foregoing resolutions are hereby approved, ratified and confirmed in all respects as the act and deed of the Company.

Exhibit A

Grant Date	Award Type	Number of Equity
01-Feb-2004	Options (NQ)	1,250
01-Mar-2004	Options (NQ)	1,250
26-Mar-2004	Options (NQ)	12,500
01-Apr-2004	Options (NQ)	1,250
13-Apr-2004	Options (ISO)	9,375
01-May-2004	Options (NQ)	1,250
01-Jun-2004	Options (NQ)	1,250
16-Aug-2004	Options (ISO)	3,750
18-Aug-2004	Options (ISO)	3,750
24-Sep-2004	Options (ISO)	1,563
24-Sep-2004	Options (ISO)	3,125
01-Oct-2004	Options (ISO)	31,250
01-Nov-2004	Options (ISO)	3,750
03-Jan-2005	Options (ISO)	2,500
01-Feb-2005	Options (ISO)	6,250
07-Feb-2005	Options (ISO)	2,500
12-Feb-2005	Options (ISO)	2,500
01-Apr-2005	Options (ISO)	250
01-Apr-2005	Options (ISO)	2,500
04-Apr-2005	Options (NQ)	500
11-Apr-2005	Options (ISO)	25,000
18-Apr-2005	Options (ISO)	625
20-Apr-2005	Options (ISO)	938
27-Apr-2005	Options (ISO)	938
02-May-2005	Options (ISO)	9,625
11-May-2005	Options (ISO)	625
01-Aug-2005	Options (ISO)	1,875
01-Aug-2005	Options (ISO)	1,875
06-Sep-2005	Options (NQ)	625
03-Oct-2005	Options (ISO)	1,375
13-Feb-2006	Options (ISO)	3,750
06-Mar-2006	Options (ISO)	1,875
13-Mar-2006	Options (ISO)	1,250
01-May-2006	Options (ISO)	938
01-May-2006	Options (ISO)	3,750
08-Aug-2006	Options (NQ)	12,500
21-Aug-2006	Options (ISO)	625
21-Aug-2006	Options (ISO)	625
25-Sep-2006	Options (ISO)	625
23-Oct-2006	Options (ISO)	625
02-Nov-2006	Options (ISO)	625
30-Nov-2006	Options (NQ)	1,500
11-Dec-2006	Options (ISO)	1,875
08-Jan-2007	Options (NQ)	1,084
08-Jan-2007	Options (NQ)	8,032
16-Jan-2007	Options (ISO)	1,875
26-Feb-2007	Options (ISO)	5,625
04-Apr-2007	Options (ISO)	1,250
09-Apr-2007	Options (ISO)	625
16-Apr-2007	Options (ISO)	1,875
03-May-2007	Options (ISO)	2,500
03-May-2007	Options (ISO)	6,250

03-May-2007	Options (NQ)	6,250
03-May-2007	Consultant Options (NQ)	770
03-May-2007	Consultant Options (NQ)	2,980
10-May-2007	Options (ISO)	3,750
16-Jul-2007	Options (ISO)	938
06-Aug-2007	Options (ISO)	1,250
11-Sep-2007	Options (ISO)	1,250
01-Oct-2007	Options (ISO)	1,875
10-Oct-2007	Options (ISO)	157
25-Oct-2007	Options (ISO)	938
04-Dec-2007	Options (NQ)	1,250
15-Feb-2008	Options (NQ)	7,500
04-Mar-2008	Options (ISO)	5,625
01-Apr-2008	Options (ISO)	1,250
09-Oct-2008	Options (ISO)	1,875
27-Jan-2009	Options (ISO)	625
07-Apr-2009	Options (NQ)	7,500
28-Oct-2009	Options (ISO)	625
07-Dec-2009	Consultant Options (NQ)	5,000
10-Feb-2010	Options (ISO)	938
01-Mar-2010	Options (ISO)	1,250
26-Jul-2010	Options (ISO)	625
07-Sep-2010	Options (ISO)	1,875
18-Nov-2010	Options (ISO)	1,250
16-Dec-2010	Options (ISO)	938
03-Jan-2011	Options (ISO)	625
03-Jan-2011	Options (ISO)	313
16-Feb-2011	Options (ISO)	938
04-Apr-2011	Options (ISO)	3,750
23-May-2011	Options (ISO)	9,375
24-May-2011	Options (ISO)	1,875
13-Jun-2011	Options (ISO)	625
01-Jul-2011	Options (ISO)	2,500
01-Jul-2011	Options (ISO)	2,500
01-Jul-2011	Options (ISO)	2,500
12-Sep-2011	Options (ISO)	5,625
19-Sep-2011	Options (ISO)	313
20-Oct-2011	Options (ISO)	938
24-Oct-2011	Options (ISO)	1,250
02-Nov-2011	Options (ISO)	313
02-Nov-2011	Options (ISO)	3,750
05-Dec-2011	Options (ISO)	625
19-Dec-2011	Options (ISO)	625
03-Jan-2012	Options (ISO)	12,500
29-Feb-2012	Options (ISO)	625
01-Mar-2012	Consultant Options (NQ)	12,500
23-Mar-2012	Options (ISO)	3,750
26-Mar-2012	Options (NQ)	18,750
09-Apr-2012	Options (ISO)	1,875
16-Apr-2012	Options (ISO)	3,750
23-Apr-2012	Options (ISO)	5,625
29-May-2012	Options (ISO)	12,500
11-Jun-2012	Options (ISO)	7,500
26-Jun-2012	Options (ISO)	1,250
25-Jul-2012	Options (ISO)	313

30-Jul-2012	Options (ISO)	938
04-Sep-2012	Options (ISO)	1,875
24-Sep-2012	Options (ISO)	313
22-Oct-2012	Options (ISO)	1,875
03-Dec-2012	Options (ISO)	1,875
31-Dec-2012	Options (ISO)	1,875
04-Feb-2013	Options (ISO)	1,875
11-Feb-2013	Options (ISO)	1,875
08-Apr-2013	Options (ISO)	1,250
20-May-2013	Options (ISO)	938
15-Jul-2013	Options (ISO)	625
29-Jul-2013	Options (ISO)	625
05-Aug-2013	Options (ISO)	1,875
07-Aug-2013	Options (ISO)	625
06-Sep-2013	Options (ISO)	12,500
20-Sep-2013	Options (ISO)	938
23-Sep-2013	Options (ISO)	938
07-Oct-2013	Options (ISO)	1,875
12-Nov-2013	Options (ISO)	1,875
14-Nov-2013	Options (ISO)	1,875
05-Dec-2013	Options (ISO)	313
05-Dec-2013	Options (ISO)	157
02-Jan-2014	Options (ISO)	10,000
06-Jan-2014	Options (ISO)	20,000
20-Jan-2014	Options (ISO)	938
10-Feb-2014	Options (ISO)	625
13-Feb-2014	Options (ISO)	1,875
18-Feb-2014	Options (ISO)	30,000
01-Apr-2014	Options (ISO)	25,000
23-Apr-2014	Options (ISO)	938
28-Apr-2014	Options (ISO)	1,875
01-May-2014	Options (ISO)	1,250
05-May-2014	Options (ISO)	938
05-May-2014	Options (ISO)	938
05-May-2014	Options (ISO)	1,250
20-May-2014	Options (ISO)	3,750
02-Jun-2014	Options (ISO)	1,875
16-Jun-2014	Options (ISO)	5,000
22-Jul-2014	Options (ISO)	938
24-Jul-2014	Options (ISO)	625
28-Jul-2014	Options (ISO)	1,250
04-Sep-2014	Options (ISO)	3,750
08-Sep-2014	Options (ISO)	1,250
22-Sep-2014	Options (ISO)	20,000
29-Sep-2014	Options (ISO)	5,625
06-Oct-2014	Options (ISO)	5,625
15-Oct-2014	Options (ISO)	3,750
27-Oct-2014	Options (ISO)	9,375
03-Nov-2014	Options (ISO)	6,500
01-Dec-2014	Options (ISO)	3,750
17-Dec-2014	Options (ISO)	20,000
05-Jan-2015	Options (ISO)	3,750
05-Jan-2015	Options (ISO)	3,750
26-Jan-2015	Options (ISO)	25,000
26-Jan-2015	Consultant Options (NQ)	5,000

30-Jan-2015	Options (ISO)	938
02-Feb-2015	Options (ISO)	938
03-Feb-2015	Options (ISO)	5,625
16-Feb-2015	Options (ISO)	1,875
17-Feb-2015	Options (ISO)	625
17-Feb-2015	Options (ISO)	1,250
23-Feb-2015	Options (ISO)	5,625
23-Feb-2015	Options (ISO)	1,875
23-Feb-2015	Options (ISO)	625
23-Feb-2015	Options (ISO)	20,000
27-Feb-2015	Options (ISO)	10,000
27-Feb-2015	Options (ISO)	12,000
09-Mar-2015	Options (ISO)	938
09-Mar-2015	Options (ISO)	938
09-Mar-2015	Options (ISO)	1,250
09-Mar-2015	Options (ISO)	1,250
16-Mar-2015	Options (ISO)	1,250
25-Mar-2015	Options (ISO)	1,250
30-Mar-2015	Options (ISO)	10,000
06-Apr-2015	Options (ISO)	625
13-Apr-2015	Options (ISO)	3,750
13-Apr-2015	Options (ISO)	938
21-Apr-2015	Options (ISO)	1,250
28-Apr-2015	Options (ISO)	5,625
11-May-2015	Options (ISO)	1,250
18-May-2015	Options (ISO)	1,250
19-May-2015	Options (ISO)	938
26-May-2015	Options (ISO)	9,375
29-Jun-2015	Options (ISO)	938
13-Jul-2015	Options (ISO)	9,375
16-Jul-2015	Options (ISO)	5,625
27-Jul-2015	Options (ISO)	1,250
03-Aug-2015	Options (ISO)	3,750
03-Aug-2015	Options (ISO)	625
10-Aug-2015	Options (ISO)	3,750
10-Aug-2015	Options (ISO)	938
10-Aug-2015	Options (ISO)	625
24-Aug-2015	Options (ISO)	1,875
31-Aug-2015	Options (ISO)	1,250
31-Aug-2015	Options (ISO)	3,750
08-Sep-2015	Options (ISO)	625
08-Sep-2015	Options (ISO)	625
08-Sep-2015	Options (ISO)	1,000
08-Sep-2015	Options (ISO)	625
14-Sep-2015	Options (ISO)	938
23-Sep-2015	Options (ISO)	625
12-Oct-2015	Options (ISO)	938
14-Oct-2015	Options (ISO)	313
14-Oct-2015	Options (ISO)	3,750
19-Oct-2015	Options (ISO)	1,875
19-Oct-2015	Options (ISO)	5,625
19-Oct-2015	Options (ISO)	3,750
02-Nov-2015	Options (ISO)	938
02-Nov-2015	Options (ISO)	1,250
09-Nov-2015	Options (ISO)	1,875

23-Nov-2015	Options (ISO)	938
23-Nov-2015	Options (ISO)	625
23-Nov-2015	Options (ISO)	938
23-Nov-2015	Options (ISO)	938
30-Nov-2015	Options (ISO)	625
30-Nov-2015	Options (ISO)	625
30-Nov-2015	Options (ISO)	3,750
30-Nov-2015	Options (ISO)	3,750
01-Dec-2015	Options (ISO)	1,250
09-Dec-2015	Options (ISO)	625
14-Dec-2015	Options (ISO)	625
14-Dec-2015	Options (ISO)	5,625
15-Dec-2015	Options (ISO)	1,875
31-Dec-2015	Options (ISO)	938
04-Jan-2016	Options (ISO)	20,000
04-Jan-2016	Options (ISO)	5,625
05-Jan-2016	Options (ISO)	1,250
11-Jan-2016	Options (ISO)	625
11-Jan-2016	Options (ISO)	1,875
11-Jan-2016	Options (ISO)	625
25-Jan-2016	Options (ISO)	1,250
25-Jan-2016	Options (ISO)	3,750
01-Feb-2016	Options (ISO)	1,250
16-Feb-2016	Options (ISO)	1,875
29-Feb-2016	Options (ISO)	1,875
14-Mar-2016	Options (ISO)	10,000
21-Mar-2016	Options (ISO)	3,750
24-Mar-2016	Options (ISO)	1,875
28-Mar-2016	Options (ISO)	938
04-Apr-2016	Options (ISO)	5,625
04-Apr-2016	Options (ISO)	938
04-Apr-2016	Options (ISO)	938
18-Apr-2016	Options (ISO)	938
18-Apr-2016	Options (ISO)	938
25-Apr-2016	Options (ISO)	625
26-Apr-2016	Options (ISO)	3,750
26-Apr-2016	Options (ISO)	5,625
02-May-2016	Options (ISO)	313
09-May-2016	Options (ISO)	9,375
09-May-2016	Options (ISO)	1,250
16-May-2016	Options (ISO)	625
16-May-2016	Options (ISO)	1,875
16-May-2016	Options (ISO)	3,750
16-May-2016	Options (ISO)	625
23-May-2016	Options (ISO)	938
30-May-2016	Options (ISO)	1,875
31-May-2016	Options (ISO)	1,250
01-Jun-2016	Options (ISO)	938
01-Jun-2016	Options (ISO)	1,250
06-Jun-2016	Options (ISO)	5,625
13-Jun-2016	Options (ISO)	625
14-Jun-2016	Options (ISO)	5,625
16-Jun-2016	Options (ISO)	12,500
20-Jun-2016	Options (ISO)	3,750
20-Jun-2016	Options (ISO)	938

27-Jun-2016	Options (ISO)	938
27-Jun-2016	Options (ISO)	625
05-Jul-2016	Options (ISO)	625
11-Jul-2016	Options (ISO)	9,375
13-Jul-2016	Options (ISO)	5,625
18-Jul-2016	Options (ISO)	3,750
18-Jul-2016	Options (ISO)	1,875
20-Jul-2016	Options (ISO)	938
21-Jul-2016	Options (ISO)	1,250
25-Jul-2016	Options (ISO)	1,250
29-Jul-2016	Options (ISO)	3,750
29-Jul-2016	Options (ISO)	1,875
01-Aug-2016	Options (ISO)	313
01-Aug-2016	Options (ISO)	1,875
15-Aug-2016	Options (ISO)	625
15-Aug-2016	Options (ISO)	938
22-Aug-2016	Options (ISO)	3,750
22-Aug-2016	Options (ISO)	1,875
22-Aug-2016	Options (ISO)	625
29-Aug-2016	Options (ISO)	1,875
29-Aug-2016	Options (ISO)	9,375
29-Aug-2016	Options (ISO)	3,750
29-Aug-2016	Options (ISO)	3,750
29-Aug-2016	Options (ISO)	3,750
06-Sep-2016	Options (ISO)	1,875
06-Sep-2016	Options (ISO)	1,250
12-Sep-2016	Options (ISO)	938
19-Sep-2016	Options (ISO)	625
19-Sep-2016	Options (ISO)	3,750
19-Sep-2016	Options (ISO)	938
19-Sep-2016	Share Units (RSU)	10,000
26-Sep-2016	Options (ISO)	30,000
26-Sep-2016	Share Units (RSU)	15,000
30-Sep-2016	Options (ISO)	625
30-Sep-2016	Options (ISO)	20,000
30-Sep-2016	Share Units (RSU)	3,000
03-Oct-2016	Options (ISO)	938
03-Oct-2016	Options (ISO)	938
03-Oct-2016	Options (ISO)	20,000
03-Oct-2016	Options (ISO)	938
03-Oct-2016	Share Units (RSU)	5,000
05-Oct-2016	Options (ISO)	20,000
05-Oct-2016	Share Units (RSU)	10,000
17-Oct-2016	Options (ISO)	1,875
24-Oct-2016	Options (ISO)	3,750
24-Oct-2016	Options (ISO)	1,875
26-Oct-2016	Options (ISO)	1,875
31-Oct-2016	Options (ISO)	938
31-Oct-2016	Options (ISO)	3,750
14-Nov-2016	Options (ISO)	625
14-Nov-2016	Options (ISO)	1,250
14-Nov-2016	Options (ISO)	625
14-Nov-2016	Options (ISO)	625
14-Nov-2016	Options (ISO)	3,750
28-Nov-2016	Options (ISO)	3,750

28-Nov-2016	Options (ISO)	1,250
30-Nov-2016	Share Units (RSU)	12,500
05-Dec-2016	Options (ISO)	625
05-Dec-2016	Options (ISO)	313
05-Dec-2016	Options (ISO)	625
12-Dec-2016	Options (ISO)	1,875
14-Dec-2016	Options (ISO)	938
19-Dec-2016	Options (ISO)	938
19-Dec-2016	Options (ISO)	938
03-Jan-2017	Options (ISO)	625
03-Jan-2017	Options (ISO)	625
09-Jan-2017	Options (ISO)	3,750
30-Jan-2017	Options (ISO)	9,375
06-Feb-2017	Options (ISO)	1,875
06-Feb-2017	Options (ISO)	625
13-Feb-2017	Options (ISO)	1,250
21-Feb-2017	Options (ISO)	938
27-Feb-2017	Options (ISO)	938
28-Feb-2017	Options (ISO)	9,375
13-Mar-2017	Options (ISO)	938
27-Mar-2017	Options (ISO)	3,750
27-Mar-2017	Options (ISO)	1,875
17-Apr-2017	Options (ISO)	938
17-Apr-2017	Options (ISO)	3,750
24-Apr-2017	Options (ISO)	3,750
01-May-2017	Options (ISO)	1,875
01-May-2017	Options (ISO)	1,250
08-May-2017	Options (ISO)	1,875
15-May-2017	Options (ISO)	938
15-May-2017	Options (ISO)	12,500
22-May-2017	Options (ISO)	3,750
22-May-2017	Options (ISO)	1,875
30-May-2017	Options (ISO)	12,500
05-Jun-2017	Options (ISO)	9,375
19-Jun-2017	Options (ISO)	625
19-Jun-2017	Options (ISO)	625
10-Jul-2017	Options (ISO)	625
10-Jul-2017	Options (ISO)	625
10-Jul-2017	Options (ISO)	1,250
24-Jul-2017	Options (ISO)	1,250
24-Jul-2017	Options (ISO)	625
24-Jul-2017	Options (ISO)	3,750
31-Jul-2017	Options (ISO)	625
31-Jul-2017	Options (ISO)	938
31-Jul-2017	Options (ISO)	938
04-Aug-2017	Share Units (RSU)	10,000
07-Aug-2017	Options (ISO)	1,250
07-Aug-2017	Options (ISO)	1,250
07-Aug-2017	Options (ISO)	625
07-Aug-2017	Options (ISO)	5,625
07-Aug-2017	Options (ISO)	1,875
07-Aug-2017	Options (ISO)	938
21-Aug-2017	Options (ISO)	3,750
21-Aug-2017	Options (ISO)	938
28-Aug-2017	Options (ISO)	1,875

28-Aug-2017	Options (ISO)	3,750
31-Aug-2017	Options (ISO)	1,875
31-Aug-2017	Options (ISO)	1,875
05-Sep-2017	Options (ISO)	1,875
11-Sep-2017	Options (ISO)	1,875
18-Sep-2017	Options (ISO)	3,750
25-Sep-2017	Options (ISO)	3,750
29-Sep-2017	Options (ISO)	1,875
29-Sep-2017	Options (ISO)	15,625
29-Sep-2017	Options (ISO)	938
02-Oct-2017	Options (ISO)	625
09-Oct-2017	Options (ISO)	938
09-Oct-2017	Options (ISO)	938
16-Oct-2017	Options (ISO)	1,250
16-Oct-2017	Options (ISO)	15,625
16-Oct-2017	Options (ISO)	9,375
06-Nov-2017	Options (ISO)	1,875
13-Nov-2017	Options (ISO)	938
13-Nov-2017	Options (ISO)	1,250
20-Nov-2017	Options (ISO)	1,875
27-Nov-2017	Options (ISO)	5,625
29-Nov-2017	Options (ISO)	5,625
15-Dec-2017	Options (ISO)	625
18-Dec-2017	Options (ISO)	10,000
08-Jan-2018	Options (ISO)	1,875
08-Jan-2018	Options (ISO)	938
08-Jan-2018	Options (ISO)	5,625
29-Jan-2018	Options (ISO)	3,750
05-Feb-2018	Options (ISO)	3,750
12-Feb-2018	Options (ISO)	1,250
30-Mar-2018	Options (ISO)	9,375
02-Apr-2018	Options (ISO)	1,875
09-Apr-2018	Options (ISO)	25,000
09-Apr-2018	Options (ISO)	938
09-Apr-2018	Share Units (RSU)	5,000
16-Apr-2018	Options (ISO)	938
16-Apr-2018	Options (ISO)	15,625
23-Apr-2018	Options (ISO)	625
01-May-2018	Options (ISO)	938
29-May-2018	Options (ISO)	1,250
04-Jun-2018	Options (ISO)	938
04-Jun-2018	Options (ISO)	625
11-Jun-2018	Options (ISO)	1,875
18-Jun-2018	Options (ISO)	1,875
29-Jun-2018	Options (ISO)	5,625
29-Jun-2018	Options (ISO)	625
02-Jul-2018	Options (ISO)	938
09-Jul-2018	Options (ISO)	3,750
09-Jul-2018	Options (ISO)	938
23-Jul-2018	Options (ISO)	1,875
30-Jul-2018	Options (ISO)	5,625
30-Jul-2018	Options (ISO)	625
01-Aug-2018	Consultant Options (NQ)	12,000
13-Aug-2018	Options (ISO)	1,875
27-Aug-2018	Options (ISO)	1,875

04-Sep-2018	Options (ISO)	1,250
17-Sep-2018	Options (ISO)	938
24-Sep-2018	Options (ISO)	625
24-Sep-2018	Options (ISO)	938
24-Sep-2018	Options (ISO)	938
24-Sep-2018	Options (ISO)	3,750
24-Sep-2018	Options (ISO)	938
08-Oct-2018	Options (ISO)	938
29-Oct-2018	Options (ISO)	625
05-Nov-2018	Options (ISO)	1,875
12-Nov-2018	Options (ISO)	1,875
12-Nov-2018	Options (ISO)	1,250
26-Nov-2018	Options (ISO)	5,625
30-Nov-2018	Options (ISO)	3,750
30-Nov-2018	Options (ISO)	5,625
10-Dec-2018	Options (ISO)	938
10-Dec-2018	Options (ISO)	938
31-Dec-2018	Options (ISO)	1,875
31-Dec-2018	Options (ISO)	1,875
07-Jan-2019	Options (ISO)	938
07-Jan-2019	Options (ISO)	12,500
07-Jan-2019	Options (ISO)	3,750
14-Jan-2019	Options (ISO)	3,750
14-Jan-2019	Options (ISO)	938
14-Jan-2019	Options (ISO)	1,875
30-Jan-2019	Options (ISO)	625
11-Feb-2019	Options (ISO)	625
11-Feb-2019	Options (ISO)	1,250
25-Feb-2019	Options (ISO)	625
05-Mar-2019	Options (ISO)	3,750
18-Mar-2019	Options (ISO)	15,625
18-Mar-2019	Options (ISO)	1,875
25-Mar-2019	Options (ISO)	1,875
29-Mar-2019	Options (ISO)	3,750
08-Apr-2019	Options (ISO)	1,875
08-Apr-2019	Options (ISO)	625
15-Apr-2019	Options (ISO)	625
22-Apr-2019	Options (ISO)	1,875
22-Apr-2019	Options (ISO)	938
22-Apr-2019	Options (ISO)	1,875
22-Apr-2019	Options (ISO)	625
25-Apr-2019	Options (ISO)	713
25-Apr-2019	Options (ISO)	713
25-Apr-2019	Options (ISO)	558
20-May-2019	Options (ISO)	938
20-May-2019	Options (ISO)	938
28-May-2019	Options (ISO)	1,875
28-May-2019	Options (ISO)	938
10-Jun-2019	Options (ISO)	3,750
10-Jun-2019	Options (ISO)	1,250
08-Jul-2019	Options (ISO)	3,750
11-Jul-2019	Consultant Options (NQ)	35,000
29-Aug-2019	Options (ISO)	1,250
16-Sep-2019	Options (ISO)	1,875
16-Sep-2019	Options (ISO)	3,750

21-Oct-2019	Options (ISO)	1,250
21-Oct-2019	Options (ISO)	1,875
21-Oct-2019	Options (ISO)	5,625
31-Oct-2019	Options (ISO)	3,750
18-Nov-2019	Options (ISO)	3,750
20-Nov-2019	Consultant Options (NQ)	10,000
02-Dec-2019	Options (ISO)	625
16-Dec-2019	Options (ISO)	625
16-Dec-2019	Options (ISO)	625
16-Dec-2019	Options (ISO)	1,875
16-Dec-2019	Options (ISO)	938
16-Dec-2019	Options (ISO)	1,875
16-Dec-2019	Options (ISO)	625
31-Dec-2019	Options (ISO)	1,875
06-Jan-2020	Options (ISO)	938
06-Jan-2020	Options (ISO)	3,750
06-Jan-2020	Options (ISO)	938
21-Jan-2020	Options (ISO)	938
27-Jan-2020	Options (ISO)	5,625
27-Jan-2020	Options (ISO)	1,250
27-Jan-2020	Options (ISO)	938
03-Feb-2020	Options (ISO)	1,875
03-Feb-2020	Options (ISO)	938
18-Feb-2020	Options (ISO)	1,250
24-Feb-2020	Options (ISO)	1,875
09-Mar-2020	Options (ISO)	5,000
09-Mar-2020	Options (ISO)	1,875
09-Mar-2020	Options (ISO)	625
16-Mar-2020	Options (ISO)	938
16-Mar-2020	Options (ISO)	9,375
30-Mar-2020	Options (ISO)	1,875
30-Mar-2020	Options (ISO)	625
30-Mar-2020	Options (ISO)	938
30-Mar-2020	Options (ISO)	3,750
13-Apr-2020	Options (ISO)	938
27-Apr-2020	Options (ISO)	5,625
27-Apr-2020	Options (ISO)	938
04-May-2020	Options (ISO)	938
04-May-2020	Options (ISO)	5,625
04-May-2020	Options (ISO)	12,500
11-May-2020	Options (ISO)	5,625
11-May-2020	Options (ISO)	1,250
11-May-2020	Options (ISO)	1,250
19-May-2020	Share Units (RSU)	24,000
19-May-2020	Share Units (RSU)	36,000
26-May-2020	Options (ISO)	1,875
26-May-2020	Options (ISO)	1,875
26-May-2020	Options (ISO)	1,875
29-May-2020	Options (ISO)	3,750
15-Jun-2020	Options (ISO)	1,000
15-Jun-2020	Options (ISO)	3,750
17-Jun-2020	Options (ISO)	1,875
22-Jun-2020	Options (ISO)	3,750
22-Jun-2020	Options (ISO)	938
06-Jul-2020	Options (ISO)	12,500

06-Jul-2020	Options (ISO)	625
13-Jul-2020	Options (ISO)	1,000
13-Jul-2020	Options (ISO)	1,875
13-Jul-2020	Options (ISO)	1,875
20-Jul-2020	Options (ISO)	12,500
27-Jul-2020	Options (ISO)	625
27-Jul-2020	Options (ISO)	12,500
27-Jul-2020	Options (ISO)	5,625
27-Jul-2020	Options (ISO)	15,625
31-Jul-2020	Options (ISO)	1,875
31-Jul-2020	Options (ISO)	15,625
10-Aug-2020	Options (ISO)	15,625
10-Aug-2020	Options (ISO)	1,875
10-Aug-2020	Options (ISO)	625
10-Aug-2020	Options (ISO)	5,625
10-Aug-2020	Options (ISO)	9,375
10-Aug-2020	Options (ISO)	1,250
10-Aug-2020	Options (ISO)	938
10-Aug-2020	Options (ISO)	1,875
31-Aug-2020	Options (ISO)	1,250
31-Aug-2020	Options (ISO)	1,875
08-Sep-2020	Options (ISO)	5,625
14-Sep-2020	Options (ISO)	1,875
14-Sep-2020	Options (ISO)	3,750
14-Sep-2020	Options (ISO)	3,750
14-Sep-2020	Options (ISO)	20,000
14-Sep-2020	Options (ISO)	1,250
14-Sep-2020	Options (ISO)	15,625
28-Sep-2020	Options (ISO)	12,500
28-Sep-2020	Options (ISO)	625
05-Oct-2020	Options (ISO)	15,625
05-Oct-2020	Options (ISO)	3,750
05-Oct-2020	Options (ISO)	15,625
12-Oct-2020	Options (ISO)	3,750
12-Oct-2020	Options (ISO)	938
19-Oct-2020	Options (ISO)	5,625
30-Oct-2020	Options (ISO)	3,750
30-Oct-2020	Options (ISO)	9,375
30-Oct-2020	Options (ISO)	3,750
16-Nov-2020	Options (ISO)	938
30-Nov-2020	Options (ISO)	1,250
30-Nov-2020	Options (ISO)	9,375
30-Nov-2020	Options (ISO)	1,250
07-Dec-2020	Options (ISO)	9,375
07-Dec-2020	Options (ISO)	12,500
07-Dec-2020	Options (ISO)	625
14-Dec-2020	Options (ISO)	1,875
14-Dec-2020	Options (ISO)	9,375
16-Dec-2020	Options (ISO)	3,750
21-Dec-2020	Options (ISO)	1,875
21-Dec-2020	Options (ISO)	5,625
21-Dec-2020	Options (ISO)	12,500
11-Jan-2021	Options (ISO)	3,750
11-Jan-2021	Options (ISO)	3,750
18-Jan-2021	Options (ISO)	5,625

25-Jan-2021	Options (ISO)	5,625
25-Jan-2021	Options (ISO)	1,875
29-Jan-2021	Options (ISO)	3,750
31-Jan-2021	Options (ISO)	25,000
31-Jan-2021	Share Units (RSU)	5,000
08-Feb-2021	Options (ISO)	938
16-Feb-2021	Options (ISO)	12,500
22-Feb-2021	Options (ISO)	1,875
08-Mar-2021	Options (ISO)	9,375
15-Mar-2021	Options (ISO)	938
29-Mar-2021	Options (ISO)	12,500
29-Mar-2021	Options (ISO)	5,625
19-Apr-2021	Options (ISO)	5,625
19-Apr-2021	Options (ISO)	9,375
26-Apr-2021	Options (ISO)	1,875
26-Apr-2021	Options (ISO)	625
26-Apr-2021	Options (ISO)	1,875
26-Apr-2021	Options (ISO)	12,500
26-Apr-2021	Options (ISO)	1,875
26-Apr-2021	Options (ISO)	625
26-Apr-2021	Options (ISO)	3,750
26-Apr-2021	Options (ISO)	625
30-Apr-2021	Options (ISO)	20,000
30-Apr-2021	Options (ISO)	5,625
17-May-2021	Options (ISO)	5,625
17-May-2021	Options (ISO)	5,625
24-May-2021	Options (ISO)	3,750
28-May-2021	Options (ISO)	938
14-Jun-2021	Options (ISO)	25,000
14-Jun-2021	Options (ISO)	625
14-Jun-2021	Share Units (RSU)	5,000
21-Jun-2021	Options (ISO)	1,875
21-Jun-2021	Options (ISO)	625
21-Jun-2021	Options (ISO)	625
28-Jun-2021	Options (ISO)	1,250
28-Jun-2021	Options (ISO)	5,625
28-Jun-2021	Options (ISO)	1,875
12-Jul-2021	Options (ISO)	20,000
19-Jul-2021	Options (ISO)	20,000
19-Jul-2021	Share Units (RSU)	5,000
26-Jul-2021	Options (ISO)	3,750
26-Jul-2021	Options (ISO)	938
26-Jul-2021	Options (ISO)	3,750
26-Jul-2021	Options (ISO)	1,875
30-Jul-2021	Options (ISO)	1,875
30-Jul-2021	Options (ISO)	1,875
02-Aug-2021	Options (ISO)	3,750
09-Aug-2021	Options (ISO)	1,875
09-Aug-2021	Options (ISO)	9,375
13-Aug-2021	Options (ISO)	20,000
16-Aug-2021	Options (ISO)	1,250
16-Aug-2021	Options (ISO)	625
16-Aug-2021	Options (ISO)	25,000
16-Aug-2021	Share Units (RSU)	5,000
23-Aug-2021	Options (ISO)	1,875

23-Aug-2021	Options (ISO)	5,625
23-Aug-2021	Options (ISO)	938
30-Aug-2021	Options (ISO)	1,875
30-Aug-2021	Options (ISO)	625
30-Aug-2021	Options (ISO)	3,750
30-Aug-2021	Options (ISO)	625
30-Aug-2021	Options (ISO)	625
30-Aug-2021	Options (ISO)	1,875
07-Sep-2021	Options (ISO)	1,250
13-Sep-2021	Options (ISO)	1,875
20-Sep-2021	Options (ISO)	3,750
20-Sep-2021	Options (ISO)	1,875
23-Sep-2021	Options (ISO)	1,875
27-Sep-2021	Options (ISO)	3,750
04-Oct-2021	Options (ISO)	3,750
04-Oct-2021	Options (ISO)	1,250
11-Oct-2021	Options (ISO)	1,875
11-Oct-2021	Options (ISO)	12,500
11-Oct-2021	Options (ISO)	12,500
14-Oct-2021	Options (ISO)	15,625
18-Oct-2021	Options (ISO)	9,375
18-Oct-2021	Options (ISO)	9,375
25-Oct-2021	Options (ISO)	3,750
25-Oct-2021	Options (ISO)	938
29-Oct-2021	Options (ISO)	5,625
29-Oct-2021	Options (ISO)	12,500
01-Nov-2021	Consultant Options (NQ)	6,000
01-Nov-2021	Share Units (RSU)	4,000
08-Nov-2021	Options (ISO)	20,000
08-Nov-2021	Options (ISO)	12,500
08-Nov-2021	Options (ISO)	938
08-Nov-2021	Options (ISO)	938
15-Nov-2021	Options (ISO)	938
15-Nov-2021	Options (ISO)	938
15-Nov-2021	Options (ISO)	3,750
15-Nov-2021	Options (ISO)	938
15-Nov-2021	Options (ISO)	5,625
15-Nov-2021	Options (ISO)	1,875
22-Nov-2021	Options (ISO)	938
22-Nov-2021	Options (ISO)	625
29-Nov-2021	Options (ISO)	938
29-Nov-2021	Options (ISO)	938
06-Dec-2021	Options (ISO)	3,750
06-Dec-2021	Options (ISO)	12,500
13-Dec-2021	Options (ISO)	938
13-Dec-2021	Options (ISO)	5,625
13-Dec-2021	Options (ISO)	12,500
13-Dec-2021	Options (ISO)	938
20-Dec-2021	Options (ISO)	1,875
10-Jan-2022	Options (NQ)	61,668
10-Jan-2022	Options (ISO)	1,875
10-Jan-2022	Options (ISO)	9,375
10-Jan-2022	Options (ISO)	3,750
10-Jan-2022	Options (ISO)	83,332
10-Jan-2022	Options (ISO)	3,750

10-Jan-2022	Share Units (RSU)	95,000
24-Jan-2022	Options (ISO)	938
31-Jan-2022	Options (ISO)	25,000
31-Jan-2022	Options (ISO)	3,750
31-Jan-2022	Share Units (RSU)	5,000
7-Feb-2022	Options (ISO)	1,250