INOVIO PHARMACEUTICALS, INC.
Form 10-K
March 16, 2015

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

FORM 10-K

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2014

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 100 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:	
COMMON STOCK, $0.001 PAR VALUE	NASDAQ
(Title of Class)	(Name of Each Exchange on Which Registered)

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 x
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 x
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 x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files). Yes x No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x

Non-accelerated filer ¨ (Do not check if a smaller reporting company) Smaller reporting company ¨
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No x
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, 2014 was approximately $614,635,315 based on $10.81, the closing price on that date of the Registrant's Common Stock on the NYSE MKT.
The number of shares outstanding of the Registrant's Common Stock, $0.001 par value, was 60,741,082 as of March 9, 2015.

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 2015 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, 2014.

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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 subsidiaries.

PART I

ITEM 1. BUSINESS

This Annual Report (including the following section regarding Management's Discussion and Analysis of Financial Condition and Results of Operations) contains forward-looking statements regarding our business, financial condition, results of operations and prospects. Words such as "expects," "anticipates," "intends," "plans," "believes," "seeks," "estimates" 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.

Overview

We are developing active DNA immunotherapies and vaccines focused on treating and preventing cancers and infectious diseases. Our DNA-based immunotherapies, in combination with our proprietary electroporation delivery devices, are intended to generate robust immune responses, in particular T cells, to fight such diseases. In 2014 we reported that in a large, controlled phase II clinical study we achieved clinically relevant efficacy against a targeted disease (HPV-associated cervical dysplasia) by generating antigen-specific T cells. Our novel SynCon® immunotherapy design has shown the ability to help break the immune system's tolerance of cancerous cells. Alternatively, our SynCon® product design is also intended to facilitate cross-strain protection against known as well as new unmatched strains of pathogens such as influenza. Given the recognized role of killer T cells in eliminating cancerous or infected cells from the body, our scientists believe that our active immunotherapies may play an important role in helping fight such diseases. Human data to date have shown a favorable safety profile of our DNA immunotherapies delivered using electroporation.

We have completed, current or planned clinical programs of our proprietary SynCon® immunotherapies for HPV-caused pre-cancers and cancers, prostate cancer, breast/lung/pancreatic cancer, hepatitis C virus (HCV), hepatitis B virus (HBV), HIV, influenza, and Ebola. Our partners and collaborators include F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. ("Roche"), University of Pennsylvania, Drexel University, National Microbiology Laboratory of the Public Health Agency of Canada, , National Institute of Allergy and Infectious Diseases ("NIAID"), United States Military HIV Research Program ("USMHRP"), U.S. Army Medical Research Institute of Infectious Diseases ("USAMRIID"), HIV Vaccines Trial Network ("HVTN"), Defense Advanced Research Projects Agency ("DARPA") and MedImmune, LLC.

Industry Background

Apart from the benefits provided by sanitation and clean water, we believe that the idea of stimulating the immune system, to date via preventive vaccines, has saved more lives and prevented more human suffering than any other human invention. As recently as a century ago, infectious diseases were the main cause of death worldwide, even in the most developed countries. Today, there is a vast range of vaccines available to protect against more than two dozen infectious diseases, especially for children, completely or virtually eradicating diseases such as smallpox and polio.

Today the idea of stimulating the immune system to prevent or treat infections and cancers is an even more compelling concept, with significant time and capital being applied by the scientific community to advance promising

new approaches. While conventional vaccine technology long ago reached its technical boundaries, the emergence of new areas of scientific knowledge such as genomics and technologies like rapid sequencing have opened many doors to new ways to enable the development of new preventive vaccines for challenging infectious diseases and new treatments for diseases such as cancer, HIV, and hepatitis. Today the opportunity for immune stimulating technologies with the potential to fight cancers and chronic infectious diseases has never appeared more promising given notable technology advancements such as checkpoint inhibitors. Yet, while yielding promising results, in many respects the surface has been barely scratched. There remains a significant need and opportunity for further advancements.

Inovio's Solution

With our immunotherapy platform comprising our SynCon® products as well as our proprietary CELLECTRA® electroporation delivery technology, we have developed a rich pipeline of pre-clinical and clinical stage products that have generated, in vivo (in the body), best-in-class immune responses, in particular T cells, which are fundamental to eliminating cancerous or infected cells. They are showing their potential to be used against any targeted cancer or infectious disease. Our lead immunotherapy (for treating HPV-associated precancer) met its primary and secondary endpoints in a large, controlled phase II clinical study, achieving statistically significant and clinically relevant efficacy in association with robust T cell activation. This was accomplished without serious adverse events and the only statistically significant adverse event being injection site redness (our immunotherapies are non-live and non-replicating therefore they cannot cause the disease; they work most naturally with the immune system and within its controls to reduce or minimize the risk of unwanted inflammatory responses; no serious adverse events have been attributed to our immunotherapies in human studies to date). These results suggest significant market potential not only for the lead product but for the broad spectrum of products that may be created based on our technology platform.

The Next Generation of Cancer and Infectious Disease Treatment: Inovio's SynCon® Immunotherapies

Our immunotherapies are designed to prevent a disease (prophylactic) or treat an existing disease (therapeutic) by activating and magnifying an immune response to one or more disease-specific antigens (proteins associated with a cancer or infectious disease that the body will recognize as foreign or not normal). Without the quality control and manufacturing challenges and costs of specifically personalized medicines, we can direct the immune response directly in the patient's own body to fight specific organisms or cells. We do this simply by introducing the genetic code for the target antigen(s) into the tissues of the body that will serve as a temporary antigen production facility. Our immunotherapies consist of one or more DNA plasmids (circular string of DNA as a backbone) encoding one or more selected antigen that are introduced into cells (directly in the body) of humans or animals. Our approach uniquely enables dramatic uptake of the DNA plasmids by the cells in a local tissue area. After the DNA code for the targeted antigen(s) is introduced to cells, the cells' natural machinery for making their own proteins useful to the body temporarily produces the selected antigen(s) encoded by the DNA sequences delivered to the cell. The antigenic protein manufactured through this process, is then presented to the immune system and triggers one or both of two arms of the immune system: the production of preventive antibodies, known as a humoral immune response, and/or the activation of therapeutic T-cells, known as a cellular or cell-mediated immune response. These responses are then ready to neutralize or eliminate infectious agents (e.g. viruses, bacteria, and other microorganisms) or abnormal cells (e.g. malignant tumor or infected cells).

Our SynCon® DNA immunotherapies are designed to generate specific antibody and T cell responses. First we identify one or more antigens that we believe are the best targets to help direct the immune system toward a particular cancer or infectious disease. We then apply our SynCon® design process, which employs the extensive data available from genomic databases. This SynCon® design uses the genetic make-up of the selected antigen(s) from multiple variants of a cancer or strains of a virus. We synthetically create a new genetic sequence of the antigen that represents a consensus of the slightly different DNA from multiple variants or strains of the targeted antigen. We can create a differentiated SynCon variant to help the immune system better recognize a cancer self-antigen (a cell and antigen grown in the body). Alternatively, we have proof of principle in human studies that we can generate immune responses with SynCon immunotherapies not matched to different strains of an infectious disease, e.g. influenza, creating a proof-of-concept of the ability to move beyond today's "one bug, one drug" paradigm in which a vaccine must match the strain of the circulating virus in order to provide protection. These SynCon® constructs may provide a solution to the genetic "shift" and "drift" that is typical of many infectious diseases. These new synthetic consensus DNA sequences do not exist in nature and are patentable.

Technically speaking, SynCon® immunotherapies are designed by taking the primary amino acid sequence from multiple strains or variants of a target disease antigen. We align the multiple amino acid sequences and at each position of the sequence choose the individual amino acid that is most immunologically dominant, conserved or important. In this process we create a new sequence that is a consensus of all the input sequences. This new synthetically engineered sequence is similar to the originating sequences but does not match any. It does not exist in nature and is therefore patentable.

The SynCon sequences are further optimized at the DNA level for codon usage, improved mRNA stability, and are provided with enhanced leader sequences for ribosome loading. The DNA inserts are therefore optimized at the genetic level to give them high expression capability particularly 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 to enhance the overall ability of the immunotherapy to induce the desired immune response.

The SynCon sequence is then inserted into a circular DNA plasmid. The plasmids are manufactured in a bacterial fermentation process using proven scalable technology. These DNA-based immunotherapies can be stable under normal environmental conditions for extended periods of time.

Inovio's immunotherapies are injected in a local area of selected tissue (muscle or skin) and then electroporated (see next section) to facilitate cellular uptake and gene expression. The resulting immune response to the produced antigens results in significant production of antibodies or T cells. Memory cells are created for durable effects and, in the case of therapeutic applications, T cells can be immediately "trafficked" to parts of the body where cells are displaying the target antigen.

Published human data from two different SynCon® DNA immunotherapies--one for treating HPV-caused pre-cancers and cancers as well as one for treating HIV infection--have generated best-in-class T cell responses in terms of magnitude, durability, and killing effect, providing evidence (demonstrated in three peer-reviewed clinical study publications) of their potential to provide preventive and therapeutic capabilities against cancers and infectious diseases. This compelling data is supported by the first clinically significant efficacy data generated in a large controlled phase II study by any DNA-based immunotherapy with Inovio's data reported in 2014.

Electroporation Delivery Technology

Despite how compelling the idea of delivering DNA encoding an antigen has been, delivering the DNA directly into a cell through the cell's protective membrane has been a significant challenge. Our immunotherapies are delivered into cells of the body into a small local area of tissue using our highly efficient, proprietary electroporation (EP) DNA delivery technology, which uses brief, locally applied electric fields to create temporary and reversible permeability, or pores, in the cell membrane. Using this method allows us to increase the cellular uptake of the DNA plasmids by a thousand-fold or more compared to just delivering the "naked DNA" alone. This extent of cellular uptake has proven to enable the best-in-class immune responses that we have reported, along with the efficacy results generated by these immune responses.

Alternative delivery approaches based on the use of viruses and lipids are complex and expensive and have in the past created concerns regarding safety and caused unwanted immune responses against the carriers themselves (believed to compromise their ability to deliver their DNA "payload" and provide protection). We have published data showing the superior immune responses generated by our SynCon® immunotherapies delivered using our CELLECTRA® electroporation technology directly compared to a leading viral vector (Adenovirus type 5) based approach. We have not seen any published data indicating the capability of alternative technologies focused on using genetic code to generate preventive or therapeutic antigens to exceed Inovio's immune response data obtained to date, nor match the efficacy and immune responses data generated in our large controlled phase II study.

We believe electroporation provides a relatively straightforward, cost effective method for delivering DNA into cells with high efficiency, minimal complications, and importantly the ability to enable what we believe to be clinically relevant levels of gene expression, immune responses, and efficacy.

Products and Product Development

Inovio's primary focus is to independently and/or in partnerships advance the products developed from its integrated platform consisting of its SynCon® immunotherapy and CELLECTRA® electroporation technologies. We are currently developing a number of DNA-based immunotherapies for the prevention or treatment of cancer and chronic infectious diseases. The table below summarizes the status of our product development programs as of December 31, 2014.

Inovio SynCon® Immunotherapy Development

Product Area	Product and Indication(s)	Development Status				Partner/Funding/Sponsor
		Pre-Clinical	Phase I	Phase II	Phase III	
Cancer	Cervical dysplasia (CIN 2/3) (VGX-3100)	X	X	X	P	Inovio
	Cervical cancer (INO-3112) (VGX-3100 + DNA-based IL-12 cytokine)	X	IP			Inovio
	Head/neck cancer (INO-3112) (VGX-3100 + DNA-based IL-12 cytokine)	X	IP			Inovio
	Aerodigestive cancer (INO-3106 +/- DNA-based IL-12 cytokine)	X	IP			Inovio
	Prostate cancer (INO-5150 +/- DNA-based IL-12 cytokine)	X	P			Inovio
	hTERT expressing cancers (breast, lung, pancreatic) INO-1400	X	IP			Inovio
Infectious Disease	Hepatitis B Virus INO-1800	X	P			Roche
	Hepatitis C Virus INO-1800 + DNA-based IL-28 cytokine)	X	IP			GeneOne Life Sciences
	HIV (preventive & therapeutic) (PENNVAX®-GP)	X	P			NIH/NIAID
	HIV (preventive) (PENNVAX®-G)	X	IP			US MHRP/NIH/NIAID
	Universal influenza (INO-3510)	X	X			NIH
	Avian influenza (VGX-3400x)	X	X			Inovio

Ebola (VGX-4200)	X		P	GeneOne Life Sciences
Biodefense targets	IP			US AMRIID

X = Completed
IP = In Progress
P = Planning

Cancer Vaccines/Immunotherapies

Previous Immune Therapy Successes Point to the Potential of Inovio's Immunotherapy Approach

In recent years there have been multiple technology advancements and product approvals that have highlighted the potential of immunotherapies to usher in a new era of cancer therapeutics. Monoclonal antibodies (Mabs) such as Herceptin® and dendritic cell therapy Provenge® for prostate cancer have had their varying degrees of success. Herceptin has been used to treat over 420,000 women (Genentech Inc., 2010). While a significant step forward, suitable monoclonal antibodies with the appropriate characteristics have been difficult to design or identify and expensive to produce, and the technology does not lend itself to designing Mabs for many diseases. Dendritic or other cell-based therapy is a highly personalized medicine involving removing cells from the patient, modifying them, multiplying them, then returning them to the body. Besides the high cost and complex processes to manufacture the product, one of the glaring weaknesses of this approach is that it has not been shown to generate high levels of cancer-specific T cells.

More recently, progress in the field of immune checkpoint inhibitors (CIs) has created further optimism regarding the potential for new immunotherapies against a spectrum of cancers. The immune system relies on a safeguard system of checkpoint mechanisms to prevent excessive or incorrectly directed immune responses. Many cancer cells have the ability to "hijack" these checkpoints and neutralize T cells sent by the immune system to eliminate them. Checkpoint inhibitors prevent

cancer cells' ability to interfere with these checkpoints and enable T cells (especially CD8 killer T cells) to complete their appropriate and intended killing function against the cancer cell. Clinical studies by multiple companies of different checkpoint inhibitors have shown notable therapeutic impact against melanoma and other cancers - yet with response rates in the 20 - 50% range, there remains an important opportunity to further improve these results. They have also been associated with certain undesirable side effects. Observations suggest that CIs may be less effective if there is not a high enough pre-existing level of antigen-specific CD8 T cells. Nevertheless, they provide significant encouragement that a strong T cell generating "active" immunotherapy used as a monotherapy or in combination with a checkpoint inhibitor may unleash or enhance significant therapeutic potential. The first PD-1 CI therapies were approved for commercial use in 2014.

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 has achieved dramatic results in B cell cancers. Unfortunately it has also been associated with significant side effects. When this technology has been applied to solid tumors it has generated significant cytokine storms that have resulted in severe side effects including deaths. Moreover, adoptive cell transfer such as CAR-T, like dendritic cell therapy, involves removing T cells from a patient, modifying them to better target a cancer cell, multiplying the T cells, then returning them to the patient. This is a highly personalized approach and as such this very complex therapeutic product needs to be manufactured and released for each patient, leading to expensive manufacturing and increased supply chain complexity. Moreover, this technology is still in early clinical development.

So while the last two decades have yielded promising technology advancements that better harness or activate capable killer T cells, there is a world of untapped potential to develop "ideal" immunotherapies to fight cancers and infectious diseases.

What is an "ideal" active immunotherapy? To state the obvious, we want products that are effective, efficient, and safe. More specifically, we want immunotherapies that:

- Target disease-specific antigens (i.e. proteins unique to a cancer or infectious disease)
- Do not depend upon being patient-specific and personalized (why remove from, modify, and reintroduce cells to a patient if you can do the most important work in the patient?)
- Activate functional killer T cells with the necessary killing tools (e.g. granzyme and perforin)
- Generate robust T cell responses (e.g. a significant number of T cells) that are persistent and durable over time (memory response)
- Do not induce unwanted immune responses
- Do not induce toxic inflammatory responses
- Are capable of "breaking tolerance" of cancer cells grown in the body.

Our phase II data (discussed under HPV Immunotherapy-VGX-3100) shows we are achieving these ideal characteristics with our active immunotherapy approach to activating highly capable, antigen-targeted T cells in vivo (in the body) and we are advancing a growing pipeline of pre-clinical and clinical immunotherapies products.

HPV Immunotherapy-VGX-3100

Late Stage Cervical Dysplasia (CIN 2/3)

Human papillomavirus (HPV) is the causative agent responsible for cervical pre-cancers (cervical dysplasia), cervical cancer, other anogenital cancers and one of the most rapidly growing cancers in men - head & neck cancer. At any given time, approximately 11% of the world's population is infected with HPV.

HPV is the most common viral infection of the reproductive tract and is recognized as the major cause of cervical cancers. 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. Every year over 500,000 new cases of cervical cancer are diagnosed world-wide and approximately half of these women die. Virtually all cases are linked with persistent infection with HPV. Challenges with acceptance, accessibility, and compliance of preventive vaccines have resulted in only a third of young women are being vaccinated in the US, and even less in other countries around the world.

While roughly 90% of HPV infections are cleared by the body on its own (i.e. by the person's immune system), persistent HPV infection can lead to high grade cervical dysplasia (CIN 3) and, if untreated, eventually invasive cervical cancer. Researchers have estimated the global prevalence of clinically pre-cancerous HPV infections at

between 28 and 40

6

million. HPV 16/18 are the two most prevalent high-risk types of HPV worldwide, causing the vast majority of HPV-related cancers. HPV 16/18 are found in 52% of all high grade pre-cancerous cervical lesions and 70% of cervical cancers.

There is an annual incidence rate of CIN 1 caused by HPV types 16 and 18 of 1.4M in the US and 1.3M in the top 5 European countries. There is an annual incidence rate of CIN 2/3 caused by HPV types 16 and 18 of 270.8K in the US and 267.4K in the top 5 European countries. These represent a significant market opportunity. CIN 1 has no treatment. CIN 2/3 is served only by an invasive surgical procedure.

There are currently two FDA approved preventive vaccines, Gardasil® and Cervarix®, that protect against HPV types 16 and 18, as well as types 6 and 11(Gardasil). However, studies have shown that preventive HPV vaccines cannot treat or protect those already infected with HPV, which is a large population. In addition, not all girls and women eligible to be vaccinated are receiving these vaccines. In 2013, a US national survey found that 57% of girls aged 13-17 years had received at least one dose of the HPV vaccine series, but only 38% had received all 3 doses in the series. Currently there is no viable immunotherapy or drug to fight established HPV infection or treat cervical dysplasia and/or cancer caused by HPV.

Current treatment options for cervical dysplasia are unappealing. The “watch-and-wait” process associated with low grade dysplasia (CIN 1) is a stressful approach. The only available treatment option for high grade cervical dysplasia (CIN 2/3) is surgery, which involves ablating or cutting a women’s cervix to remove the pre-cancerous lesions. While surgical procedures are generally effective in removing lesions, they can lead to cervical scarring and longer-term reproductive risks such as pre-term birth, miscarriage, and infertility. Anticipation of these procedures produces significant anxiety for patients, despite their doctor’s reassurances, and full recovery from surgery can take up to several weeks. Because surgery does not clear the underlying HPV infection, pre-cancer lesions can recur as a result of persistent infection or incomplete removal of the lesion during surgery.

Inovio's VGX-3100 is an immunotherapy designed to dramatically increase immune responses (humoral and cell mediated) against the E6 and E7 antigens of HPV types 16 and 18 that are present in both pre-cancerous and cancerous cells transformed by these HPV types. E6 and E7 are oncogenes that play an integral role in transforming HPV-infected cells into pre-cancerous and cancerous cells. The goal of the immunotherapy is to stimulate the body's immune system to mount a killer T cell response strong enough to cause the killing of cells producing the E6/E7 protein. The potential of such an immunotherapy would be to treat pre-cancerous dysplasias as well as cancers caused by these HPV types.

Phase I Study Results

We completed a phase I study of our cervical dysplasia immunotherapy (VGX-3100) in 2010. This dose escalation study tested the safety and immunogenicity of VGX-3100 in women previously treated for moderate or severe cervical intraepithelial neoplasia (CIN 2/3), a high grade premalignant lesion that is a precursor of cervical cancer. The trial enrolled patients in three cohorts of six subjects each with VGX-3100 doses of 0.6 mg (0.3 mg each of two DNA plasmids), 2.0 mg, and 6.0 mg. Each subject was dosed at months 0, 1 and 3.

In September 2010, we presented top-line data showing achievement of best-in-class immune responses in this dose escalation study. Data from the trial included:

- Antigen-specific, dose-related T cell responses across the three dose groups;
- Strong antigen-specific antibody responses in all three dose groups;
- VGX-3100 delivered using Inovio’s proprietary CELLECTRA® intramuscular electroporation delivery device was generally safe and well tolerated at all dose levels; and
- No immunotherapy-related serious adverse events (SAEs). Reported adverse events and injection site reactions were mild to moderate and required no treatment.

Immunological analyses of blood samples collected before and after treatment indicate that antigen-specific immune responses were induced against the target proteins produced by Inovio's immunotherapy. We assessed the cellular immune responses by different analytical assays that measure the production of antigen specific T cells as well as their ability to kill in an antigen specific manner. Overall, 17/18 (94%) patients, including 6/6 (100%) of the high dose group, demonstrated vaccine induced antigen specific T cell responses by at least one measurement. Using a validated, standard interferon- ELISpot assay, antigen-specific cytotoxic T-lymphocyte (CTL, or killer T cell) responses were observed against all four antigens (E6 and E7 proteins for HPV types 16 and 18). Overall, in all three dose cohorts

combined, 14 out of 18 immunized subjects (78%) developed significant CTL responses, with positive responses ranging from under 100 to over 5000 SFU per million cells; 72% (13 of 18) responded to at least two antigens; and 50% (9 of 18) responded to all four antigens.

In the 6 mg cohort, five of six immunized subjects (83%) developed significant CTL responses by ELISpot, with average responses of 1362 SFU per million cells after three immunizations. This was a 118% increase compared to the 2 mg cohort average of 626 SFU per million cells (four responders out of six) and a 174% increase compared to the 0.6 mg dose cohort average of 497 SFU per million cells (four responders out of six).

Moreover, these ELISpot responses persisted 24 weeks after the last immunization in 86% of evaluable patients, indicating that T cell responses, in addition to antibody responses, persist for at least six months after the final immunization at month 3.

In July 2011, we reported data demonstrating long-term durability of T cell immune responses of up to two years (at the latest time measured) in 7 of 8 evaluated patients following a fourth vaccination of VGX-3100.

In October, 2012, we reported that the immune responses generated in this study displayed a powerful killing effect on cells changed by HPV into precancerous dysplasias. These results appeared in the peer-reviewed journal, Science-Translational Medicine, in an article entitled, "Immunotherapy against HPV 16/18 generates potent Th1 and cytotoxic cellular immune responses." In this study, 91% of patients who developed T cell responses showed the presence of CD8 T cells capable of the desired killing activity. Direct killing by CTLs was observed in all immunized subjects (6 of 6) in the 6 mg cohort.

Antibody responses to E6 and E7 antigens were also measured. Specific antibody responses to tumor antigens can function as an important surrogate potency marker for determining the immunogenicity (immune response characteristics) of an immunotherapy, i.e. its ability to induce an immune response. Antibodies were generated against all four antigens, as tested by the enzyme-linked immunosorbent assay (ELISA). Overall, 100% of the study participants (18 of 18) reported antibody positivity to at least two immunotherapyantigens, and 94% (17 of 18) reported positivity to three antigens; 56% (10 of 18) were positive to all four antigens.

In March 2011, we initiated a randomized, placebo-controlled, double-blind phase II study of VGX-3100 delivered using our CELLECTRA® intramuscular electroporation device in women with HPV type 16 or 18 and diagnosed with, but not yet treated for, high grade cervical intraepithelial neoplasia (CIN 2/3). The women in the study received either 6 mg of VGX-3100 (the highest dose used in our phase I study) or a placebo using the CELLECTRA® in vivo electroporation device at months 0, 1, and 3. The study assessed efficacy by measuring regression of cervical lesions from CIN 2/3 to CIN 1 or normal in the treated versus control subjects. Immunological responses were also measured in this clinical study to assess the ability of this therapy to generate strong T cell responses in a larger, controlled study. Safety was also assessed (ClinicalTrials.gov NCT01304524).

Phase II Study Results

In July 2014, Inovio released top line efficacy data from this phase II clinical trial (HPV-003) for VGX-3100. The primary endpoint, histologic regression, was evaluated 36 weeks after the first treatment. In the per protocol analysis of this three-immunization regimen, CIN2/3 resolved to CIN1 or no disease in 53 of 107 (49.5%) women treated with VGX-3100 compared to 11 of 36 (30.6%) who received placebo. This difference was statistically significant (p=0.017). Intent to treat results were also statistically significant.

There was also a high level of complete clearance of CIN 2/3. In a post-hoc analysis, CIN 2/3 resolved to no disease in 43 of 107 (40.2%) women treated with VGX-3100 compared to 6 of 36 (16.7%) who received placebo (p=0.006).

We also reported that women treated with VGX-3100 on average experienced a robust increase in CD8 T cells specific to the E6 and E7 HPV antigens. This response increased with each of the three immunizations, then declined modestly to a sustained and durable level of T cells (memory T cells) measured through 36 weeks (24 weeks post-treatment).

This trial also demonstrated virological clearance of HPV 16 or 18 from the cervix in conjunction with histopathological regression of cervical dysplasia to CIN1 or no disease, a secondary endpoint of the trial, in 43 of 107 (40.2%) VGX-3100 recipients compared to 5 of 35 (14.3%) placebo recipients (p=0.001).

We have taken the steps to publish the phase II results in a peer-reviewed medical journal. Over many months we have conducted multiple, sophisticated immune assays (measurements) to characterize the CD8 T cell responses and their association with our efficacy results, and completed a rigorous analysis and preparation of the data for publishing. We expect to see this paper published in 2015.

Preparation and launch of VGX-3100 registration phase III study

Based on the preliminary phase II results we have stated our intention to advance VGX-3100 into a phase III study in early 2016. Following is an update on the steps we are taking toward launching this clinical study.

We await completion of all follow-up in the study (week 88) which extends a full 52 weeks after the primary endpoint visits that were reached in the spring of 2014. We intend to obtain alignment with the FDA and various global regulatory agencies on the details of the pivotal phase III program to support an indication in CIN2/3.

In preparation for pivotal phase III development and commercialization, we have taken steps to scale-up manufacturing for both our VGX-3100 product and our proprietary electroporation device to support higher volume production requirements associated with commercial use while continuing to meet the highest quality assurance standards, to which we already adhere.

We have already identified highly qualified manufacturing partners and are currently working with them to establish manufacturing for phase III and beyond.

We have conducted additional market research with physicians and patients that have further characterized the unmet medical needs relating to the treatment of high grade cervical dysplasia (CIN 2/3). These include a preference for a non-invasive, non-surgical procedure for removing cervical lesions; a treatment that can clear HPV, the cause of the pre-cancer, throughout the body and not just in the limited area of the lesion; and a treatment that has no risk of causing pre-term births or infertility. CIN 2/3 represents a unique market opportunity for a novel therapy capable of providing a first-line alternative to surgery. This market research will help guide our communication and interaction with the physician, patient, and support communities.

VGX-3100 has the potential to be a less-invasive first-line treatment option, and to spare women from the anxiety of surgery and the risks it poses to their reproductive health. It strengthens the body’s immune response to the HPV infection to clear the underlying HPV infection that causes cervical cancer. It can eliminate pre-cancerous lesions that, left untreated, would evolve to cancer.

In short, VGX-3100 has potential to offer women the first non-surgical treatment for pre-cancerous cervical dysplasia. As a novel therapy advancing toward commercialization, we are pleased that the various steps necessary to launch the phase III study in early 2016 are advancing in a timely and successful manner.

HPV Immunotherapy-INO-3112 (VGX-3100 +DNA-Based IL-12 Cytokine INO-9012)

Head & Neck Cancer and Cervical Cancer

HPV is also associated with head and neck cancers, especially those in the oropharynx and larynx but also the oral cavity and nose/nasal passages. The incidence of HPV-caused oropharyngeal cancer has increased significantly within the last 20 years and has been increasing at an epidemic rate. Approximately 15-20% of the 400,000 new head and neck cancers globally are HPV related. HPV associated head and neck cancer is growing fastest in developed countries, such as the US, and in younger men. In the US, approximately 12,000 new cases of HPV-associated head and neck cancer are diagnosed annually. The estimated prevalence of HPV-caused oropharyngeal cancer in the U.S. in 2012 was nearly 212,000.

By 2020, scientists estimate that HPV will cause more cases of oropharyngeal cancer than cervical cancer and by 2025 HPV will be the causative factor of 90% of all head & neck cancers (HPV currently causes 63% of head & neck cancers). Greater than 70% of cancers of the oropharynx are linked to HPV, with HPV16 being the most prevalent serotype.

Improvements in primary treatment modalities (surgery and radiation) have produced significant improvements in morbidity but intensive radiation has a profound long-term impact on mortality and quality of life. Based on these factors, we believe there is a significant opportunity for an effective immunotherapy.

In June 2014 we initiated a phase I/IIa clinical study assessing the immunogenicity and safety of INO-3112 (VGX-3100 in combination with a DNA-based IL-12 cytokine (INO-9012)) in head & neck cancer patients. We added our DNA-based IL-12 immune activator to VGX-3100 for this cancer study because our HIV immunotherapy clinical study (HVTN-080) showed that the addition of IL-12 to our DNA immunotherapy can enhance the activation of CD8 T cells.

Up to twenty adults with HPV-positive head & neck squamous cell carcinoma (HNSCC) will be treated with INO-3112 and followed for safety, immune and clinical responses in an open-label study called HPV-005. In one part of the study, up to ten patients will be treated with INO-3112 before and after resection of their tumor. In the second part of the study, up to ten patients will be treated with INO-3112 after completion of chemotherapy and radiation therapy. Each INO-3112 treatment will be administered using Inovio's CELLECTRA® delivery system. In addition to assessing safety, this study will analyze T cell immune responses to INO-3112. Pre- and post-immunotherapy tumor tissue will be analyzed to evaluate infiltration of T cells into the tumor and tumor bed. Clinical responses characterized by anti-tumor effects, using RECIST criteria, and progression free survival will also be measured.

Cervical cancer is the most commonly occurring cancer among women in developing countries and is the second most commonly occurring cancer amongst women worldwide. Without consistent HPV vaccination or improvements in screening and treatments, current incidence trends suggest that the incidence of cervical cancer could rise from roughly 530,000 cases per year to approximately 1 million cases per year in 2050. The prognosis for advanced cervical cancer patients is characteristically poor and treatment options are palliative at best.

In June of 2014 we initiated a phase I/IIa clinical study assessing the immunogenicity and safety of INO-3112 (VGX-3100 in combination with INO-9112) in cervical cancer patients. Twenty patients with HPV-caused inoperable invasive cervical cancer will be evaluated in an open-label study called HPV-004. Women will receive four treatments of INO-3112 every four weeks after completion of a standard chemoradiation regimen. Each INO-3112 treatment will be a combination of 6 mg of VGX-3100 and 1 mg of INO-9012 delivered together intramuscularly with the CELLECTRA® delivery system. The study team will evaluate clinical responses at the tumor site (tumor shrinkage or regression) and assess disease-free survival

and disease recurrence up to 12 months after the initial immunotherapy with Inovio's INO-3112. T cell immune responses will be analyzed pre- and post-immunotherapy in the tumor tissue as well as in the periphery (bloodstream). We expect to report interim data from these studies in 2015.

HPV Immunotherapy-INO-3106 +/- DNA-Based IL-12 Cytokine

Aerodigestive Cancer

Further expanding our HPV portfolio, we launched a compassionate phase I clinical trial in patients with HPV-caused aerodigestive cancer. Aerodigestive cancer is a condition that affects the lips, mouth, tongue, nose, throat, vocal cords, larynx, and parts of the esophagus and windpipe. Current treatment for HPV-associated aerodigestive cancers includes chemotherapy, radiation, and surgery, all of which have negative side effects.

This phase I study is testing INO-3106 alone or in combination with DNA-based IL-12 in subjects with HPV-6 associated invasive aerodigestive malignancies who have exhausted other treatment options (chemotherapy, radiation and surgery). Successful results could open a path to pursuing an FDA orphan designation (special status granted for therapies for rare diseases) for aerodigestive cancers.

Prostate Cancer Immunotherapy-INO-5150

The development of a new treatment for prostate cancer would be a significant medical advance given that present treatment options (surgery, radiation and hormone deprivation), while somewhat effective, all carry deleterious side effects and often do not confer long-term cure. Across the United States, there were 238,000 new cases of prostate cancer and more than 29,000 deaths in 2013.

In January 2011, we announced the publication of a scientific paper in the journal Human Vaccines detailing potent immune responses in a pre-clinical study of our SynCon® immunotherapy for prostate cancer targeting two antigens, prostate specific antigen (“PSA”) and prostate specific membrane antigen (“PSMA”). While current prostate cancer therapies target single antigens, in this study we tested the hypothesis in mice that multiple antigens administered with Inovio's electroporation delivery technology would improve the breadth and effectiveness of a prostate cancer immunotherapeutic.

This study, conducted by our scientists and collaborators, is described in the published paper entitled, “Co-delivery of PSA and PSMA DNA vaccines with electroporation induces potent immune responses.” The SynCon® immunotherapy evaluated in this study consists of PSA and PSMA synthetic consensus immunogens based on human and macaque amino acid sequences, which enabled the sequences for these antigens to differ slightly from the native proteins associated with prostate cancer in humans. In humans, this difference may help overcome self-tolerance of cancer cells displaying these prostate-related proteins and enable the generation of an anti-tumor immune response. Mice received two immunizations of highly optimized immunotherapy delivered by electroporation. Immunogenicity was evaluated one week after the second immunization. The resultant data showed the induction of strong PSA and PSMA-specific cellular immune responses and also significant antigen specific seroconversion, illustrating that both humoral and cellular immune responses can be generated by this approach.

In 2013 we established a license agreement with Roche (described in more detail under Corporate Development) that included Inovio’s prostate immunotherapy product. In November 2014 Roche terminated its license for INO-5150, while still maintaining its license to and collaboration with Inovio’s hepatitis B immunotherapy. All rights to INO-5150 will be returned by Roche to Inovio.

We plan to initiate a phase I clinical trial for INO-5150 in the first half of 2015.

hTERT Immunotherapy-INO-1400

Human telomerase reverse transcriptase (hTERT) is an attractive cancer immunotherapy target. High levels of hTERT have been detected in more than 85% of all human cancers, including breast, lung, and pancreatic cancers, while normal cells showed undetectable levels of telomerase expression. Immunological analysis indicated that hTERT is a widely applicable target recognized by T-cells and can be potentially used as a universal cancer immunotherapy. Lung, breast, and pancreatic cancer mortality rates are ranked first, third, and fourth, respectively, among cancer types in the United States, despite improvement in detection and treatment. In each of these three cancer types, significant numbers of patients undergo surgical resection and adjuvant therapy with an attempt at cure, but only a fraction remain in remission. This study will evaluate our novel immunotherapy with the ultimate goal of reducing the risk of relapse in these patients.

In July 2013, we announced that our hTERT DNA cancer immunotherapy administered with our CELLECTRA® adaptive electroporation delivery device generated robust and broad immune responses, induced T cells with a tumor-killing function, and increased the rate of survival in pre-clinical studies.

In December 2014, we initiated a phase I clinical trial for our hTERT (human telomerase reverse transcriptase) DNA immunotherapy (INO-1400) alone or in combination with our IL-12 immune activator (INO-9012) in adults with breast, lung, or pancreatic cancer at high risk of relapse after surgery and other cancer treatments. This trial is an open label, dose escalation study in approximately 54 subjects.

Infectious Disease Vaccines/Immunotherapies

Hepatitis B Virus-INO-1800

Although an effective preventive vaccine against hepatitis B virus (HBV) infection has existed for over three decades, HBV remains a major epidemic, especially among people of Asian and African descent. The World Health Organization estimates that 2 billion people globally have been infected with HBV, with over 350 million people chronically infected with the virus and at risk of developing cirrhosis or liver cancer. It is estimated that upwards of 1.4 million people in the US are infected with the virus. Currently, the only therapies available for chronically infected individuals are interferon-alpha and nucleoside analog treatments, which function by controlling viral replication but unfortunately do not clear infection. Interferon can prevent viral replication in only 30% of patients and does so with undesirable side effects.

Liver cancer is the second most common cause of death from cancer worldwide, killing most patients within five years of diagnosis. About 782,000 new cases arise each year. One of the major causes and risk factors for liver cancer is infection by hepatitis B. Chronically infected individuals may develop a permanent scarring of the liver (a condition called cirrhosis). Liver cirrhosis can evolve into hepatocellular carcinoma, which claims 746,000 lives annually.

In November 2012, we announced data indicating that our HBV immunotherapy generated strong T cell responses that eliminated targeted liver cells in mice. Results from this pre-clinical study appeared in the peer-reviewed journal, Cancer Gene Therapy, in an article entitled, "Synthetic DNA immunogen encoding hepatitis B core antigen drives immune response in liver."

In this study, we developed a DNA immunotherapy which is encoded for the HBcAg antigen and represents a consensus of the unique HBcAg DNA sequences of all major HBV genotypes (A through E). When delivered by electroporation, our researchers first demonstrated that this therapy elicited strong HBcAg-specific T cell and antibody responses in the periphery (outside of the liver) by ELISpot, ICS and cell proliferation assays. Researchers observed that the immunization could also induce antigen-specific CD8 and CD4 T cells that produced both IFN-y and TNF-a in the liver, indicating a strong immunotherapy-induced T cell response was also present in the liver.

Furthermore, study researchers found the immunotherapy-specific T cells exhibited a killing function, and could migrate to and stay in the liver and cause clearance of target cells without any evidence of liver injury. Taken together, this is the first study to provide evidence that intramuscular immunization can induce killer T cells that can migrate to the liver and eliminate target cells.

In September, 2013, Roche exclusively licensed this SynCon® immunotherapy in conjunction with the use of Inovio's CELLECTRA® electroporation technology for this immunotherapy as part of a broader partnership agreement with Inovio. We expect that a phase I study of this immunotherapy will be initiated in the first half of 2015. The initiation of the trial will trigger a milestone payment from Roche. Roche is paying for all costs associated with the development of this immunotherapy.

Hepatitis C Virus (HCV)-INO-8000/VGX-6150

Hepatitis C virus is a major cause of acute hepatitis. HCV is spread primarily by direct contact with human blood, the major causes worldwide being the use of unscreened blood transfusions and re-use of needles and syringes that have not been adequately sterilized. As many as 75% -85% of newly infected patients may progress to develop chronic infection. Of those with chronic liver disease, 5% - 20% may develop cirrhosis. About 1%-5% of infected people may die from the consequences of long term infection (due to liver cancer or cirrhosis). Globally, an estimated 150 million people are chronically infected with HCV, which represents a reservoir sufficiently large for HCV to persist, and 3 to 4 million people are newly infected each year. In the US, while new incidences of HCV have dropped dramatically, an estimated 3.2 million Americans are chronically infected. People with chronic HCV infection face an increased risk of developing hepatocellular cancer, a difficult-to-treat cancer with a poor prognosis. More than 350,000 deaths each year are attributed to HCV-caused liver cirrhosis and hepatocellular cancer.

In April, 2010, we announced, along with our collaborators from Drexel University, Cheyney University, and the University of Pennsylvania, that we received a combined $2.8 million grant from the PA Commonwealth Universal

Research Enhancement Program (CURE), to advance our proprietary immunotherapy to treat HCV using our CELLECTRA® electroporation delivery system. The grant funded pre-clinical studies using an expanded set of SynCon® immunogens to test

the safety and effect on the immune system of our novel immunotherapy designed to treat persons who are chronically infected with HCV and have not responded to currently available therapies.

The HCV therapy market has been recently transformed by the launch and rapid adoption of Sovaldi® and other combo drugs in its class. Yet prices for these products remain high and out of reach for most of the patients in the world. Furthermore, there is no immune system stimulating approach that may provide a better solution for many HCV-infected people.

At the end of 2011 we announced positive pre-clinical results from our HCV immunotherapy, INO-8000, which were published in Molecular Therapy. This multi-antigen DNA immunotherapy covers hepatitis C virus genotypes 1a and 1b and targets the antigens NS3/4A, which includes HCV nonstructural proteins 3 (NS3) and 4A (NS4A), as well as NS4B and NS5A proteins. Following immunization, rhesus macaques mounted strong HCV-specific T cell immune responses strikingly similar to those reported in patients who have cleared the virus on their own. The responses included strong NS3-specific interferon-gamma (IFN-g) induction, robust CD4 and CD8 T cell proliferation, and induction of polyfunctional T cells. Importantly, we also observed functional T cells in the liver.

In October 2013, our partner GeneOne (formerly VGX International Inc.) launched a phase I study of this HCV immunotherapy. Under a 2011 development agreement, GeneOne is fully funding IND-enabling, phase I, and phase II studies for this immunotherapy. They are currently testing VGX-6150 (INO-8000 with DNA-based IL-28 cytokine) in phase I testing in Korea. We intend to report interim data from this phase I study in 2015.

We are also planning to evaluate INO-8000 at additional clinical study sites in the U.S.

HIV Preventive and Therapeutic Immune Therapies

Since its discovery in 1981, HIV, the virus which causes AIDS, has killed more than 36 million people. In 2011, there were roughly 2.5 million new cases of HIV diagnosed. In 2012, approximately 35 million people were living with HIV worldwide. Each year in the United States, about 50,000 people become newly infected with HIV. At the end of 2010, 1.1 million people in the US were living with HIV.

Effective vaccines have been actively pursued for over 20 years, without success. HIV represents one of the most confounding targets in medicine. The virus' high mutagenicity (ability to mutate) has made effective vaccine development very challenging. Its outer envelope, swathed in sugar molecules, is difficult to attack, and HIV strikes the very cells that the immune system launches to thwart such an infection. Although several drugs (anti-retrovirals) are available to treat the patients once they are infected, vaccines and immunotherapies are necessary to stop the spread of disease and perhaps reduce the need for anti-retroviral treatment.

Noting that many long-term survivors have high counts of killer CD8 T cells, the HIV vaccine and immunotherapy field has turned to stimulating the immune system to generate those cells. Recent HIV vaccine candidates adopted the use of an adenovirus or a common human cold virus that had been genetically modified to contain code for HIV antigens to prevent viral replication. These vaccines have proven to not be effective. More recently the RV-144 trial, which employed an ALVAC™ (canary pox) vaccine prime followed by a protein vaccine boost, demonstrated 30% efficacy in preventing acquisition of infection amongst the vaccinated population compared to the control group. Although the efficacy was relatively modest, the finding has for the first time showed that an immunotherapy may be able to combat spread of HIV and has spurred the development of newer immunotherapy candidates. We believe, however, that a different approach is needed to develop an effective vaccine or immunotherapy for HIV.

In October 2009, along with the HIV Vaccines Trial Network (“HVTN”), we initiated a phase I study (HVTN-080) of PENNVAX®-B (with and without a DNA cytokine, DNA IL-12) delivered with electroporation using the CELLECTRA® delivery device in healthy, uninfected individuals. The vaccine consists of SynCon® immunogens targeting HIV gag, pol, and env proteins from HIV subtype, or clade, B. This randomized, double-blind, multi-center study was sponsored by the NIAID, an agency of the National Institutes of Health (the “NIH”), and conducted by the NIAID-funded HVTN, and vaccinated 48 healthy, HIV-negative volunteers at several clinical sites to assess safety and levels of immune responses.

Of the 48 total volunteers, eight subjects received a placebo, 10 subjects received a 1 mg dose of PENNVAX®-B immunotherapy, and 30 subjects received a 1 mg dose of PENNVAX®-B along with IL-12 DNA. All volunteers received vaccine or placebo administered with electroporation at months 0, 1, and 3. T-cell immune responses were detected using a validated flow cytometry-based intracellular cytokine staining (ICS) assay at the HVTN core immunology laboratory at the Fred Hutchinson Cancer Research Center in Seattle, WA.

We reported final data from this study in September 2011. These data indicate that antigen-specific T-cell responses were generated by the immunotherapy in a majority of subjects. Overall, either CD4 or CD8 or both T-cell responses were observed against at least one of the immunotherapy antigens in 83.3% (30 of 36) of evaluated subjects after three immunizations using electroporation. The response rate increased to 88.9% (24 of 27) of evaluated subjects after three immunizations with electroporation plus the IL-12 cytokine gene adjuvant. The investigators in this study concluded that PENNVAX®-B + IL-12

plasmid delivered via electroporation led to frequencies and magnitudes of cellular immune responses equal to or greater than those reported from current vector-based HIV vaccines such as adenovirus or traditional DNA vaccination without electroporation. These results represent best-in-class immune responses that have not been observed with other platforms.

Other specific results included:

- Antigen-specific CD4 T cell responses were generated by the immunotherapy in 80.8% of evaluated immunotherapy recipients (21 of 26).
- Significantly strong antigen-specific CD8 T cell responses were also generated by the immunotherapy in 51.9% of evaluated immunotherapy recipients (14 of 27).
- In an assessment of immune response durability out to six months post dose 3, 53.6% (15 of 28) of the subjects maintained positive CD4 T cell responses and 42.9% (12 of 28) of the subjects maintained positive CD8 T cell responses out to six months.
- Compared to the previously conducted HVTN 070 phase I study, which assessed PENNVAX®-B with cytokine adjuvant IL-12 at double the dose, with four immunizations, but without electroporation delivery, response rates in HVTN 080 with electroporation were significantly higher for both CD4 responses (40.7%) and CD8 T cell responses (3.6%). Samples from eight placebo recipients and pre-vaccine samples from vaccine recipients were also tested and were negative for both CD4 T cell responses and CD8 T cell responses.
- PENNVAX®-B delivered using the CELLECTRA® intramuscular electroporation delivery device with or without IL-12 was safe and generally well tolerated. There were no immunotherapy-related serious adverse events. Reported adverse events and injection site reactions were mild to moderate and required no treatment.

This data was published in July 2013 in the peer-reviewed Journal of Infectious Diseases in the article, “Safety and comparative immunogenicity of an HIV-1 DNA vaccine in combination with plasmid IL-12 and impact of intramuscular electroporation for delivery.”

A second clinical study testing PENNVAX®-B in a therapeutic setting was conducted in collaboration with the University of Pennsylvania. The HIV-001 open label, phase I study enrolled 12 adult HIV-positive volunteers to assess safety and levels of immune responses generated by Inovio's PENNVAX®-B immunotherapy delivered with our CELLECTRA® electroporation device. Study volunteers were required to be on a highly active antiretroviral therapy (HAART) regimen, have undetectable plasma viral load (<75 copies/mL), and have CD4 T lymphocyte counts above 400 cells/μL with nadirs over 200 cell/μL. Twelve (12) eligible subjects were administered a four dose series (day 0, weeks 4, 8 and 16) of PENNVAX®-B containing 3 mg of DNA/dose via intramuscular electroporation. T cell responses were measured using a validated ELISpot assay at the University of Pennsylvania Immunology Core Facility. Overall, significant immunotherapy-specific T cell responses were observed in 75% (9 out of 12) of subjects against at least one of the three immunotherapy antigens (gag. pol, or env) following immunization. Fifty percent of the subjects (6 out of 12) had strong immunotherapy induced antigen-specific responses above the pre-immunization levels to at least two of the antigens. Importantly, the responses induced by immunization were predominantly antigen-specific (i.e. gag, pol and env) CD8 T-cells, which are considered to be paramount in clearing chronic viral infections and an important measurement of the performance of an immunotherapeutic. These results are in stark contrast to previously reported studies with other DNA immunotherapies delivered without electroporation that yielded poor overall T cell immune responses.

Subsequent to year end, the results from this clinical study appeared in the peer-reviewed journal Molecular Therapy, in the article, "Synthetic consensus HIV-1 DNA induces potent cellular immune responses and synthesis of granzyme B, perforin in HIV infected individuals," authored by Inovio researchers and collaborators.

Our HIV immunotherapy was found to have significantly increased antigen-specific CD8+ T-cell responses in all 12 patients. We observed that these activated CD8+ killer T cells produced the cell-killing substances granzyme B and perforin (both necessary to kill targeted cells and viruses) in quantities and characteristics similar to those of long-term non-progressors. (HIV-infected individuals who, without treatment, do not progress to further stages of the disease). It is believed that in these extremely rare individuals who self-regulate their HIV infection, part of their ability to control the infection may lie in their unique immune responses.

Another striking result of this HIV study was that PENNVAX®-B increased the number of HIV-specific CD8+ killer T cells displaying the receptor integrin, which is associated with the ability to carry T cells to the gastrointestinal tract

(GIT), the most important target organ for HIV.

We believe these positive results demonstrate the potency of our immunotherapy technology platform and raise the potential for the development of immunotherapies against HIV.

The valuable proof of concept data achieved with the PENNVAX®-B (targeting clade B envelope viruses) clinical studies provided a strong and positive basis with which to advance our HIV immunotherapy development program via an HIV Vaccine Design and Development Teams (HVDDT) contract for PENNVAX®-GP (discussed below).

In September 2010, the United States Military HIV Research Program (MHRP) initiated a phase I trial (RV262) using one of our prophylactic HIV immunotherapies in a unique prime-boost strategy. This program was developed to protect against diverse subtypes of HIV-1 prevalent in North America, Europe, Africa, and South America. The study is being conducted by the United States MHRP through its clinical research network in the US and East Africa. The prime is a plasmid immunotherapy, Inovio's PENNVAX®-G, and the boost is a virus vector vaccine, Modified Vaccinia Ankara-Chiang Mai Double Recombinant (MVA-CMDR). Together, the vaccines are designed to deliver a diverse mixture of antigens for HIV-1 subtypes A, B, C, D and E. The study will test PENNVAX®-G delivered with electroporation in conjunction with the MVA-CMDR boost. The NIAID is sponsoring the study, which is intended to enroll 92 total participants and assess safety and immune responses. The study is being conducted in two parts. Part A enrolled 12 subjects in the US (open label study) and is complete. This study confirmed the safety profile of the vaccine and opened the door to initiate the larger placebo controlled international study. Part B has completed the targeted enrollment and dosing of 80 subjects in three African countries (Kenya, Tanzania and Uganda). Immune analyses are being performed by the MHRP and are ongoing. Interim data presented at the HIV R4P meeting in Capetown in October 2014 showed that the vaccine administration was generally safe and well tolerated. Antigen specific T cell responses were detected by interferon gamma ELISpot assay in 12/27 subjects and antibody responses were noted by ELISA in 10/11 subjects whose samples had been analyzed at that time.

Based on the proof-of-concept established with PENNVAX®-B, we were awarded a contract under the NIAID's HIV Vaccine Design and Development Teams program to advance a more optimized preventive HIV DNA vaccine, PENNVAX®-GP, delivered using intradermal electroporation delivery. The contract provides up to $25.3 million of funding over seven years, including a five-year base period and follow-on option years. The funding and development program covers pre-clinical optimization, immunogenicity and challenge studies in animal models, IND-enabling toxicology studies, cGMP (current good manufacturing practices) manufacturing of all components of the immunotherapy and intradermal CELLECTRA® electroporation device, and the conduct of a phase I human clinical trial. cGMP manufacture of the PENNVAX®-GP constructs to support clinical trials is being conducted at the manufacturing facility of our affiliate, GeneOne/VGXI.

We expect that the HVTN will launch a phase I clinical study of PENNVAX®-GP in a preventive setting in the first half of 2015. A phase I clinical study of PENNVAX®-GP as an immunotherapy is planned for the second half of 2015.

HIV remains a challenging and tremendously important area of medical research, and we value the NIH's support to further evaluate the immunogenicity and efficacy of our electroporation delivery system and novel preventive HIV immunotherapy candidate.

Avian Influenza Immunotherapies

Influenza is one of the most communicable diseases and typically affects children and elderly most severely. Complications from influenza cause more than 200,000 hospitalizations and cause between 3,000-49,000 deaths each year in the United States alone, according to the Centers for Disease Control. The world is annually subjected to two influenza sessions (one per hemisphere), between three and five million cases of severe illness, and up to 500,000 deaths. A pandemic occurs every ten to twenty years, which infects a large proportion of the world's population and can kill tens of millions of people as the “Spanish Flu” did in just two years (50-100 million deaths during 1918-1919). New influenza viruses are constantly produced by mutation or reassortment, and can develop resistance to standard antiviral drugs. The H5N1 flu virus has been spreading from Asia despite the belief that it was under control immediately after outbreaks there in 2004. In 2005, there were reports of H5N1 in wild birds in Europe. In 2006, there were reports of an H5N1 strain in wild birds and poultry in Africa and the Near East. According to the World Health Organization, the H5N1 bird flu has infected 650 people and resulted in 386 deaths (approximately 60% death rate) in 15 countries since 2003 (WHO, February 2014). While H5N1 has never been passed person-to-person and has not spread widely, one concern is the potential for the lethal H5N1 to “reassort” with another of the influenza sub-types that have been prone to spread more rapidly in humans, possibly creating a more dangerous influenza strain. Through 2006, over 140 million birds had been killed and over $10 billion spent to try to contain H5N1 avian influenza, which has a death rate of 90%-100% in birds.

Our VGX-3400X candidate targets H5N1. The immunotherapy consists of three distinct DNA plasmids coded for a consensus hemagglutinin (HA) antigen derived from different H5N1 virus strains; a consensus neuraminidase (NA)

antigen derived from different N1 sequences; and a consensus nucleoprotein (NP) fused to a small portion of the m2 protein (m2E) based on a broader cross-section of influenza viruses in addition to H5N1 and H1N1.

In our first proof of principle study of our universal flu immunotherapy program, VGX-3400X was delivered with intramuscular electroporation using our CELLECTRA® electroporation device. The primary objectives of this clinical trial were to assess safety and tolerability. The secondary objective was the measurement of antigen-specific T cell and antibody responses, including binding and hemagglutination inhibition (HAI) responses, i.e. a measure of protection, against multiple strains of H5N1 influenza.

The study assessed a total of 60 healthy volunteers, 30 in the US and 30 in Korea (in a separate, parallel clinical trial sponsored by Inovio affiliate GeneOne. Three dose cohorts of 10 subjects were each given two injections of 0.2 mg, 0.67 mg, or 2.0 mg of each plasmid at months 0 and 1.

In a report in July, 2011 of interim data, VGX-3400X was found to be generally safe and well tolerated at all dose levels. There were no vaccine-related serious adverse events. Reported adverse events and injection site reactions were mild to moderate and required no treatment.

We tested for antibody responses against the target antigens and observed high levels of binding antibodies in 26 of 27 evaluated subjects (96%). Antibodies were generated against all three antigens, as tested by the enzyme-linked immunosorbent assay (ELISA). Positive antibody responses persisted to seven months, the latest time point tested.

In testing for HAI responses against the Vietnam (A/H5N1/1203/04) strain, 3 of 27 subjects (11%) showed HAI titers greater than 1:40, which is considered to be an indicator of protection against influenza in humans. Two of the three subjects with HAI titers exceeding 1:40 against the Vietnam strain also demonstrated greater than 1:40 titers against the Indonesia (A/H5N1/5/2005) strain, demonstrating cross-reactive responses in these volunteers.

Significantly, antigen-specific cytotoxic T-lymphocyte (CTL) responses were also observed against all three antigens (HA, NA and NP). After two vaccinations, 13 of 18 vaccinated subjects (72%) from the first two cohorts developed strong CTL responses to at least one of the immunotherapy components. After cohort 3 samples were analyzed, 20 of 29 immunized subjects (69%) in all 3 cohorts developed strong CTL responses to at least one of the immunotherapy components. These positive T cell responses were measured up to seven months after the first immunization.

Generation of influenza antigen-specific T cell responses is believed to be important for generating universal, long-lasting immunity against influenza as well as to generate a stronger immune response against flu in elderly people.

In another component of the study, participants received a booster vaccination using just the H5 HA immunotherapy component of VGX-3400X delivered using intradermal (rather than intramuscular) electroporation. The intradermal (ID) part of the study was the first flu study using ID electroporation delivery in humans. ID electroporation delivers our SynCon® immunotherapies into skin, which contains large amounts of immune cells such as dendritic cells and macrophages considered most important for generating protective antibodies. Our new ID electroporation device uses a patented miniaturized needle array which creates electroporation conditions uniquely optimized for skin delivery. The goal of this booster vaccination was to determine if ID delivery of the H5 HA construct can increase HAI titers beyond those achieved by the initial intramuscular immunizations. Twenty-two participants received the ID booster immunization.

Immune response data measured one month after this boost were reported in November 2011. Ten of 20 subjects (50%) exhibited a four-fold or greater rise in geometric mean titers (GMT) in the HAI assay (ranging from 1:20 to 1:80 HAI titers) against the Clade 1 A/Vietnam/1203/04 strain. Significantly, a four-fold or greater rise in GMT titers against five other Clade 2 (Clade 2.1, 2.2; 2.3.2; 2.3.4) and Clade 0 H5N1 viruses was also noted in 10-25% of the vaccinated subjects, further demonstrating cross-reactive immune responses in these volunteers. One subject displayed greater than 1:40 HAI titers against all six different H5N1 viruses tested. ID immunization was found to be generally safe and well tolerated.

HAI measurements from the blood of an immunized subject are used to assess the generation of protective antibody responses. A four-fold rise in HAI titers (compared to pre-vaccination) is considered to be an important indicator of immune activation. Generating an HAI titer of 1:20 is generally regarded as a positive vaccine response, with a titer of 1:40 or higher in the blood of immunized subjects generally associated with protection against influenza in humans.

Seventeen subjects boosted with the minimally invasive ID vaccination were subsequently given a second ID booster vaccination. In May 2012 we reported that 100% and 89% of immunized subjects demonstrated high-titer binding antibody responses against the more common Clade 1 A/Vietnam/1203/04 and Clade 2 A/Indo/5/05 strains, respectively, demonstrating vaccine-specific immune activation. We also tested the immunotherapy's ability to generate protective HAI responses against six distinct H5N1 virus strains (Clades 0, 1, 2.1, 2.2, 2.3.2 and 2.3.4), representing all major genetic branches of the H5N1 genetic tree. Of the 17 subjects who completed the full immunization regimen:

- Eight of 17 (47%) immunized subjects had an HAI titer of 1:40 or higher against at least one of the tested H5N1 viruses.

- Twelve of 17 (71%) vaccinated subjects had an HAI titer of 1:20 or higher against at least one H5N1 strain.
- Seven of 17 (41%) had an HAI titer of 1:40 or higher against the Clade 2.2 A/Turkey/1/05 strain.
- Five of 17 immunized subjects (29%) displayed an HAI titer of 1:20 or higher against at least three different H5N1 viruses tested.
- In an unprecedented result, two immunized subjects demonstrated an HAI titer of 1:20 or higher against all six strains tested.

Hemagglutination inhibition (HAI) measurements from the blood of an immunized subject are used to assess the generation of protective HA antibody responses generated by a vaccine. All HAI titer data are presented in geometric mean

titers (GMT). Generating an HAI titer of 1:20 is generally regarded as a positive response to the vaccine; a titer of 1:40 or higher in the blood of immunized subjects is generally associated with protection against seasonal influenza viruses and has been observed in multiple subtypes.

Although a number of companies have well-developed avian influenza programs and lead vaccine candidates have entered into national stockpiles (US and EU), we believe there exists a need for broadly protective and easily scalable technologies to prepare for the as yet unknown target presented by the next form of avian influenza. Our SynCon® technology provides protection from known avian influenza viruses (in animal studies) and has also shown the ability to protect against newly emergent, unmatched strains.

Responding to the 2013 H7N9 influenza outbreak, we completed the design, optimization, and manufacturing of an H7N9 DNA immunotherapy within two weeks. A pre-clinical study of this DNA therapy showed that 100% of vaccinated mice were protected against sickness and death when they were challenged with a lethal dose of H7N9 virus. This study further highlights the ability of Inovio's SynCon® immunotherapies to create cellular immune responses that could reduce the severity of H7N9 infection in a person that acquires the virus and limit the spread of the virus in a pandemic setting. Data from this study was published in Vaccine in a paper titled “Protective immunity to H7N9 influenza viruses elicited by DNA vaccine.”

We are seeking additional grant funding to advance this program further.

Universal Influenza Immunotherapy

Conventional vaccines are strain-specific and have limited ability to protect against genetic shifts in the influenza strains they target. They are therefore modified annually in anticipation of the next flu season’s new strain(s). If a significantly different, unanticipated new strain emerges, such as the 2009 swine-origin pandemic strain, then the current vaccines provide little or no protective capability. In contrast, we believe that our design approach to characterize a broad consensus of antigens across variant strains of each influenza sub-type creates the ability to protect against new strains that have common genetic roots, even though they are not perfectly matched. By formulating a single immunotherapy with some or all of the key sub-types, protection may be achieved against seasonal as well as pandemic strains such as swine flu or pandemic-potential strains such as avian influenza noted above. We are focused on developing DNA-based influenza immunotherapies able to provide broad protection against known as well as newly emerging, unknown seasonal and pandemic influenza strains.

Instead of targeting a specific strain or strains, we have developed a universal vaccine strategy to deal with the ever-changing flu threats. Using our SynCon® process, our scientists designed immunotherapies targeting an optimal consensus of HA, NA, and NP proteins derived from multiple strains of each of the Type A sub-types H1N1, H2N2, H3N2 (these three influenza sub-types having been responsible for the majority of seasonal and pandemic influenza outbreaks in humans during the last century), as well as H5N1. In theory, consensus HA vaccine constructs from each sub-type, delivered using our electroporation device, could potentially protect immunized subjects from 90-95% of all human seasonal and pandemic influenza concerns. Additionally, we have also developed an optimal consensus of HA sequences derived from influenza Type B strains. Type B is one of three components of current seasonal influenza vaccinations. Thus, using our SynCon® constructs, we have now developed immunotherapy elements that can target both pandemic-risk (H5N1, H7N9, H1N1) as well as seasonal influenza strains (H3N2, H1N1, influenza B).

Moreover, using our approach the immunotherapies might not have to be administered annually after the first few priming sessions. Rather, the same combination could be used to boost the immune system every few years.

In September 2012, we announced that an interim analysis of a SynCon® universal H1N1 influenza vaccine showed that it generated protective HAI titers against some of the most prevalent strains of H1N1 influenza from the past 100 years in a phase I clinical trial. The open label phase I study evaluated two H1N1 hemagglutinin (HA) plasmids designed to broadly protect against unmatched influenza strains within different branches of the H1N1 subtype. These plasmids were delivered in healthy adults with Inovio's CELLECTRA® intradermal electroporation device up to three times. The delivered immunotherapy was well tolerated; reported adverse events and injection site reactions were mild to moderate and required no treatment.

Researchers exposed blood samples from the vaccinated subjects to each of the nine key H1N1 viruses in circulation over the last 100 years: eight were H1N1 strains used to formulate the seasonal vaccines of the last 25 years; one was the H1N1 strain that caused the 1918 Spanish flu. These unmatched influenza strains were used to assess the

generation of hemagglutination inhibition (HAI) titers meeting or exceeding 1:40. Demonstrating Inovio's vaccine's broad cross-reactive coverage, a significant percentage of subjects immunized with Inovio's SynCon® immunotherapy had an HAI titer of 1:40 or higher against each of the nine H1N1 strains tested, ranging from a 30% response rate to the A/Brisbane/59/07 strain to a 100% response rate to the A/Beijing/262/95 strain. The benchmark for the current licensed seasonal flu vaccines, which are based on matching the vaccine HA sequence to that of the circulating strain, is to have greater than 65% of vaccinees generate an HAI titer of 1:40 or higher against the matched vaccine strain.

By design, our SynCon® universal flu immunotherapy is not matched to any single virus and was not matched to any of the strains tested in this study. The immunotherapy recipients generated protective HAI responses against the H1N1 A/South Carolina/1/18 strain from the 1918 Spanish flu as well as all the H1N1 strains which were part of the annual seasonal trivalent inactivated flu vaccines (TIV) since 1986, including: A/Taiwan/1/86, A/Texas/36/91, A/Bayern/07/95, A/Beijing/262/95, A/New Caledonia/20/99, A/Solomon Islands/03/06, A/Brisbane/59/07, A/California/07/09. The HAI titers in the positive responders ranged from 1:40 to greater than 1:1280.

Compared to the seasonal TIV (trivalent influenza vaccine)-immunized control group, which was matched to the current H1N1 seasonal flu strain (A/California/07/09), those immunized with our immunotherapy generated a higher or similar percentage of positive HAI titer responders against all of the strains except for A/California/07/09. As anticipated, the TIV recipients generated the best HAI titers against the matched strain, but did not generate vaccine-induced response rates against the unmatched strains.

We are conducting optimization studies in animal models to further strengthen our H1N1 immunotherapy's potency against all strains, especially the current circulating strain, A/California/07/09, as well as to reduce the number of injections needed to generate protective responses against multiple strains.

In December 2012 we reported interim results of a phase I trial that showed that a single dose of our H1N1 universal SynCon® flu immunotherapy followed with a dose of a seasonal flu vaccine generated protective immune responses in 40% of trial subjects compared with a 20% response rate in elderly patients who received the seasonal flu vaccine alone.

People over 65 years of age represent about 90% of annual influenza deaths in the US. Older people's immune systems typically mount much weaker protective immune responses to seasonal vaccines, often in only 10 to 20% of this population. In younger adults, the same flu vaccines generate protective immune responses in at least 65% of the vaccine recipients. Other approaches, such as the use of higher vaccine doses and novel adjuvants, have not significantly improved the seasonal vaccine's impact in the older population. Thus, there is a significant need for a new approach to provide better protection in this more vulnerable population.

With the vulnerability of the elderly in mind, this phase I study evaluated the ability of Inovio's SynCon® immunotherapy alone, as well as in combination with the 2012 seasonal influenza vaccine, to generate protective levels of antigen-specific antibody immune responses in a greater proportion of the elderly population as well as to assess the potential for more universal protection against both matched and unmatched seasonal influenza strains.

In the trial, conducted at the University of Manitoba in Winnipeg, Canada, 50 healthy elderly patients were divided into three groups: one group of 20 subjects received a two-dose regimen of Inovio's H1N1 universal SynCon® flu immunotherapy delivered using Inovio's proprietary CELLECTRA® intradermal electroporation device 16 weeks apart; a second group of 20 subjects received one dose of Inovio's SynCon® immunotherapy delivered using electroporation followed by a dose of seasonal flu vaccine 16 weeks later; a third group of 10 subjects received placebo delivered by electroporation followed by a dose of the seasonal flu vaccine 16 weeks later. The study's objectives were to assess the tolerability, safety, and immune responses of these different immunization regimens. Serum samples from the immunized subjects were used to assess the generation of hemagglutination inhibition (HAI) titers meeting or exceeding a dilution of 1:40 to the current H1N1 seasonal flu strain (A/California/07/09). An HAI titer of 1:40 is the level recognized as a protective immune response against influenza in humans. Because of generally high HAI titer background rates to the A/California/07/09 strain, immunotherapy-specific, protective response rates were determined by assessing the number of patients in each group who had HAI titers greater than 1:40 and HAI titers at least 4-fold higher than the background value at the start of the trial. In reported interim data, immunization with the H1N1 universal SynCon® flu immunotherapy followed with a dose of a seasonal flu vaccine generated protective immune responses in 40% (8 of 20) of trial subjects compared with a 20% (2 of 10) response rate in elderly patients who received the seasonal flu vaccine alone. We are analyzing the final data with the intent to prepare a paper for submission to a peer-reviewed scientific publication.

Finally, on our path to develop a universal seasonal flu immunotherapy we are completing tests in animal models of our immunotherapy constructs for A/H3N2 and Type B influenza. Our goal is to develop immunotherapies that can also generate HAI titers exceeding 1:40 against unmatched strains within the H3N2 and Type B subtypes. In January 2012, we reported that our immunotherapies for influenza Type A H3N2 and Type B achieved protective antibody responses in immunized animals against multiple unmatched strains.

In the study of our SynCon® H3N2 immunotherapy, investigators immunized small animals (mice and guinea pigs) with a vaccine designed to produce the influenza hemagglutinin (HA) antigen in the animals. Inovio investigators have to date tested blood samples from the animals for immune responses against unmatched strains from several clades of H3N2. (Like the branches of a tree, there are dozens of distinct strains within each of these clades). The animals immunized with the SynCon® H3N2 immunotherapy developed HI titers exceeding the 1:40 level commonly associated with protective immunity against several clades of H3N2 tested. These included strains circulating in the 2000-01, 2006-07, and 2008-09 influenza seasons, which had necessitated a change in the composition of the seasonal flu vaccine for those years. Additional animal

testing of the remaining few H3N2 clades continued through 2012 and was to include a new strain, H3N2v (A/Indiana/10/2011 X203), which was selected in January 2012 by the CDC as a pandemic vaccine target.
Similarly, in the study of our SynCon® Type B immunotherapy, investigators tested blood samples from immunized mice for immune responses against multiple, unmatched strains of Type B influenza. All the animals immunized with the SynCon® Type B immunotherapy developed HI titers exceeding the 1:40 level against all of the strains of Type B tested, including those circulating and consequently a part of the vaccine formulation in 2001-02, 2008-09, and 2011-12. Type B influenza mutates more slowly than Type A, but enough to preclude lasting immunity. Type B influenza can lead to life-threatening complications, including pneumonia, in young children, persons over 50, those with chronic diseases (e.g. diabetes) or suppressed immune systems, and others at risk for complications.
We are seeking additional grant and/or partner funding to advance this program further.

Ebola

The Ebola virus has been described as one of the most virulent viral diseases known to man with lethality rates approaching 90%. 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.
According to the CDC, the 2014 Ebola epidemic is the largest in history, resulting in 20,747 laboratory confirmed cases and 8,235 deaths. This virus is also mutating into diverse strains. There are no preventive vaccines or effective therapeutic treatments for Ebola and the ease with which Ebola is generating genetic variations will complicate the process of creating such solutions. In addition, various experimental approaches have already been associated with undesirable side effects and limited ability to scale manufacturing.
In 2014, we announced our intent to advance our DNA immunotherapy for Ebola into a phase I clinical trial in collaboration with GeneOne Life Science Inc. In the collaboration, Inovio and GeneOne will co-develop Inovio's DNA-based Ebola immunotherapy through a phase I clinical trial. We plan to initiate the clinical study in the first half of 2015. In parallel with this effort, we are seeking additional third party support and resources to further develop and commercialize this product.
The decision to advance our Ebola immunotherapy is based on positive results achieved in preclinical studies. We observed that 100% of immunized guinea pigs and mice were protected from death after being exposed to the Ebola virus. Unlike the non-immunized animals, immunized animals were also protected from weight loss, a measure of morbidity. Researchers found significant increases in neutralizing antibody titers and strong and broad levels of immunotherapy-induced T-cells, including "killer" T-cells, suggesting that this product could provide both preventive and treatment benefits. This data was published in 2013 in the peer-reviewed journal Molecular Therapy in a paper, "Induction of Broad Cytotoxic T Cells by Protective DNA Vaccination Against Marburg and Ebola."

Immunotherapies for Biodefense and Biosecurity

A number of infectious agents that are relatively rare today are poised for an upsurge in incidence by either “natural” or terrorism-related means. For example, natural threats are posed by the influenza strains H5N1 and H7N9. At the same time, an engineered influenza virus for intentional release would pose a significant human threat.
Since 2001, the United States government has spent or allocated over a billion dollars in funding to address the threat of biological weapons. United States funding for bioweapons-related activities focuses primarily on research for and acquisition of medicines for defense. Biodefense funding also goes toward stockpiling protective equipment, increased surveillance and detection of biological agents, and improving state and hospital preparedness. The increase in this type of funding recently is mainly due to the Project BioShield Act adopted in 2004.
There are opportunities to secure development funding and for proof-of principle immunotherapy studies for biowarfare pathogens. Over the past five years, we have been successful at securing funding from the US government for such projects.
The company continues to actively pursue grant and contract funding from the NIH, Department of Defense and other government funding agencies as an important source of non-dilutive funding to support development of specific technologies that are broadly applicable across multiple product development programs in the areas of cancer, infectious diseases and biodefense. Based on various initiatives and with the support of NIH funding we are an active collaborator with the Department of Defense (U.S. Army) and continue research and development of DNA-based

immunotherapies delivered via our proprietary electroporation system. Specifically, our projects are focused on identifying immunotherapy candidates with the potential to provide rapid, robust immunity to protect against bio-warfare and bioterror attacks as well as development of our electroporation devices.

In April 2012, we received a U.S. Department of Defense Small Business Innovation Research Grant to advance the development of a low-cost, non-invasive surface electroporation (EP) delivery device and test its utility in combination with

our novel DNA immunotherapies against viruses with bioterrorism potential, including hanta, puumala, arenavirus and pandemic influenza. This project is a continuation of a first-stage DOD grant in 2011 that initiated Inovio's development of this skin delivery system.

In the first phase of this project, Inovio focused on optimizing the device design of our current minimally invasive surface EP device. In this second phase, the objective is to further advance and validate this device and the resulting immune responses in appropriate animal models. We will also investigate the development and manufacture of low-cost sterile disposables for the device and the possibility of integrating dermal injection capabilities into a combined inject/EP device platform.

DNA Based Monoclonal Antibodies (dMAb™)

Monoclonal antibodies (mAb) have become one of the most valuable therapeutic technologies of recent years. In 2012, global sales of monoclonal antibodies exceeded $50 billion. Among the top 10 best-selling drugs in 2012, six of them were monoclonal antibodies, each with annual sales exceeding $5 billion.

Monoclonal antibodies (mAbs) are designed to enhance the immune system's ability to regulate cell functions. They 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 unique 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 Remicade®). The global market for therapeutic mAb products was estimated at $44.6 billion in 2011.

However, mAb technology has limitations. As a passive immunotherapy, meaning they are manufactured outside the body, mAbs require costly large-scale laboratory development and production. Additional limitations include high cost to develop and manufacture and their limited duration of in vivo potency. We have created DNA based monoclonal antibodies that overcome many of the limitations associated with conventional mAb technology.

With our core platform technology, the DNA sequence for a specific monoclonal antibody is encoded in a DNA plasmid and delivered directly into cells of the body using electroporation, causing the mAbs to be "manufactured" in the body by these cells - not outside of the body like conventional mAb technology. We believe we can create dMAbsfor many diseases that are not currently addressable with conventional mAbs. This is a new application of our core technology platform consisting of encoded DNA plasmids delivered using electroporation and represents another potentially paradigm-shifting transformation in the immunotherapy field with very significant business potential. This capability we can potential make make dMAbs not only for new disease targets; we can also target existing, commercially successful mAbs and produce a competitive DmAb with a more attractive dosing regimen and cost structure.

Chikungunya Virus

Chikungunya virus (CHIKV) is a serious mosquito-borne alpha-virus responsible for several recent epidemics in tropical Africa and Asia. Recent evidence in the Caribbean suggests that CHIKV, which is primarily transmitted to humans from mosquitoes, is spreading to other parts of the world. There is currently no vaccine or therapeutic against this virus. We have developed a novel DNA plasmid encoding a highly engineered immunoglobulin encoding a CHIKV monoclonal antibody (mAb) to directly generate in vivo production of an anti-CHIKV mAb.

In a preclinical study, we demonstrated that our DNA-based mAb targeting CHIKV completely protected mice from a lethal CHIKV challenge. We demonstrated that the serum of transfected animals exhibited the specific ability to bind to the CHIKV envelope antigen and this serum possessed CHIKV-neutralizing activity. Importantly, the treatment of the animals with anti-CHIKV mAb plasmids protected 100% of the treated animals from a lethal injection of CHIKV virus while 100% of the control animals died. The treated animals were also spared of virus-related morbidity, as measured by dramatic weight loss and lethargy. Results from this study were presented as a poster at the 17th Annual Meeting of the American Society of Gene & Cell Therapy in Washington, DC.

Other Disease Indications

In 2014, we announced that the Defense Advanced Research Projects Agency (DARPA) awarded $12.2 million to scientists from the Perelman School of Medicine at the University of Pennsylvania, Inovio Pharmaceuticals, and MedImmune to develop and assess dMAbs in preclinical studies.

This collaboration aims to demonstrate that the DNA plasmids containing optimized DNA sequences encoded to generate disease-specific dMAbs can activate sufficient quantities of specific monoclonal antibodies in the body to be protective against a pathogen challenge. Using the capabilities and advantages of DNA plasmids delivered using

electroporation, the team will construct and evaluate multiple dMAbsfocused on influenza virus and antibiotic resistant bacteria (Pseudomonas aeruginosa and Staphylococcus aureus). Successful completion of the initial preclinical activities under the DARPA grant would aim to lead to clinical studies on selected product candidates to be funded under a future increment to

the award. Perhaps more significant to Inovio, this and other external funding will be utilized to build out other dMAb product candidates with significant market potential against multiple types of infection as well as cancer.

Our Electroporation Delivery Technology

Choice of Tissue for DNA Delivery

Skeletal muscle has been a core focus for delivery of DNA-based immunotherapies via electroporation because it is mainly composed of large elongated cells with multiple nuclei. Muscle cells are non-dividing, hence long-term expression can be obtained without integration of the gene of interest into the genome. Muscle cells have been shown to have a capacity for secretion of proteins into the blood stream. Secreted therapeutic proteins may therefore act systemically and produce therapeutic effects in distant tissues of the body. In this respect, the muscle functions as a factory for the production of the biopharmaceutical needed by the body. We envision that delivery of DNA by electroporation to muscle cells will circumvent the costly and complicated production procedures of viral gene delivery vectors, protein-based drugs, conventional vaccines and monoclonal antibodies. This approach may provide long-term stable expression of a therapeutic protein or monoclonal antibody at a sustained level.

For immunization, the DNA causes muscle cells to produce antigenic proteins that the immune system will identify as foreign and against which it will mount an immune response. As with conventional vaccines, the immune system will then develop memory of this antigen (and related disease) for future reference. Intramuscular delivery by electroporation of DNA encoded antigens has been shown to induce both humoral (antibody) and cellular (T cell) immune responses.

While we have generated pre-clinical and preliminary clinical evidence that intramuscular electroporation-based DNA delivery will be effective for a number of immunotherapies, electroporation of the skin may also be a relevant route of administration. Skin or intradermal administration is important and is becoming an attractive site for immunization given its high density of antigen presenting cells (APCs). Unlike muscle, skin is the first line of defense against most pathogens and is therefore very rich in immune cells and molecules. Skin specifically contains certain cells that are known to help in generating a robust immune response. With intradermal administration of electroporation, we may be able to demonstrate a comparable immune response to muscle delivery. Drug delivery into skin, or dermal tissue, is the most attractive method given that the skin is the largest, most accessible, and most easily monitored organ of the human body, and it is highly immuno-competent (able to recognize antigens and mount an immune response to them).

Our Electroporation Systems

Our current electroporation systems consist of an electrical pulse generator box the size of a large laptop attached by a cord to a separate needle-electrode applicator. We have also developed a series of hand-held, cordless electroporation devices which bring together groundbreaking design and engineering advancements to combine all components into a self-contained, easy-to-use portable device the size of a cordless hand tool.

CELLECTRA® System

There are several configurations in the CELLECTRA® device family. The first covers intramuscular (IM) delivery of DNA; the second covers the intradermal/subcutaneous delivery (ID) of DNA. Both devices have been validated, manufactured under Current Good Manufacturing Practices (cGMP) and are being used in human clinical trials. We have filed a device master file (MAF) with the FDA covering the use of the CELLECTRA®-IM EP device in human clinical trials. These devices are intended to be used in combination with a DNA plasmid-based immunotherapy.

The new CELLECTRA®-SP products combine the functionality of our current generation of skin and intramuscular electroporation devices in clinical testing with enhanced form, design, and portability. All components from the pulse generator and applicator are integrated into a cordless, rechargeable device. The rechargeable battery can enable immunization of several hundred subjects, making the device highly amenable to mass vaccination. The devices are designed to accommodate different electrode arrays to meet the requirements of the particular immunotherapy and tissue for delivery (skin or muscle).

Next Generation Devices

All of our electroporation delivery systems noted above can increase levels of gene expression (i.e. production of the immune-stimulating protein the immunotherapy was coded to produce) of DNA immunotherapies by 1000-fold or more compared to delivery of DNA immunotherapies via conventional injection alone. Delivery of our SynCon® immunotherapies into muscle or skin tissue with our electroporation systems have generated robust immune responses in humans against cervical dysplasia, influenza (H5N1 and H1N1), and HIV, as well as against other diseases in

animal models.

While our current intramuscular (IM) delivery technologies are well tolerated, we are also advancing next generation, minimally invasive intradermal electroporation delivery devices. One ID device penetrates to no more than 3 mm, compared to intramuscular devices that go deeper. Furthermore, a second ID device is a surface electroporation (SEP) device that sits on

the surface of the skin and uses a virtually undetectable scratch to facilitate delivery of the immunotherapy. With the advancement of these devices, our aim is to make electroporation delivery amenable to mass prophylactic vaccination by decreasing dose levels, increasing tolerability of the vaccination, and increasing the breadth of viable immunotherapy targets. Our data related to influenza, HIV, malaria, and smallpox antigens demonstrate that DNA delivery with this newer generation of ID delivery including SEP devices yields levels of immunogenicity in terms of both antibody and T cell responses and/or efficacy against a virus challenge that is comparable to intramuscular electroporation devices currently in the clinic.

These results were highlighted in September 2012, in the peer-reviewed journal, Human Gene Therapy, in a paper ("Intradermal DNA vaccination enhanced by low-current electroporation improves antigen expression and induces robust cellular and humoral immune responses") which described the positive immunological effects of the optimized electroporation parameters for its minimally invasive skin (intradermal) EP delivery devices.

We also previously announced (February 2011) a new needle-free, contactless electroporation technology for immunotherapy delivery, which provides the powerful enabling capabilities of electroporation without contacting the skin. Our pre-clinical research was highlighted in a paper published in the scientific journal Human Vaccines. The paper appearing in Human Vaccines, "Piezoelectric permeabilization of mammalian dermal tissue for in vivo DNA delivery leads to enhanced protein expression and increased immunogenicity," described an innovative electroporation method optimized for delivery into skin. This new method is based on piezoelectricity, which is the generation of an electric field or electric potential by certain materials in response to applied mechanical stress.

We have recently unveiled an efficient, tolerable, and non-invasive multi-headed intradermal electroporation device designed to deliver multiple DNA plasmids simultaneously but spatially separated, allowing the tailoring of delivery sites for combination immunotherapies. Results from a preclinical study reveal this device could allow for the delivery of multi-plasmid formulations without the risk of interference of immune responses. This could be useful for combination immunotherapies that are rapidly formulated such as in response to emerging infectious disease threats or pandemics, and could overcome the limited dosing issues often associated with intradermal delivery. Results from this study were published in Human Vaccines Immunotherapeutics in a paper titled, "A multi-head intradermal electroporation device allows for tailored and increased dose DNA immunotherapy delivery to the skin."

Corporate Development

We have entered into various arrangements with corporate, academic, and government collaborators, licensors, licensees and others. These arrangements are summarized below and elsewhere in this annual report. In addition, we conduct ongoing discussions with potential collaborators, licensors and licensees.

On September 10, 2013, we entered into an exclusive worldwide license agreement with Roche to research, develop and commercialize our multi-antigen DNA immunotherapies targeting prostate cancer (INO-5150) and hepatitis B (INO-1800). Under the terms of the agreement, Roche made an upfront payment of $10 million to Inovio and agreed to pay for all ongoing development costs and certain development, regulatory and commercial event based payments. Roche also agreed to potentially pay additional development event based payments if Roche pursues other indications with INO-5150 or INO-1800.

In November, 2014, Roche terminated their 2013 collaboration, option, and license agreement to co-develop INO-5150 as well as their research collaboration in prostate cancer. All of Roche's rights to INO-5150, including the right to license the product to other parties, will be returned to us. Due to the termination, the potential future event based payments have been reduced. We plan to independently advance INO-5150 into a phase I clinical trial in the first half of 2015.

Inovio and Roche will continue to collaborate and co-develop Inovio's DNA immunotherapy (INO-1800) against hepatitis B virus under this existing license agreement. The partnership is on track to move INO-1800 collaboratively into a phase I study in 2015.

On March 24, 2010, we entered into a Collaboration and License Agreement (the "Agreement") with GeneOne (formerly VGX International Inc.). Under the Agreement, we granted GeneOne an exclusive license to our SynCon® universal influenza vaccine (the "Product") delivered with electroporation to be developed in certain countries in Asia. As consideration for this license we have received a research and development initiation fee, as well as research support and annual license maintenance fees, and will receive royalties on net product sales. In addition, contingent upon achievement of clinical and regulatory milestones, we will receive development payments over the term of the

Agreement. The Agreement also provides us with exclusive rights to supply devices for clinical and commercial purposes (including single use components) to GeneOne for use in the Product.

The term of the Agreement commenced upon execution and will extend on a country by country basis until the last to expire of all Royalty Periods for the territory (as such term is defined in the Agreement) for any Product in that country, unless the Agreement is terminated earlier in accordance with its provisions as a result of breach, by mutual agreement, or by GeneOne's right to terminate without cause upon prior written notice.

In October 2011, we entered into a product development collaboration agreement with GeneOne to co-develop our SynCon® immunotherapies for hepatitis B and C infections. Under the terms of the agreement, GeneOne received marketing rights for these immunotherapies in Asia, excluding Japan, and in return was to fully fund IND-enabling and initial phase I and II clinical studies. We will receive payments based on the achievement of clinical milestones and royalties based on sales in the licensed territories and will retain all commercial rights in all other territories.
In conjunction with our announcement of our Roche partnership we also announced that we reacquired the rights, title and interest to the SynCon® hepatitis B immunotherapy in Asia from GeneOne.
Under the terms of an original license agreement with the University of Pennsylvania (UPenn) completed in 2007 we obtained exclusive worldwide rights to develop multiple DNA plasmids and constructs with the potential to treat and/or prevent HIV, HCV, HPV and influenza. The agreement also included molecular adjuvants. This agreement and subsequent amendments provide for royalty payments, based on future sales, to UPenn. The technology was developed in the University of Pennsylvania laboratory of Professor David B. Weiner, a pioneer in the field of DNA-based vaccines and chairman of our scientific advisory board.
In January 2010, we announced that we expanded our existing license agreement with UPenn, adding exclusive worldwide licenses for technology and intellectual property for novel immunotherapies against pandemic influenza, Chikungunya, and FMD. The amendment also encompassed new chemokine and cytokine molecular adjuvant technologies.
In July 2011, we expanded this license agreement by adding exclusive worldwide licenses for technology and intellectual property for novel immunotherapies against prostate cancer, herpes viruses, including CMV (cytomegalovirus), malaria, hepatitis B, RSV (respiratory syncytial virus), and MRSA (methicillin-resistant staphylococcus aureus). The amendment also encompassed a new optimized IL-12 cytokine gene adjuvant.
In November 2012, we expanded this license agreement by adding worldwide rights to technology and intellectual property for novel vaccines against intestinal infections including Clostridium difficile, or C. difficile; cancer therapeutic vaccines targeting Wilms' tumor gene or WT1; and biodefense pathogens including Ebola and the family of Filovirus such as Marburg.
In 2014 we added to our license agreement with UPenn by in-licensing expanded patents covering candidate products for DNA based antibodies and those covering dengue fever, H7N9 influenza, additional HPV serotypes, as well as certain other undisclosed cancer antigen targets. In addition, the amended agreement provides us global rights to DNA-based antibodies, immune activators (IL-21, IL-23 & IL-33), Middle East Respiratory Syndrome (MERS), and tuberculosis.
In 2009, we announced an agreement with the PATH Malaria Vaccine Initiative (MVI) to evaluate in a pre-clinical feasibility study our SynCon® immunotherapy development platform. In 2010, MVI agreed to provide follow-on research funding to continue evaluation and development of our malaria vaccine candidate in non-human primates. In 2013, we announced a follow-on collaboration with MVI focused on initiating human studies.
In 2013 we published the successful pre-clinical immunogenicity data in mice and non-human primate models in the peer-reviewed journal Infection and Immunity, demonstrating the feasibility and benefits of developing a first of its kind, five-antigen formulation vaccine targeting malaria. Animal model data in the two species demonstrated the induction of strong malaria specific T-cells (including CD8+ T cells with cell killing activity) and antibody responses to the circumsporozoite surface protein (CSP) - both responses thought to be important in treating and/or preventing malaria infection and hitherto difficult to achieve with other vaccine modalities. By 2014 Inovio had successfully met all objectives of the funded research and feasibility programs.
In 2014, MVI decided not to fund a phase I malaria vaccine due to their focus on later-stage products. Inovio possesses the global commercial rights to the vaccine and will seek other development and commercialization partners from among government, non-government, and commercial entities.
In 2014 we acquired worldwide rights (excluding China) for early preclinical therapies addressing Alzheimer's disease and multiple sclerosis based on the academic research of Dr. Bin Wang, a professor at Fudan University's Shanghai Medical College. These newly licensed technologies are based on patent-protected and published discoveries from Dr. Wang and his collaborator, who found a novel way to generate inducible regulatory T cells, or iTregs. These novel approaches could be used to develop therapies targeting major inflammatory diseases.

In 2014 we along with the Perelman School of Medicine at the University of Pennsylvania and MedImmune were awarded $12.2 million from the Defense Advanced Research Projects Agency (DARPA) to develop DNA-based monoclonal antibodies (mAbs) for infectious disease treatment. Together we will develop and assess the dMAbs in preclinical studies using technology developed by Penn and licensed by Inovio. The collaboration will focus on influenza virus, Pseudomonas aeruginosa and Staphylococcus aureus. Successful completion of the initial preclinical activities under the DARPA grant aims to lead to clinical studies on selected product candidates to be funded under a future increment to the award.

In 2014 VGX Animal Health, Inc. (VAH), Inovio's 91%-owned subsidiary, concluded an agreement for the sale of its animal health assets to Plumbline Life Sciences, Inc. (PLS) of Korea. The assets transferred included an exclusive license with Inovio for animal applications of our growth hormone-releasing hormone (GHRH) technology and animal DNA vaccines plus a non-exclusive license to our electroporation delivery systems. VGX Animal Health will receive $2 million in cash in multiple payments and 20% of the outstanding shares of PLS. VAH's 20% equity ownership position in PLS will be maintained without dilution up to $10 million of additional equity fundraising by PLS. We will receive milestone payments and royalties on product sales as well as retain the human applications of our GHRH technology.

Competition

We face competition at two levels. At the highest level we face competition by 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 pharmaceuticals, which are broadly engaged in vaccine/immunotherapy research and development. These include Crucell N.V (now part of J&J), Sanofi-Aventis, Novartis, Inc., GlaxoSmithKline plc, Merck, Pfizer, and MedImmune, Inc., a wholly owned subsidiary of AstraZeneca, Inc. There are also various development stage biotechnology companies involved in different immunotherapy technologies. As these companies develop their technologies, they may develop proprietary technologies which may materially and adversely affect our business.

A number of companies are developing products to specifically address diseases we are also targeting. 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 dysplasias; LEEP is the current standard of care for treating high grade cervical dysplasia; Advaxis and Kite have therapeutic cervical cancer product candidates under development. Many companies are pursuing different approaches to prostate, breast, lung and other cancers we are targeting.

At another level we 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. Today the key competitive DNA delivery technologies include viral vectors, lipid vectors, and electroporation. All of these technologies have shown promise, but they each also have their unique obstacles to overcome. We believe our electroporation system is strongly positioned to succeed as the dominant delivery method for DNA-based immunotherapies.

Viral DNA Delivery

This technology utilizes a virus as a carrier to deliver genetic material into target cells. The method is very 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.

Ballistic DNA Delivery (Gene Gun)

This technology utilizes micron sized DNA-coated gold particles that are shot into the skin using compressed gas. The method has matured considerably over the last 15 years and has been shown to be an efficient method to deliver a number of immunotherapy antigens. Since the DNA is dry coated, excellent stability of the immunotherapy can be achieved. The method is limited to use in skin and only a few micrograms of genetic material can be delivered each time. This may limit the utility of the method for targets such as cancer where higher doses of immunotherapy antigens and stronger T cell responses are needed.

Lipid DNA Delivery

A number of lipid formulations have been developed that increase the effect of DNA immunotherapies. These work by either increasing uptake of the DNA into cells or by acting as an adjuvant, alerting the immune system. While there has been progress in this field, lipid delivery tends to be less efficient than viral vectors and is hampered by concerns regarding toxicity and increased complexity.

DNA Immunotherapy Delivery With Electroporation

When an antigen-targeting DNA immunotherapy plasmid injection is followed by electroporation of the injected tissue, local cellular uptake (transfection) is significantly greater with resultant gene expression generally enhanced 1000-fold. This level of cellular uptake has been shown to facilitate significant antigen production by the transfected cells and induce significant levels of antigen-related immune responses. In fact, as described in earlier sections, this approach has achieved best-in-class CD8+ killer T cells which in turn been translated into clinically relevant efficacy in a large controlled phase II study, a first for Inovio and the field of immunotherapies. There have been no serious adverse events attributed to our DNA immunotherapies delivered using our electroporation devices in these clinical studies.

We believe that the greatest obstacle to making immunotherapies a reality has been the lack of effective, efficient, and safe delivery of DNA plasmid constructs into target cells and that electroporation may become the method of choice for DNA delivery into cells in many applications.

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. Together with our partners and collaborators, we have been the leader in establishing proof-of-principle of electroporation-delivered immunotherapies.
- We have a broad product line of electroporation instruments designed to enable DNA delivery in tumors, muscle, and skin.
- We have been very 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 products, 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 the 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.

Government Regulation

DNA Vaccine Product Regulation

Any pharmaceutical products we develop will require regulatory clearances prior to clinical trials and additional regulatory approvals prior to commercialization. New gene-based products for vaccine or therapeutic applications are subject to extensive regulation by the FDA and comparable agencies in other countries. Our potential products will be regulated as biological products that are used to treat or prevent disease. In the United States, drugs are subject to regulation under the Federal Food, Drug and Cosmetic Act, or the FDC Act. Biological products, in addition to being subject to provisions of the FDC Act, are regulated in the United States under the Public Health Service Act. Both statutes and related regulations govern, among other things, testing, manufacturing, safety, efficacy, labeling, storage, record keeping, advertising, and other promotional practices.

Obtaining FDA approval or comparable approval from similar agencies in other countries is a costly and time-consuming process. Generally, FDA approval requires that pre-clinical studies be conducted in the laboratory and in animal model systems to gain preliminary information on efficacy and to identify any major safety concerns. In the United States, the results of these studies are submitted as a part of an IND application which the FDA must review and allow before human clinical trials can start. The IND application includes a detailed description of the proposed clinical investigations.

A company must submit an IND application or equivalent application in other countries for each proposed product and must conduct clinical studies to demonstrate the safety and efficacy of the product necessary to obtain FDA

approval or comparable approval from similar agencies in other countries. For example, in the United States, the FDA receives reports on the progress of each phase of clinical testing and may require the modification, suspension, or termination of clinical trials if an unwarranted risk is presented to patients.

To obtain FDA approval prior to marketing a pharmaceutical product in the United States typically requires several phases of clinical trials to demonstrate the safety and efficacy of the product candidate. Clinical trials are the means by which experimental treatments are tested in humans, and are conducted following pre-clinical testing. Clinical trials may be

conducted within the United States or in foreign countries. If clinical trials are conducted in foreign countries, the products under development as well as the trials are subject to regulations of the FDA and/or its counterparts in the other countries. Upon successful completion of clinical trials, approval to market the treatment for a particular patient population may be requested from the FDA in the United States and/or its counterparts in other countries.

Clinical trials for therapeutic products are normally done in three phases. Phase I clinical trials are typically conducted with a small number of patients or healthy subjects to evaluate safety, determine a safe dosage range, identify side effects, and, if possible, gain early evidence of effectiveness. Phase II clinical trials are conducted with a larger group of patients to evaluate effectiveness of an investigational product for a defined patient population, and to determine common short-term side effects and risks associated with the drug. Phase III clinical trials involve large scale, multi-center, comparative trials that are conducted to evaluate the overall benefit-risk relationship of the investigational product and to provide an adequate basis for product labeling. In some special cases where the efficacy testing of a product may present a special challenge to testing in humans, such as in the case of a vaccine to protect healthy humans from a life-threatening disease that is not a naturally occurring threat, effectiveness testing may be required in animals.

After completion of clinical trials of a new product, FDA marketing approval must be obtained or equivalent approval in comparable agencies in other countries. For the FDA, if the product is regulated as a biologic, a Biologics License Application, or BLA, is required. The BLA must include results of product development activities, pre-clinical studies, and clinical trials in addition to detailed chemistry, manufacturing and control information.

Applications submitted to the FDA are subject to an unpredictable and potentially prolonged approval process. Despite good-faith communication and collaboration between the applicant and the FDA during the development process, the FDA may ultimately decide, upon final review of the data, that the application does not satisfy its criteria for approval or requires additional product development or further pre-clinical or clinical studies. Even if FDA regulatory clearances are obtained, a marketed product is subject to continual review, and later discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or withdrawal of the product from the market as well as possible civil or criminal sanctions. Before marketing clearance for a product can be secured, the facility in which the product is manufactured must be inspected by the FDA and must comply with cGMP regulations. In addition, after marketing clearance is secured, the manufacturing facility must be inspected periodically for cGMP compliance by FDA inspectors.

In addition to the FDA requirements, the NIH has established guidelines for research involving human genetic materials, including recombinant DNA molecules. The FDA cooperates in the enforcement of these guidelines, which apply to all recombinant DNA research that is conducted at facilities supported by the NIH, including proposals to conduct clinical research involving gene therapies. The NIH review of clinical trial proposals and safety information is a public process and often involves review and approval by the Recombinant DNA Advisory Committee, of the NIH.

Sponsors of clinical trials are required to register and report results for all controlled clinical investigations, other than phase I investigations, of a product subject to FDA regulation. Trial registration may require public disclosure of confidential commercial development data resulting in the loss of competitive secrets, which could be commercially detrimental.

Medical Device Manufacturing Regulation

In addition, we are subject to regulation as a medical device manufacturer. We must comply with a variety of manufacturing, product development and quality regulations in order to be able to distribute our electroporation devices commercially around the world. In Europe, we must comply with the Medical Device Directives. We have a Quality System certified by its international Notified Body to be in compliance with the international Quality System Standard, ISO13485, and meeting the Annex II Quality System requirements of the MDD. We completed Annex II Conformity Assessment procedures to allow for the CE Mark of our electroporation devices.

In the United States, we are required to maintain facilities, equipment, processes and procedures that are in compliance with quality systems regulations. Our systems have been constructed to be in compliance with these regulations and our ongoing operations are conducted within these systems. Commercially distributed devices within the United States must be developed under formal design controls and be submitted to the FDA for clearance or approval. All development activity is performed according to formal procedures to ensure compliance with all design control regulations.

We employ modern manufacturing methods and controls to optimize performance and control costs. Internal capabilities and core competencies are strategically determined to optimize our manufacturing efficiency. We utilize contract manufacturers for key operations, such as clean room assembly and sterilization, which are not economically conducted in-house. We outsource significant sub-assemblies, such as populated printed circuit boards, for which capital requirements or manufacturing volumes do not justify vertical integration.

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.

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.

Relationship with GeneOne (Formerly VGX International Inc.)

In March 2014, the Company's affiliated entity VGX International Inc. changed its name to GeneOne Life Sciences ("GeneOne").

We acquired an equity interest in GeneOne in 2005. As of December 31, 2014, we owned 10.6% of the outstanding capital stock of GeneOne and GeneOne owned 73,590 shares of our common stock. None of our current officers, directors, or key employees beneficially owns, directly or indirectly, any securities of GeneOne.

In 2008 we sold our manufacturing operations (including patent rights to certain manufacturing technology) to VGXI, Inc., a wholly-owned United States subsidiary of GeneOne. In connection with this transfer we entered into a Supply Agreement pursuant to which VGXI, Inc., a cGMP contract manufacturer, produces and supplies the DNA plasmids for all of our research and early clinical trials. The price of the plasmids we purchase from VGXI, Inc. is determined by us and GeneOne at the time of order placement or, with respect to product supplied in connection with a grant contract, based on the contracted bid provided by the applicable agency. We agreed to treat GeneOne and its subsidiary as our most favored supplier for DNA plasmids and GeneOne and its subsidiary agreed to treat us as their most favored customer. Before we can manufacture DNA plasmids on our own behalf or engage a third party other than GeneOne or its subsidiary to manufacture DNA plasmids for us, we must first offer such manufacturing work to GeneOne or its subsidiary.

We have also entered into license and collaboration agreements pursuant to which we have granted GeneOne exclusive rights to certain of our product candidates in certain jurisdictions. For example, GeneOne has exclusive rights in countries in Asia including Korea to our VGX-3400X and INO-3510 for treatment of flu and our hepatitis C program. In exchange for these rights, GeneOne shares the development costs for some of our product candidates. Prior to signing the Roche Agreement, we reacquired the rights, title and interest to hepatitis B in Asia previously licensed to GeneOne. As a result, we paid $300,000 to GeneOne as of December 31, 2013 based on the up-front payment received from Roche.

On September 23, 2014, we entered into a Collaborative Development Agreement with GeneOne to co-develop an Ebola vaccine through phase I clinical trials.

For the years ended December 31, 2014 and 2013, we recognized revenue from GeneOne of $479,000 and $425,000, respectively, which consisted of licensing, collaborative research and development arrangements and other fees. Operating expenses related to GeneOne for the years ended December 31, 2014 and 2013 were $4.2 million and $2.3 million, respectively, primarily related to biologics manufacturing. At December 31, 2014 and 2013 the Company had an accounts receivable balance of $2,000 and $0, respectively, from GeneOne and its subsidiaries. At December 31, 2014 and 2013, $260,000 and $231,000 of prepayments made to GeneOne were classified as long-term other assets on the consolidated balance sheet.

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 electroporation delivery and vaccine related technologies. As of February 25, 2015, our patent portfolio included over 98 issued United States patents and 310 issued foreign counterpart patents.

Key vaccine related technology patents and published patent applications include the following:

- European patent no. 1809336B1, entitled, “Growth Hormone Releasing Hormone (GHRH) Enhances Vaccination Response”
- US Pat No. 7,846,720, entitled, “Optimized High Yield Synthetic Plasmids”
- US Pat. No. 8,168,769, entitled, “Improved Vaccines and Methods for Using the Same,” with claims directed to HPV vaccine products.
- US Pat. No. 8,389,706, entitled, “Vaccines for Human Papilloma Virus and Methods for Using the Same”
- International publication WO 08/014521, entitled, “Improved Vaccines and Methods for Using the Same,” which includes HCV, HPV, influenza, HIV, and cancer (hTERT) SynCon® DNA.
- US Pat. No. 8,133,723, entitled, “Novel Vaccines Against Multiple Subtypes Of Influenza”
- US Pat. No. 8,298,820, entitled, “Influenza Nucleic Acid Molecules and Vaccines Made Therefrom”
- US Pat No. 8,835,620, “Novel Vaccines Against Multiple Subtypes Of Influenza Virus”
- US Pat No. 8,697,084, entitled, "HIV Consensus Envelop Sequences And Methods For Using The Same"
- US Pat Nos. 8,829,174 and 8,921,536, "Improved HCV Vaccines And Methods For Using The Same"
- US Pat No. 8,535,687, entitled, "Smallpox DNA Vaccine And The Antigens Therein That Elicit An Immune Response"
- US Pat. No. 8,178,660, entitled, "Vaccines And Immunotherapeutics Using Codon Optimized IL-15 And Methods For Using The Same"
- European patent EU1976871, entitled, 'Vaccines And Immunotherapeutics Using Codon Optimized IL-15 And Methods For Using The Same"
- US Pat No. 7,173,116, entitled, "Nucleic Acid Formulations For Gene Delivery And Methods Of Use"
- US Pat No. 8,927,692, entitled, “Consensus Prostate Antigens, Nucleic Acid Molecule Encoding The Same And Vaccine And Uses Comprising The Same"
- US Pat No. 8,852,609, entitled, “Consensus Sequences of Chikungunya Viral Proteins, Nucleic Acid Molecules Encoding the Same and Compositions and Methods for Using the Same”

Key electroporation related patents covering range of field strengths include the following:

- US Pat No. 7,922,709, entitled, “Enhanced delivery of naked DNA to skin by non-invasive in vivo electroporation.”
- US Pat No. 7,328,064, entitled, “Electroporation device and injection apparatus,” with claims directed to methods of delivering an agent plus electroporation.
- US Pat No. 7,245,963, entitled, “Electrode assembly for constant-current electroporation and use”
- US Pat No. 7,664,545, entitled, “Electrode assembly for constant-current electroporation and use”
- US Pat No. 6,697,669, entitled, “Skin and muscle-targeted gene therapy by pulsed electrical field”
- US Pat No. 6,110,161 issued August 29, 2000
- US Pat No. 6,261,281 issued July 17, 2001
- US Pat No. 6,958,060 issued October 25, 2005

- US Pat No. 6,939,862 issued September 6, 2005

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.

Significant Customers and Research and Development

During the year ended December 31, 2014 and 2013, we derived 70% and 68% of our revenue from Roche, respectively. During the years ended December 31, 2014 and 2013, we derived 12% and 16% of our revenue from the NIAID, respectively.

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 $34.1 million in 2014 and $21.4 million in 2013.

Corporate History and Headquarters

Inovio Pharmaceuticals, Inc. grew out of the merger of VGX Pharmaceuticals, Inc. (“VGX”) and Inovio Biomedical Corporation. On June 1, 2009, VGX, a private company primarily focused on developing DNA immunotherapies, completed a merger with Inovio Biomedical Corporation, a publicly listed company whose main focus was developing electroporation delivery technology and devices, pursuant to the terms of an Amended and Restated Agreement and Plan of Merger dated December 5, 2008, as further amended on March 31, 2009. Subsequent to the merger, we conduct our business through our United States wholly-owned subsidiaries, VGX Pharmaceuticals, LLC and Genetronics, Inc. On May 14, 2010, the entity changed its corporate name to Inovio Pharmaceuticals, Inc. Our corporate headquarters is located at 660 W. Germantown Pike,

Suite 100, Plymouth Meeting, Pennsylvania 19462, and the telephone number is (267) 440-4200. Inovio Pharmaceuticals (NASDAQ: INO) is focused on advancing products based on its integrated technology platform consisting of its SynCon® DNA immunotherapies and vaccines delivered with its CELLECTRA® electroporation delivery devices.

VGX was originally incorporated as Viral Genomix, Inc. under the laws of Delaware on April 17, 2000, to develop new drugs and therapies to treat viral diseases and cancers. The company was renamed VGX Pharmaceuticals, Inc. on May 31, 2006. On February 21, 2007, VGX acquired Advisys, Inc., a company possessing DNA and electroporation technology, through an asset purchase agreement. On April 14, 2007, VGX entered into an exclusive license agreement with the Trustees of the University of Pennsylvania related to therapeutic and prophylactic DNA vaccines developed by Dr. David Weiner at the University of Pennsylvania School of Medicine. VGX focused on advancing its DNA immunotherapy technology targeting cancers and infectious diseases.

Inovio Biomedical Corporation originated as a company incorporated on June 29, 1983, under the laws of California as Biotechnologies & Experimental Research, Inc. The company was formed to develop electroporation devices for the research marketplace and later began to explore human applications of electroporation to deliver agents such as chemotherapeutic agents, gene therapies, and DNA immunotherapies. The company changed its corporate name to BTX, Inc. on December 10, 1991, and Genetronics, Inc. on February 8, 1994. On April 14, 1994, Genetronics, Inc. became a public company through a share exchange agreement with Consolidated United Safety Technologies, Inc., a company listed on the Vancouver Stock Exchange under the laws of British Columbia, Canada, which then changed its name to Genetronics Biomedical Ltd. on September 29, 1994. Genetronics, Inc. remained as a wholly owned operating subsidiary. On September 2, 1997, the company listed on the Toronto Stock Exchange. On December 8, 1998, the company listed on the American Stock Exchange (now owned by the NYSE and referred to as the NYSE MKT). We voluntarily de-listed from the Toronto Stock Exchange on January 17, 2003. On June 15, 2001, Genetronics Biomedical Ltd. completed a change in jurisdiction of incorporation from British Columbia, Canada, to the state of Delaware and became Genetronics Biomedical Corporation. On January 25, 2005, Genetronics Biomedical Corporation acquired Inovio AS, a gene delivery technology company. On March 31, 2005, Genetronics Biomedical Corporation was renamed Inovio Biomedical Corporation. On September 4, 2014, the Company provided notice to the NYSE MKT that it would voluntarily transfer the listing of its common stock, par value $0.001 per share (the "Common Stock"), from NYSE MKT to the NASDAQ Global Select Market ("NASDAQ"). The Common Stock was approved for listing on NASDAQ and began trading on NASDAQ on September 15, 2014.

Available Information

Our Internet website address is www.inovio.com. We make our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, Forms 3, 4, and 5 filed on behalf of directors and executive officers, and any 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. You can also read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. You can obtain additional information about the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, 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 Policy and information for contacting our board of directors is available on our Internet site (www.inovio.com). We will provide any of the foregoing information without charge upon request to Peter Kies, 10480 Wateridge Circle, San Diego, CA, 92121.

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 Internet site (www.inovio.com) or in a report on Form 8-K, as required by applicable law.

Employees

As of March 9, 2015, we employed 106 people on a full-time basis and 4 people under consulting and project employment agreements. Of the combined total, 86 were in product research, which includes research and development, quality assurance, clinical, engineering, and manufacturing, and 24 were in general and administrative, which includes corporate development, information technology, legal, investor relations, finance, and corporate administration. None of our employees are subject to collective bargaining agreements.

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 Business and Industry

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

We have experienced significant operating losses to date; as of December 31, 2014 our accumulated deficit was approximately $331.9 million. We have generated limited revenues, primarily consisting of license and grant revenue, 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 vaccine product candidates or electroporation-based synthetic vaccine delivery technology and thus may never have any significant future revenues or achieve and sustain profitability. We believe that current cash and cash equivalents plus short-term investments are sufficient to meet planned working capital requirements through the end of 2017, excluding our planned phase III clinical trial of VGX-3100. We will continue to rely on outside sources of financing to meet our capital needs beyond this time.

We have limited sources of revenue and our success is dependent on our ability to develop our vaccine and other product candidates 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.

None of our human vaccine product candidates has been approved for sale, and we may not develop commercially successful vaccine products.

Our human vaccine programs are in the early stages of research and development, and currently include vaccine product candidates in discovery, pre-clinical studies and phase I and II clinical studies. There is limited data regarding the efficiency of synthetic vaccines compared with conventional vaccines, and we must conduct a substantial amount of additional research and development before any regulatory authority will approve any of our vaccine product candidates. The success of our efforts to develop and commercialize our vaccine product candidates could fail for a number of reasons. For example, we could experience delays in product development and clinical trials. Our vaccine product candidates could be found to be ineffective or unsafe, or otherwise fail to receive necessary regulatory clearances. The products, if safe and effective, could be difficult to manufacture on a large scale or uneconomical to market, or our competitors could develop superior vaccine products more quickly and efficiently or more effectively market their competing products.

In addition, adverse events, or the perception of adverse events, relating to vaccines and vaccine delivery technologies may negatively impact our ability to develop commercially successful vaccine 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 products and could result in greater governmental regulation, stricter labeling requirements and

potential regulatory delays in the testing or approval of our potential products.

We will need substantial additional capital to develop our synthetic vaccine and electroporation delivery technology and other product candidates and for our future operations.

Conducting the costly and time consuming research, pre-clinical and clinical testing necessary to obtain regulatory approvals and bring our vaccine delivery technology and product candidates 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;
- competing technological and market developments; and
- our ability and 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 been experiencing heightened volatility and turmoil, making it more difficult to raise capital through the issuance of equity securities. Furthermore, as a result of the recent volatility in the capital markets, the cost and availability of credit has been and may continue to be adversely affected by 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, 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.

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.

We face intense and increasing competition and many of our competitors have significantly greater resources and experience.

If any of our competitors develop products with efficacy or safety profiles significantly better than our products, 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 H5N1, H1N1 and universal influenza vaccines, and several H1N1 vaccines developed by our competitors have been approved for human use. Our competitors and potential competitors include

large pharmaceutical and medical device companies 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, pre-clinical 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.

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, or may 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 a license and collaboration agreement with Roche. 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. 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 enter into agreements with other highly-regarded 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 and implement 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.

A small number of licensing partners and government contracts 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. For example, during the year ended December 31, 2014, Roche and the NIAID accounted for approximately 70% and 12%, of our consolidated revenue, respectively. 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 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 and the US Army, and we intend to continue entering into these 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.

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.

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;
- 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.

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 products 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 pre-clinical 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. 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, pre-clinical 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.

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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 pre-clinical 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 pre-clinical 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 and a product candidate are safe and effective for any indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- 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 and a product candidate's clinical and other benefits outweigh its safety risks;
- we may be unable to demonstrate that our electroporation equipment and a 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 pre-clinical 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.

Delays in the commencement 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 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. 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 gene based therapy clinical trials;
- 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;
- conducting clinical trials with sites internationally due to regulatory approvals and meeting international standards;

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- 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, terrorist activities, and economic and other external factors.

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. 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 or completion of clinical trials may adversely affect the trading price of our common stock.

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.

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. 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 approval;
- 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. 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. 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.

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 synthetic vaccine 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, health care 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.

We currently have no marketing and sales organization and have no experience in marketing products. 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 do not have a 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 any of our products for which we receive regulatory approval does 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;
- the relative convenience and ease of administration;
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- 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;
- our ability to obtain sufficient third-party coverage or 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, health care 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 reimbursement policies which, if not favorable to our product candidates, could hinder or prevent our products' commercial success.

Our ability to commercialize our electroporation equipment and product candidates successfully will depend in part on the extent to which governmental authorities, 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 generally require that drug products have been approved for marketing by the FDA. Third-party payors also are increasingly challenging the effectiveness of and prices charged for medical products and services. We may not be able to obtain third-party coverage or reimbursement for our products in whole or in part.

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 passed healthcare reform legislation, the Patient Protection and Affordable Care Act, or the ACA. The provisions of the ACA have become or will become effective on various dates. While many of the details regarding the implementation of the ACA are yet to be determined, we believe there will be continuing trends towards expanding coverage to more individuals, containing health care costs and improving quality. At the same time, the rebates, discounts, taxes and other costs associated with the ACA are expected to be a significant cost to the pharmaceutical industry.

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 and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights may be applicable to our business. We could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business, without limitation. 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 either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws 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 ACA expands the government's investigative and enforcement authority and increases the penalties for fraud and abuse, including amendments to both the False Claims Act and the Anti-Kickback Statute to make it easier to bring suit under those statutes;
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- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- the Federal Food, Drug, and Cosmetic Act, 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; 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, 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.

Additionally, the compliance environment is changing, with more states, such as California and Massachusetts, mandating implementation of compliance programs, compliance with industry ethics codes, and spending limits, and other states, such as Vermont, Maine, and Minnesota requiring reporting to state governments of gifts, compensation, and other remuneration to physicians. Under the ACA, pharmaceutical companies are required to record any transfers of value made to doctors and teaching hospitals and to disclose such data to HHS. These laws all provide for penalties for non-compliance. 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.

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 penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations 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. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

If we and the contract manufacturers upon whom we rely fail to produce our systems and product candidates in the volumes that we require on a timely basis, or fail to comply 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 systems and utilize the services of contract manufacturers to manufacture the remaining components of these systems and our product supplies for clinical trials. The manufacture of our systems and product supplies 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 products to patients in our clinical trials or to commercially launch a product would be jeopardized. Any delay or interruption in the supply of clinical trial supplies 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.

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.

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 may be subject to stockholder litigation, which would harm our business and financial condition.

We may have actions brought against us by stockholders relating to past transactions, changes in our stock price or other matters. Any such actions could give rise to substantial damages, and thereby have a material adverse effect on our consolidated financial position, liquidity, or results of operations. Even if an action is not resolved against us, the uncertainty and expense associated with stockholder actions could harm our business, financial condition and reputation. Litigation can be costly, time-consuming and disruptive to business operations. The defense of lawsuits could also result in diversion of our management's time and attention away from business operations, which could harm our business.

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 and the availability and cost of credit have contributed to increased volatility and diminished expectations for the economy and the markets going forward. These factors, combined with volatile oil prices, declining business and consumer confidence and increased unemployment, have precipitated an economic recession. Domestic and international capital markets have also been experiencing heightened volatility and turmoil. These events and the continuing market upheavals may have an adverse effect on us. In the event of a continuing 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 in 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. Given the current instability of financial institutions, we may experience losses on these deposits.

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 has evolved over recent years and continues to undergo review and revision, both in the United States. 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:

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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;
- 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.

Risks Related to Our Common Stock

The price of our common stock is expected 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 is expected to be highly volatile and can 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, in addition to the other risk factors described in this annual 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;
- fluctuating public or scientific interest in the potential for influenza pandemic or other applications for our vaccine or other product candidates;
- 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;
- 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;
- negative perception 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, terrorist activities, and economic and other external factors; and
- catastrophic weather and/or global disease pandemics.

The stock market in general has recently experienced relatively large price and volume fluctuations. 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 the common stock, which could cause a decline in the value of the common stock. In addition, price volatility may increase if the trading volume of our common stock remains limited or declines.

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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 your sole source of potential gain for the foreseeable future.

The market price for our shares may not maintain their pre-reverse stock split market price.

On June 5, 2014, we effectuated a 4-for-1 reverse split of the Company's outstanding common stock. We cannot be certain that the reverse split will have a long-term positive effect on the market price of our common stock, or increase our ability to consummate financing arrangements in the future. The market price of our common stock is based on factors that may be unrelated to the number of shares outstanding. These factors include our performance, general economic and market conditions and other factors, many of which are beyond our control. The market price for our post-reverse stock split shares may not rise or remain constant in proportion to the reduction in the number of pre-split shares outstanding before the reverse split. Accordingly, the total market capitalization of our common stock after the reverse split may be lower than the total market capitalization before the reverse split.

ITEM 1B. UNRESOLVED STAFF COMMENTS

We have no unresolved written comments from the SEC staff regarding our filings under the Exchange Act.

ITEM 2. PROPERTIES

We own no real property and have no plans to acquire any real property in the future. Our corporate headquarters is located at 660 W. Germantown Pike, Suite 100, Plymouth Meeting, Pennsylvania. This lease was signed in March 2014 and we occupied the building in June 2014. The initial term of the lease is 11.5 years for a total of approximately 21,000 square feet. The base rent adjusts periodically throughout the term of the lease, with monthly payments ranging from $0 to $58,000. In addition, we will pay the landlord our share of operating expenses and a property management fee. We have paid the landlord a security deposit of $49,000.

The lease for our former corporate headquarters located at 1787 Sentry Park West in Blue Bell, Pennsylvania, was amended in July 2014 to allow the lessor the option to recapture all or a portion of the premises. In October 2014, the lessor exercised the option to recapture 3,749 square feet of the 8,761 total square feet. The rent for the remaining space was prorated to reflect the decrease in square footage. Although we intend to sublet the remaining space, we will continue to be subject to rent and lease obligations through June 30, 2017.

The corporate office in San Diego is located at 10480 Wateridge Circle in San Diego, California. This lease was signed in April 2013 and we occupied the building in early December 2013. The initial term of the lease runs through

December 1, 2023 for a total of approximately 26,500 square feet. The base rent adjusts periodically throughout the ten year term of the

lease, with monthly payments ranging from $0 to $83,000. In addition, we pay the landlord our share of operating expenses and a property management fee. We currently use the facility for office and research and development purposes.

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

Not applicable.

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

Reverse Stock Split

On June 5, 2014, we implemented a 4-for-1 reverse stock split. All share information contained within this report, including the accompanying consolidated financial statements and footnotes, have been retroactively adjusted to reflect the effects of the reverse split.

Market Information

On September 4, 2014, we provided notice to the NYSE MKT that the Company intends to voluntarily transfer the listing of our common stock, par value $0.001 per share (the "Common Stock"), from NYSE MKT to the NASDAQ Global Select Market ("NASDAQ"). The Common Stock was approved for listing on NASDAQ, and began trading on NASDAQ on September 15, 2014 under the symbol "INO". The following table sets forth the quarterly high and low per share closing prices of our common stock for the two most recent fiscal years.

	Year Ended December 31,			
	2014		2013	
Period:	High	Low	High	Low
First Quarter	$15.28	$9.76	$3.28	$2.00
Second Quarter	$13.96	$8.00	$3.20	$2.04
Third Quarter	$13.10	$8.68	$12.00	$3.40
Fourth Quarter	$12.31	$8.21	$11.88	$6.92

As of March 9, 2015, we had approximately 490 common stockholders of record. This figure does not include beneficial owners who hold shares in nominee name. The closing price per share of our common stock on March 9, 2015 was $7.14, as reported on the NASDAQ.

Dividends

The payment of any dividends on our common stock is within the discretion of our board of directors. We have not 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 matches Inovio Pharmaceuticals Inc.'s cumulative 5-Year total shareholder return on common stock with the cumulative total returns of the NYSE MKT Composite index, the S&P SuperCap Biotechnology index and the NASDAQ Composite index. The graph tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from December 31, 2009 to December 31, 2014.

	12/09	12/10	12/11	12/12	12/13	12/14
Inovio Pharmaceuticals, Inc.	100.00	100.88	37.54	43.82	254.39	201.32
NYSE MKT Composite	100.00	129.56	133.75	140.87	150.79	153.24
S&P SuperCap Biotechnology	100.00	100.46	123.79	176.36	308.75	410.95
NASDAQ Composite	100.00	117.43	118.27	138.47	196.27	223.17

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 is not being filed for purposes of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

ITEM 6. SELECTED FINANCIAL DATA

The following table sets forth our selected consolidated financial data for the periods indicated, derived from consolidated financial statements prepared in accordance with United States generally accepted accounting principles.

	Year Ended December 31, 2014	Year Ended December 31, 2013	Year Ended December 31, 2012	Year Ended December 31, 2011	Year Ended December 31, 2010
Operations Data:					
Revenue under collaborative research and development arrangements, including from affiliated entity	$7,896,032	$9,664,547	$660,003	$567,856	$527,222
Grants and miscellaneous revenue	2,560,734	3,802,799	3,458,649	9,227,401	5,617,483
Total revenues	10,456,766	13,467,346	4,118,652	9,795,257	6,144,705
Loss from operations	(39,495,961)	(19,544,332)	(23,493,532)	(21,638,540)	(19,220,162)
Interest and other income, net	331,461	132,214	166,113	34,285	147,406
Change in fair value of common stock warrants	348,143	(45,632,669)	1,982,620	8,690,658	2,403,924
Gain (Loss) on investment in affiliated entity	2,676,224	(1,038,745)	1,631,819	(2,390,498)	(969,914)
Net loss	(36,140,133)	(66,083,532)	(19,712,980)	(15,304,095)	(17,638,746)
Net loss attributable to non-controlling interest	18,420	55,084	44,025	51,150	24,950
Net loss attributable to Inovio Pharmaceuticals, Inc.	$(36,121,713)	$(66,028,448)	$(19,668,955)	$(15,252,945)	$(17,613,796)
Net loss per common share attributable to common stockholders					
Basic	$(0.61)	(1.43)	(0.58)	(0.48)	(0.68)
Diluted	$(0.64)	$(1.43)	$(0.58)	$(0.48)	$(0.68)
Balance Sheet Data:					
Cash and cash equivalents	$40,543,982	$33,719,796	$5,646,021	$17,350,116	$19,998,489
Short-term investments	53,075,974	18,905,608	8,034,001	12,863,420	1,849,271
Total assets	131,785,097	88,287,207	45,138,754	61,106,561	56,067,391
Current liabilities	14,023,752	28,966,456	8,376,577	11,043,021	6,436,708
Noncurrent liabilities	6,223,751	6,418,068	1,904,772	2,201,878	2,529,772
Accumulated deficit	(331,910,290)	(295,788,577)	(229,760,129)	(210,091,174)	(194,838,229)
Total stockholders' equity	111,537,594	52,902,683	34,857,405	47,861,662	47,100,911

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

This report contains forward-looking statements. 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, 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 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; 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 proposals.

Overview

We are developing active DNA immunotherapies and vaccines focused on treating and preventing cancers and infectious diseases. Our DNA-based immunotherapies, in combination with our proprietary electroporation delivery devices, are intended to generate robust immune responses, in particular T cells, to fight such diseases. In 2014 we reported that in a large, controlled phase II clinical study we achieved clinically relevant efficacy against a targeted disease (HPV-associated cervical dysplasia) by generating antigen-specific T cells. Our novel SynCon® immunotherapy design has shown the ability to help break the immune system's tolerance of cancerous cells. Alternatively, our SynCon® product design is also intended to facilitate cross-strain protection against known as well as new unmatched strains of pathogens such as influenza. Given the recognized role of killer T cells in eliminating cancerous or infected cells from the body, our scientists believe that our active immunotherapies may play an important role in helping fight such diseases. Human data to date have shown a favorable safety profile of our DNA immunotherapies delivered using electroporation.

We have completed, current or planned clinical programs of our proprietary SynCon® immunotherapies for HPV-caused pre-cancers and cancers, prostate cancer, breast/lung/pancreatic cancer, hepatitis C virus (HCV), hepatitis B virus (HBV), HIV, influenza, and Ebola. Our partners and collaborators include F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. ("Roche"), University of Pennsylvania, Drexel University, National Microbiology Laboratory of the Public Health Agency of Canada, , National Institute of Allergy and Infectious Diseases ("NIAID"), United States Military HIV Research Program ("USMHRP"), U.S. Army Medical Research Institute of Infectious Diseases ("USAMRIID"), HIV Vaccines Trial Network ("HVTN"), Defense Advanced Research Projects Agency ("DARPA") and MedImmune, LLC.

All of our potential human products are in research and development phases. We have not generated any revenues from the sale of any such 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, collaborative research and development agreements, grants and government contracts. 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.

Recent Developments

On September 4, 2014, we provided notice to the NYSE MKT that the Company intends to voluntarily transfer the listing of our common stock, par value $0.001 per share (the "Common Stock"), from NYSE MKT to the NASDAQ Global Select Market ("NASDAQ"). The Common Stock was approved for listing on NASDAQ, and began trading on NASDAQ on September 15, 2014.

In May 2014, our 91% owned subsidiary VGX Animal Health, Inc. entered into an agreement for the sale of its animal health assets to Plumbline Life Sciences, Inc. ("PLS") of Korea. The assets being transferred include an exclusive license for animal applications of our growth hormone-releasing hormone ("GHRH") technology and animal DNA vaccines plus a non-exclusive license to our electroporation delivery systems. VGX Animal Health will receive $2.0 million in cash in multiple payments and 20% of the outstanding shares of PLS. VGX Animal Health will receive additional shares to maintain its 20% equity ownership position in PLS in the event of additional equity fund-raising by PLS up to $10.0 million. No receivable has been recorded for the $2.0 million due from PLS as collection is

uncertain.

On March 4, 2014, we closed an underwritten public offering of 5,452,725 shares of our common stock, including 711,225 shares of common stock issued pursuant to the underwriter’s exercise of its overallotment option, at the public offering price of $11.60 per share. The net proceeds, after deducting the underwriter’s discounts and commission and other offering expenses, were approximately $59.2 million.

In March 2014, we entered into an office lease (the "Lease") with a publicly owned real estate investment trust, located in Plymouth Meeting, Pennsylvania and occupied the new space in June 2014. The initial term of the Lease is 11.5 years and we intend to use the facility for office purposes. The base rent adjusts periodically throughout the 11.5 year term of the Lease,

with monthly payments ranging from $0 to $58,000. In addition, we will pay the landlord our share of operating expenses and a property management fee and have paid a security deposit of $49,000.

As of December 31, 2014, we had an accumulated deficit of $331.9 million. 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.

Reverse Stock Split

On June 5, 2014, we implemented a 4-for-1 reverse stock split. All share information contained within this report, including the accompanying condensed consolidated financial statements and footnotes, has been retroactively adjusted to reflect the effects of the reverse split.

Critical Accounting Policies

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 is based on our audited consolidated financial statements, which have been prepared in accordance with U.S. GAAP. There have been no changes to our critical accounting policies during the year ended December 31, 2014. The preparation of these 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. Our critical accounting policies include:

Revenue Recognition.

Grant revenue

We receive non-refundable grants under available government programs. Government grants towards current expenditures are recorded as revenue when there is reasonable assurance that we have complied with all conditions necessary to receive the grants, collectability is reasonably assured, and as the expenditures are incurred.

License fee and milestone revenue

We have adopted a strategy of co-developing or licensing our gene delivery technology for specific genes or specific medical indications. Accordingly, we have entered into collaborative research and development agreements and have received funding for pre-clinical research and clinical trials. Prior to the adoption of the Financial Accounting Standards Board's ("FASB") Accounting Standards Update ("ASU") No. 2009-13, Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements, we analyzed our multiple element arrangements to determine whether the identified deliverables could be accounted for individually as separate units of accounting. The delivered item(s) were considered a separate unit of accounting if all of the following criteria were met: (1) the delivered item(s) has value to the customer on a standalone basis; (2) there is objective and reliable evidence of the fair value of the undelivered item(s); and (3) if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item(s) is considered probable and substantially in our control. If these criteria were not met, the deliverable was combined with other deliverables in the arrangement and accounted for as a combined unit of accounting.

For new collaborative agreements or material modifications of existing collaborative agreements entered into after December 31, 2010, we follow the provisions of ASU No. 2009-13. In order to account for the multiple-element arrangements, we identify the deliverables included within the agreement and evaluate which deliverables represent separable units of accounting. Analyzing the arrangement to identify deliverables requires the use of judgment, and each deliverable may be an obligation to deliver services, a right or license to use an asset, or another performance obligation. A delivered item is considered a separate unit of accounting when the delivered item has value to the collaborator on a standalone basis based on the consideration of the relevant facts and circumstances for each arrangement.

Arrangement consideration is allocated at the inception of the agreement to all identified units of accounting based on their relative selling price. The relative selling price for each deliverable is determined using vendor specific objective evidence ("VSOE"), of selling price or third-party evidence of selling price if VSOE does not exist. If neither VSOE nor

third-party evidence of selling price exists, we use our best estimate of the selling price for the deliverable. The amount of allocable arrangement consideration is limited to amounts that are fixed or determinable. The consideration received is allocated among the separate units of accounting, and the applicable revenue recognition criteria are applied to each of the separate units. Changes in the allocation of the sales price between delivered and undelivered elements can impact revenue recognition but do not change the total revenue recognized under any agreement.

Upfront license fee payments are recognized upon delivery of the license if facts and circumstances dictate that the license has standalone value from the undelivered items, the relative selling price allocation of the license is equal to or exceeds the upfront license fee, persuasive evidence of an arrangement exists, our price to the collaborator is fixed or determinable, and collectability is reasonably assured. Upfront license fee payments are deferred if facts and circumstances dictate that the license does not have standalone value. The determination of the length of the period over which to defer revenue is subject to judgment and estimation and can have an impact on the amount of revenue recognized in a given period.

Prior to the adoption of ASU No. 2010-17, Revenue Recognition (Topic 605): Milestone Method of Revenue Recognition ("Milestone Method"), we recognized non-refundable milestone payments upon the achievement of specified milestones upon which we had earned the milestone payment, provided the milestone payment was substantive in nature and the achievement of the milestone was not reasonably assured at the inception of the agreement. We deferred payments for milestone events that were reasonably assured and recognized them ratably over the minimum remaining period of our performance obligations. Payments for milestones that were not reasonably assured were treated as the culmination of a separate earnings process and were recognized as revenue when the milestones were achieved.

Effective January 1, 2011, we adopted on a prospective basis the Milestone Method of ASU No. 2010-17. Under the Milestone Method, we will recognize consideration that is contingent upon the achievement of a milestone in its entirety as revenue in the period in which the milestone is achieved only if the milestone is substantive in its entirety. A milestone is considered substantive when it meets all of the following criteria:

1. The consideration is commensurate with either the entity's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone,
2. The consideration relates solely to past performance, and
3. The consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

A milestone is defined as an event (i) that can only be achieved based in whole or in part on either the entity's performance or on the occurrence of a specific outcome resulting from the entity's performance, (ii) for which there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and (iii) that would result in additional payments being due to the Company.

Research and Development Expenses. Since our inception, most of our activities have consisted of research and development efforts related to developing our electroporation technologies and DNA vaccines. 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 our independent research and development efforts as well as efforts associated with collaborations and licensing arrangements. We review and accrue clinical trials expense based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical 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.

Valuation and Impairment Evaluations of Goodwill and Intangible Assets. Goodwill represents the excess of acquisition cost over the fair value of the net assets of acquired businesses. As of December 31, 2014, our intangible assets resulting from the acquisition of VGX and Inovio AS, and additional intangibles including previously capitalized patent costs and license costs, net of accumulated amortization, totaled $4.8 million. Intangible assets are amortized over their estimated useful lives ranging from 5 to 18 years. We are concurrently conducting pre-clinical, Phase I, and Phase II trials using acquired intangibles, and we have entered into certain significant licensing agreements for use of these acquired intangibles.

Historically we have recorded patents at cost and amortized these costs using the straight-line method over the expected useful lives of the patents or 17 years, whichever is less. Patent costs consist of the consideration paid for

patents and related legal costs. Effective June 1, 2009, in connection with our acquisition of VGX, all new patent costs are being expensed as incurred. Patent costs currently capitalized will continue to be amortized over the expected life of the patent. The effect of this change was immaterial to prior periods. We record license costs based on the fair value of consideration paid and amortize 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.

The determination of the value of such intangible assets requires management to make estimates and assumptions that affect our consolidated financial statements. We assess 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. Our judgments regarding the existence of impairment indicators and future cash flows related to intangible assets are based on operational performance of our acquired businesses, market conditions and other factors. If impairment is indicated, we reduce the carrying value of the intangible asset to fair value. While our current and historical operating and cash flow losses are potential indicators of impairment, we believe the future cash flows to be received from our intangible assets will exceed the intangible assets' carrying value, and accordingly, we have not recognized any impairment losses through December 31, 2014.

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 more likely than not 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 more likely than not that the fair value of its reporting unit is less than its carrying amount, then no additional assessment is deemed necessary. Otherwise, the Company proceeds to perform the two-step test for goodwill impairment. The first step involves comparing the estimated fair value of the reporting unit with its carrying value, including goodwill. If the carrying amount of the reporting unit exceeds its fair value, the Company performs the second step of the goodwill impairment test to determine the amount of loss, which involves comparing the implied fair value of the goodwill to the carrying value of the goodwill. The Company may also elect to bypass the qualitative assessment in a period and elect to proceed to perform the first step of the goodwill impairment test. The Company performed its annual assessment for goodwill impairment as of November 30, 2014, identifying no impairment.

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

Stock-based Compensation. We have equity incentive plans under which we have granted incentive stock options, restricted stock units and non-qualified stock options.

Our employee stock-based compensation cost is estimated at the grant date based on the fair-value of the award and is recognized as an expense ratably over the requisite service period of the award. Determining the appropriate fair-value model and calculating the fair value of stock-based awards at the grant date requires considerable judgment, including estimating stock price volatility, expected option life and forfeiture rates. We develop our estimates based on historical data. If factors change and we employ different assumptions in future periods, the compensation expense that we record may differ significantly from what we have recorded in the current period. A small change in the estimates used may have a relatively large change in the estimated valuation. We use the Black-Scholes pricing model to value stock option awards. We recognize compensation expense using the straight-line amortization method.

Our non-employee stock-based compensation awards are measured at either the fair value of the consideration received or the fair value of the equity instruments issued, whichever is more reliably measurable. If the fair value of the equity instruments issued is used, it is measured at each reporting date using the stock price and other measurement assumptions as of the earlier of (i) the date at which a commitment for performance by the counterparty to earn the equity instruments is reached, or (ii) the date at which the counterparty’s performance is completed.

Registered Common Stock Warrants. We account for registered common stock warrants pursuant to the authoritative guidance on accounting for derivative financial instruments indexed to, and potentially settled in, a company’s own stock, on the understanding that in compliance with applicable securities laws, the registered warrants require the issuance of registered securities upon exercise and do not sufficiently preclude an implied right to net cash settlement. We classify registered warrants on the consolidated balance sheet as a current liability, which is revalued at each

balance sheet date subsequent to the initial issuance. Determining the appropriate fair-value model and calculating the fair value of registered warrants requires considerable judgment including estimating stock price volatility and expected warrant life. We develop our estimates based on historical data. A small change in the estimates used may have a relatively large change in the estimated valuation. We use the Black-Scholes pricing model to value the registered warrants. Changes in the fair market value of the warrants are reflected in the consolidated statement of operations as “Change in fair value of common stock warrants.”

Transaction costs associated with the issuance of warrants classified on the consolidated balance sheet as a current liability are expensed immediately and included as part of general and administrative expense on the consolidated statement 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

Comparison of Years Ended December 31, 2014 and 2013

The consolidated financial data for the years ended December 31, 2014 and December 31, 2013 is presented in the following table and the results of these two periods are used in the discussion thereafter.

	December 31, 2014	December 31, 2013	Increase/ (Decrease) $	Increase/ (Decrease) %
Revenues:				
Revenue under collaborative research and development arrangements, including from affiliated entity	$7,896,032	$9,664,547	$(1,768,515)	(18)%
Grants and miscellaneous revenue	2,560,734	3,802,799	(1,242,065)	(33)
Total revenues	10,456,766	13,467,346	(3,010,580)	(22)
Operating expenses:				
Research and development	34,095,039	21,368,604	12,726,435	60
General and administrative	15,857,688	13,643,074	2,214,614	16
Gain on sale of assets	—	(2,000,000)	2,000,000	(100)
Total operating expenses	49,952,727	33,011,678	16,941,049	51
Loss from operations	(39,495,961)	(19,544,332)	(19,951,629)	(102)
Interest and other income, net	331,461	132,214	199,247	151
Change in fair value of common stock warrants	348,143	(45,632,669)	45,980,812	(101)
Gain (Loss) on investment in affiliated entity	2,676,224	(1,038,745)	3,714,969	358
Net loss	(36,140,133)	(66,083,532)	29,943,399	45
Net loss attributable to non-controlling interest	18,420	55,084	(36,664)	(67)
Net loss attributable to Inovio Pharmaceuticals, Inc.	$(36,121,713)	$(66,028,448)	$29,906,735	45%

Revenue

Revenue primarily consists of revenue under collaborative research and development arrangements and grants and government contracts. Our total revenue decreased $3.0 million or 22% for the year ended December 31, 2014, as compared to the year ended December 31, 2013.

The $1.8 million decrease in revenue under collaborative research and development arrangements for the year ended December 31, 2014 as compared to 2013 was primarily due to $8.4 million of the $10.0 million upfront payment from our Agreement with Roche being recognized in September 2013 (see Note 3), offset by an increase in revenue recognized related to collaborative research and development services performed related to the Agreement of $7.4 million during the year ended December 31, 2014 as compared to $803,000 during the year ended December 31, 2013.

The $1.2 million decrease in grants and miscellaneous revenue for the year ended December 31, 2014 as compared to 2013, was primarily due to less revenue recognized from our contract with the NIAID of $1.2 million in 2014, as compared to $2.1 million for the same period in 2013, due to the timing of work performed. The decrease was also attributable to less revenue recognized under our PATH MVI contract and our subcontract with the University of Pennsylvania, partially offset by an increase in revenue recognized under our NIH research project grant.

Research and Development Expenses

The $12.7 million increase in research and development expenses for the year ended December 31, 2014 as compared to 2013 was primarily due to an increase in costs of $5.3 million incurred in conjunction with our Roche collaboration. Other increases included $2.7 million in higher employee headcount, $2.3 million in higher employee non-cash stock-based compensation, $2.2 million in higher research and development activities and $1.9 million in higher engineering and professional services for new device development, among other variances. These increases were partially offset by lower

clinical trial expenses of $1.3 million as well as $1.1 million in sub-license fee expense incurred during the year ended December 31, 2013, which was triggered by the up-front payment received from the Roche agreement. There were no comparable payments during the year ended December 31, 2014.

General and Administrative Expenses

The $2.2 million increase in general and administrative expenses for the year ended December 31, 2014 as compared to the year ended December 31, 2013 was primarily due to an increase in employee non-cash stock-based compensation, employee headcount, rent and utilities expense for the new building leases and corporate and patent legal fees of $1.4 million, $688,000, $524,000 and $494,000 respectively. These increases were offset by a decrease in the amortization of intangible assets of $828,000, among other variances.

Stock-based Compensation

Employee stock-based compensation cost is measured at the grant date, based on the fair value of the award reduced by estimated forfeitures, and is recognized as expense over the employee's requisite service period. Total employee compensation cost for our stock plans for the years ended December 31, 2014 and 2013 was $4.8 million and $1.2 million, of which $2.8 million and $550,000 was included in research and development expenses and $2.0 million and $605,000 was included in general and administrative expenses, respectively. The increase for the annual period year over year was primarily due to a higher valuation of the employee and director stock options granted during the period. At December 31, 2014, there was $5.3 million of total unrecognized compensation cost related to unvested stock options, which we expect to recognize over a weighted-average period of 2 years, as compared to $956,000 for the year ended December 31, 2013 expected to be recognized over a weighted-average period of 1.8 years. Total stock-based compensation for options granted to non-employees for the years ended December 31, 2014 and 2013 was $585,000 and $714,000, respectively.

Interest and Other Income, net

Interest and other income, net, increased by $199,000 for the year ended December 31, 2014 as compared to 2013 due to higher average cash and short-term investment balances.

Change in fair value of common stock warrants

The change in fair value of common stock warrants for the years ended December 31, 2014 and 2013 was $348,000 and $(45.6) million, respectively. The variance is primarily due to the revaluation of registered common stock warrants issued in January 2011 and March 2013, as well as fewer number of warrants classified as a current liability due to a significant number of warrants exercised during 2014. We revalue warrants at each balance sheet date to fair value. Warrants that were exercised during the period were revalued the day prior to exercise and reclassified into stockholders' equity upon exercise. If unexercised, the remaining warrants will expire in September 2018.

Gain (Loss) from investment in affiliated entity

The gain (loss) is a result of the change in the fair market value of the investment in GeneOne Life Sciences ("GeneOne") (formerly VGX International Inc.) for the year ended December 31, 2014.

Gain on Sale of Assets

The gain on sale of assets is related to the March 2011 Asset Purchase Agreement with OncoSec Medical Incorporated ("OncoSec"). The gain recorded during the year ended December 31, 2013 is related to the cash received during the year related to the sale (see Note 5).

Income Taxes

Since inception, we have incurred operating losses and accordingly have not recorded a provision for income taxes for any of the periods presented. As of December 31, 2014, we had net operating loss carry forwards for federal, California and Pennsylvania income tax purposes of approximately $159.3 million, $60.1 million and $99.3 million, respectively, net of the net operating losses that will expire due to IRC Section 382 limitations. We also had federal and state research and development tax credits of approximately $2.8 million and $2.1 million, respectively, net of the federal research and development credits that will expire due to IRC Section 383 limitations. If not utilized, the net operating losses and credits will begin to expire in 2018. Utilization of net operating losses and credits are subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended.

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Comparison of Years Ended December 31, 2013 and 2012

The consolidated financial data for the years ended December 31, 2013 and December 31, 2012 is presented in the following table and the results of these two periods are used in the discussion thereafter.

	December 31, 2013	December 31, 2012	Increase/ (Decrease) $	Increase/ (Decrease) %
Revenues:				
Revenue under collaborative research and development arrangements, including from affiliated entity	$9,664,547	$660,003	$9,004,544	1,364 %
Grants and miscellaneous revenue	3,802,799	3,458,649	344,150	10
Total revenues	13,467,346	4,118,652	9,348,694	227
Operating expenses:				
Research and development	21,368,604	17,984,825	3,383,779	19
General and administrative	13,643,074	10,778,359	2,864,715	27
Gain on sale of assets	(2,000,000)	(1,151,000)	(849,000)	74
Total operating expenses	33,011,678	27,612,184	5,399,494	20
Loss from operations	(19,544,332)	(23,493,532)	3,949,200	17
Interest and other income, net	132,214	166,113	(33,899)	(20)
Change in fair value of common stock warrants	(45,632,669)	1,982,620	(47,615,289)	(2,402)
Gain (Loss) on investment in affiliated entity	(1,038,745)	1,631,819	(2,670,564)	164
Net loss	(66,083,532)	(19,712,980)	(46,370,552)	(235)
Net loss attributable to non-controlling interest	55,084	44,025	11,059	25
Net loss attributable to Inovio Pharmaceuticals, Inc.	$(66,028,448)	$(19,668,955)	$(46,359,493)	(236)%

Revenue

Revenue primarily consists of revenue under collaborative research and development arrangements and grants and government contracts. Our total revenue increased $9.3 million or 227% for the year ended December 31, 2013, as compared to the year ended December 31, 2012.

The $9.0 million increase in revenue under collaborative research and development arrangements for the year ended December 31, 2013 as compared to 2012 was primarily due to the revenue recognized from our Agreement with Roche entered into in September 2013 (see Note 3).

The $344,000 increase in grants and miscellaneous revenue for the year ended December 31, 2013 as compared to 2012, was primarily attributable to $726,000 of revenue recognized under our PATH Malaria Vaccine Initiative ("MVI") contract during the year ended December 31, 2013 as compared to $85,000 of revenue recognized for the same period in 2012, due to the initiation of the third amendment in October 2012. There were also increases in revenue recognized from our NIH research project grant, our subcontract with the University of Pennsylvania and our U.S. Department of Defense SBIR grant of $152,000, $142,000 and $126,000, respectively, for the year ended December 31, 2013 as compared to the same period in 2012, among other variances. These increases were offset by lower revenue of $740,000 recognized from our contract with the NIAID.

Research and Development Expenses

The $3.4 million increase in research and development expenses for the year ended December 31, 2013 as compared to 2012 was primarily due to $1.3 million in expenses incurred related to the Roche Agreement, which includes $1.1 million in sub-license fees paid based on the up-front payment received from Roche. The increase was also attributable to $915,000 in higher compensation and related expenses, $606,000 in higher costs related to work performed for the MVI contract, $304,000 in higher engineering and professional services and $170,000 in higher clinical trial expenses, among other variances.

General and Administrative Expenses

The $2.9 million increase in general and administrative expenses for the year ended December 31, 2013 as compared to the year ended December 31, 2012 was primarily due to an increase in consultant stock-based compensation, rent expense

related to deferred rent on the new building lease, compensation and related expenses, outside consulting services, corporate and patent legal fees and transaction costs associated with the issuance of warrants in the March 2013 financing of $554,000, $506,000, $494,000, $394,000, $357,000 and $316,000, respectively, among other variances.

Stock-based Compensation

Employee stock-based compensation cost is measured at the grant date, based on the fair value of the award reduced by estimated forfeitures, and is recognized as expense over the employee's requisite service period. Total employee compensation cost for our stock plans for the years ended December 31, 2013 and 2012 was $1.2 million and $1.2 million, of which $550,000 and $555,000 was included in research and development expenses and $605,000 and $638,000 was included in general and administrative expenses, respectively. At December 31, 2013, there was $956,000 of total unrecognized compensation cost related to unvested stock options, which we expect to recognize over a weighted-average period of 1.8 years, as compared to $944,000 for the year ended December 31, 2012 expected to be recognized over a weighted-average period of 1.9 years. Total stock-based compensation for options granted to non-employees for the years ended December 31, 2013 and 2012 was $714,000 and $153,000, respectively.

Interest and Other Income, net

Interest and other income, net, decreased by $34,000 for the year ended December 31, 2013 as compared to 2012.

Change in fair value of common stock warrants

The change in fair value of common stock warrants for the years ended December 31, 2013 and 2012 was $(45.6) million and $2.0 million, respectively. The significant variance is due to the revaluation of registered common stock warrants issued by us in March 2013, December 2011, January 2011 and June 2009. We revalue warrants at each balance sheet date to fair value. Warrants that were exercised during the period were revalued the day prior to exercise and reclassified into stockholders' equity upon exercise. The change in fair value was primarily due to the significant increase in Company stock price during the year. If unexercised, the warrants will expire at various dates between July 2014 and September 2018.

Gain (Loss) from investment in affiliated entity

The gain (loss) is a result of the change in the fair market value of the investment in GeneOne for the year ended December 31, 2013.

Gain on Sale of Assets

The gain on sale of assets is related to the March 2011 Asset Purchase Agreement with OncoSec. The gain recorded during the year ended December 31, 2013 is related to the cash received during the year related to the sale, and the gain recorded during 2012 is related to the cash received related to the sale as well as the initial fair value of the warrants received in connection with the second amendment to the Asset Purchase Agreement signed in March 2012 (see Note 5).

Income Taxes

Since inception, we have incurred operating losses and accordingly have not recorded a provision for income taxes for any of the periods presented. As of December 31, 2013, we had net operating loss carry forwards for federal, California and Pennsylvania income tax purposes of approximately $122.4 million, $38.9 million and $75.6 million, respectively, net of the net operating losses that will expire due to IRC Section 382 limitations. We also had federal and state research and development tax credits of approximately $2.0 million and $2.1 million, respectively, net of the federal research and development credits that will expire due to IRC Section 383 limitations. If not utilized, the net operating losses and credits will begin to expire in 2018. Utilization of net operating losses and credits are subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended.

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.

Working Capital and Liquidity

As of December 31, 2014 we had cash and short-term investments of $93.6 million and working capital of $84.9 million, as compared to $52.6 million and $29.7 million, respectively, as of December 31, 2013. The increase in cash and short-term

investments during the year ended December 31, 2014 was primarily due to our March 2014 financing as well as proceeds received from warrant and stock option exercises, offset by expenditures related to our research and development activities and various general and administrative expenses related to legal, consultants, accounting and audit, and corporate development.

Net cash used in operating activities was $29.8 million and $15.4 million for the years ended December 31, 2014 and 2013, respectively.

Net cash used in investing activities was $35.8 million and $9.2 million for the years ended December 31, 2014 and 2013, respectively. The variance was primarily the result of timing differences in short-term investment purchases, sales and maturities.

Net cash provided by financing activities was $72.5 million and $52.7 million for the years ended December 31, 2014 and 2013, respectively. The increase was related to proceeds received from our March 2014 financing as well as warrant and stock option exercises.

On March 4, 2014, we closed an underwritten public offering of 5,452,725 shares of our common stock, including 711,225 shares of common stock issued pursuant to the underwriter's exercise of its overallotment option, at the public offering price of $11.60 per share. The net proceeds, after deducting the underwriter's discounts and commission and other estimated offering expenses, were approximately $59.2 million.

During the year ended December 31, 2014, warrants and stock options to purchase 2,713,867 shares of common stock were exercised for total proceeds to the Company of $13.3 million.

As of December 31, 2014, we had an accumulated deficit of $331.9 million. We have operated at a loss since 1994, 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. If these activities are successful and if we receive approval from the FDA to market our DNA vaccine products, then we will need to raise additional funding to market and sell the approved vaccine 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 current cash and cash equivalents plus short-term investments are sufficient to meet planned working capital requirements through the end of 2017, excluding our planned phase III clinical trial of VGX-3100. We will continue to rely on outside sources of financing to meet our capital needs beyond this time.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenue, expenses, and results of operations, liquidity, capital expenditures or capital resources.

Contractual Obligations

As of December 31, 2014, we did not have any other material long-term debt or other known contractual obligations, except for the operating leases for our facilities, which expire in 2017 through 2025, and operating leases for copiers, which expire in 2015 through 2017.

We are contractually obligated to make the following operating lease payments as of December 31, 2014:

	Total	Less than 1 year	1 – 3 years	3 – 5 years	More than 5 years
Operating lease obligations	$13,745,000	$621,000	$2,621,000	$2,781,000	$7,722,000

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. QUALITATIVE AND QUANTITATIVE 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.

Fair Value measurements

We account for our common stock warrants pursuant to the authoritative guidance on accounting for derivative financial instruments indexed to, and potentially settled in, a company's own stock, on the understanding that in compliance with applicable securities laws, the registered warrants require the issuance of registered securities upon exercise and do not sufficiently preclude an implied right to net cash settlement. We classify registered warrants on the consolidated balance sheet as a current liability that is revalued at each balance sheet date subsequent to the initial issuance.

The investment in affiliated entity represents our ownership interest in the Korean based company, GeneOne (formerly VGX International Inc.) We report this investment at fair value on the consolidated balance sheet using the closing price of GeneOne's shares of common stock as listed on the Korean Stock Exchange.

Common stock warrants that we have received to purchase shares of OncoSec are classified on the consolidated balance sheet as a long-term asset that is revalued at each balance sheet date subsequent to the initial receipt.

Foreign Currency Risk

We have operated primarily in the United States and most transactions during the year ended December 31, 2014, have been made in United States dollars. Accordingly, we have not had any material exposure to foreign currency rate fluctuations, with the exception of the valuation of our equity investment in GeneOne which is denominated in South Korean Won. We do not have any foreign currency hedging instruments in place.

Certain transactions related to us are denominated primarily in foreign currencies, including Euros, British Pounds, Canadian Dollars and South Korean Won. 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, including the impact of the existing crisis in the global financial markets in such countries and the impact on both the United States dollar and the noted foreign currencies.

We do not use derivative financial instruments for speculative purposes. We do not engage in exchange rate hedging or hold or issue foreign exchange contracts for trading purposes. Currently, we do not expect the impact of fluctuations in the relative fair value of other currencies to be material in 2015.

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

As of December 31, 2014, we carried out an evaluation, with the participation of our Chief Executive Officer and Chief Financial Officer, of the effectiveness of our disclosure controls and procedures (as defined in Rule 13a-15(e) under the Exchange Act). Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of the end of the period covered by this report in recording, processing, summarizing and reporting, on a timely basis, information required to be disclosed in reports that we file or submit under the Exchange Act and our disclosure controls and procedures were also effective to ensure that information we disclose in the reports we file or submit under the Exchange Act is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely

decisions regarding required disclosure.

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, 2014, 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, 2014.

Changes in Internal Control over Financial Reporting

There have not been any changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the fourth quarter of our fiscal year ended December 31, 2014, that have 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, 2014. The report appears below.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited Inovio Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2014, 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). Inovio Pharmaceuticals, Inc.'s management is responsible for 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 the standards of the Public Company Accounting Oversight Board (United States). 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 our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes 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 directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection 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 misstatements. Also, projections of any evaluation 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.

In our opinion, Inovio Pharmaceuticals, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Inovio Pharmaceuticals, Inc. as of December 31, 2014 and 2013, and 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, 2014 of Inovio Pharmaceuticals, Inc. and our report dated March 13, 2015 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California
March 13, 2015

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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 2014 fiscal year.

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 2014 fiscal year.

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 2014 fiscal year.

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 2014 fiscal year.

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 2014 fiscal year.

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(a)	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).
4.16+	Form of Restricted Stock Award Grants under the 2007 Omnibus Stock Incentive Plan (incorporated by reference to Exhibit 4.3 to the registrant's Registration Statement on Form S-8 filed on May 14, 2007).
4.17+	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 with on May 14, 2007).
4.18	Form of Common Stock Warrant issued by Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 4.1 to the registrant's Form 8-K current report filed on January 24, 2011).
4.19	Form of Warrant to Purchase Common Stock issued by Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 4.1 to the registrant's Form 8-K current report filed December 1, 2011).
4.20	Form of Warrant to Purchase Common Stock issued by Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 4.1 to the registrant's Form 8-K current report filed March 7, 2013).
10.1	Lease Agreement by and between the registrant and 1787 Sentry Park West LLC dated December 10, 2009, as amended by First Amendment dated August 18, 2010, as amended by Second Amendment dated February 16, 2012, as amended by Third Amendment dated May 14, 2014, as amended by Fourth Amendment dated July 25, 2014 and as amended by Fifth Amendment dated January 30, 2015 (incorporated by reference to Exhibit 10.1 of the registrant's Form 10-K annual report for the year ended December 31, 2009 filed on March 26, 2010).
10.2†	License Agreement dated June 30, 2013 by and between the registrant and the University of South Florida Research Foundation, Inc. (incorporated by reference to Exhibit 10.5 of the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2000 filed on November 9, 2000).
10.3†	Intentionally omitted.

10.4	Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.2 of the registrant's Form 8-K current report filed on August 6, 2007).

Exhibit Number	Description of Document
10.5+	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).
10.6	Termination of Voting Trust Agreement dated as of November 8, 2013 by and among Inovio Pharmaceuticals, Inc., the stockholders parties thereto, Simon Benito and Dr. Morton Collins (incorporated by reference to Exhibit 10.2 to the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2013, filed on November 11, 2013).
10.7+	Employment Agreement dated December 27, 2010 between Inovio Pharmaceuticals, Inc. and Niranjan Y. Sardesai (incorporated by reference to Exhibit 10.7 to the registrant's Form 10-K report for the year ended December 31, 2011 filed on March 15, 2012).
10.8	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).
10.9	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).
10.12+	Amended and Restated 2007 Omnibus Incentive Plan, as amended (filed herewith).
10.15†	Collaboration, Option and License Agreement dated as of September 9, 2013 by and among F. Hoffman-La Roche Ltd, Hoffman-La Roche Inc. and Inovio Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.1 as filed with registrant's Form 8-K current report filed on September 12, 2013).
10.16†	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).
10.17†	Asset Purchase Agreement dated February 21, 2007 by and among Ronald O. Bergan, Mary Alice Bergan, and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.32 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.18†	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).
10.23†	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).

10.24†	Sales and Marketing Agreement dated February 28, 2008 by and between VGX International and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.42 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).

Exhibit Number	Description of Document
10.25+	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).
10.26†	CELLECTRA® Device License Agreement dated April 16, 2008 by and between VGX International and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.44 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.27	Asset Purchase Agreement dated June 10, 2008 by and among VGXI, Inc. and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.48 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.29†	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).
10.30+	2001 Equity Compensation Plan for VGX Pharmaceuticals, Inc., as amended (incorporated by reference to Exhibit 10.62 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.31+	2007 Equity Compensation Plan for VGX Animal Health, Inc. (incorporated by reference to Exhibit 10.63 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.32	Memorandum of NIH Research Grant Agreement by and between National Institute of Allergy and Infectious Diseases and VGX Pharmaceuticals, Inc. (incorporated by reference to Exhibit 10.66 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.33	Form of Warrant to Purchase Common Stock issued by VGX Pharmaceuticals, Inc. since 2003 (incorporated by reference to Exhibit 10.67 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.34	Form of Warrant Purchase Agreement for Warrants to Purchase Common Stock issued by VGX Pharmaceuticals, Inc. since 2003 (incorporated by reference to Exhibit 10.68 as filed with the registrant's Registration Statement on Form S-4 (File No. 333-156035) on April 27, 2009).
10.35†	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).
10.36	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).
10.37	Intentionally omitted.

10.38	Intentionally omitted.
10.39+	Employment Agreement dated December 10, 2009 between Inovio Pharmaceuticals, Inc. and Mark L. Bagarazzi (incorporated by reference to Exhibit 10.39 to the registrant's Form 10-K report for the year ended December 31, 2011 filed on March 15, 2012).
10.40+	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).

Exhibit Number	Description of Document
10.41+	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).
10.42+	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).
10.43+	First Amendment to Employment Agreement dated as of December 31, 2012 between Inovio Pharmaceuticals, Inc. and Mark L. Bagarazzi (incorporated by reference to Exhibit 10.43 of the registrant's Form 10-K annual report for the year ended December 31, 2012 filed on March 18, 2013).
10.44+	First Amendment to Employment Agreement dated as of December 31, 2012 between Inovio Pharmaceuticals, Inc. and Niranjan Sardesai (incorporated by reference to Exhibit 10.44 of the registrant's Form 10-K annual report for the year ended December 31, 2012 filed on March 18, 2013).
10.45+	Second Amendment to Employment Agreement dated November 7, 2014 by and between Inovio Pharmaceuticals, Inc. and Dr. Mark Bagarazzi (incorporated by reference to Exhibit 10.1 of the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2014 filed on November 10 , 2014).
10.46+	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).
10.47+	Second Amendment to Employment Agreement dated November 7, 2014 by and between Inovio Pharmaceuticals, Inc. and Dr. Niranjan Sardesai (incorporated by reference to Exhibit 10.3 of the registrant's Form 10-Q quarterly report for the quarter ended September 30, 2014 filed on November 10 , 2014).
21.1	Subsidiaries of the registrant.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on signature page).
31.1	Certification of the Chief Executive Officer pursuant Securities Exchange Act Rule 13a-14(a).
31.2	Certification of the Chief Financial Officer pursuant Securities Exchange Act Rule 13a-14(a).
32.1	Certification pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance 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.

+ Designates management contract, compensatory plan or arrangement.
† Portions redacted pursuant to confidential treatment applications.

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 13, 2015.

Inovio Pharmaceuticals, Inc.

By: /s/ J. JOSEPH KIM
J. Joseph Kim
President, Chief Executive Officer and Director

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 13, 2015
/s/ AVTAR DHILLON Avtar Dhillon	Chairman of the Board of Directors	March 13, 2015
/s/ PETER KIES Peter Kies	Chief Financial Officer (Principal Accounting Officer and Principal Financial Officer)	March 13, 2015
/s/ SIMON X. BENITO Simon X. Benito	Director	March 13, 2015
/s/ ANGEL CABRERA Angel Cabrera	Director	March 13, 2015
/s/ MORTON COLLINS Morton Collins	Director	March 13, 2015
/s/ ADEL MAHMOUD Adel Mahmoud	Director	March 13, 2015
/s/ NANCY J. WYSENSKI Nancy J. Wysenski	Director	March 13, 2015

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INOVIO PHARMACEUTICALS, INC.
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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited the accompanying consolidated balance sheets of Inovio Pharmaceuticals, Inc. as of December 31, 2014 and 2013, and 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, 2014. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Inovio Pharmaceuticals, Inc. at December 31, 2014 and 2013, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2014, 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), Inovio Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2014, 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 13, 2015 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California
March 13, 2015

Inovio Pharmaceuticals, Inc.
CONSOLIDATED BALANCE SHEETS

	December 31, 2014	2013
ASSETS		
Current assets:		
Cash and cash equivalents	$40,543,982	$33,719,796
Short-term investments	53,075,974	18,905,608
Accounts receivable	2,804,207	3,301,563
Prepaid expenses and other current assets	797,973	637,433
Prepaid expenses from affiliated entity	1,382,375	2,057,350
Deferred tax asset	342,573	61,839
Total current assets	98,947,084	58,683,589
Restricted cash	—	100,762
Fixed assets, net	4,583,204	2,886,545
Investment in affiliated entity	12,340,811	9,664,587
Intangible assets, net	4,776,059	5,718,778
Goodwill	10,113,371	10,113,371
Common stock warrants	550,000	717,500
Other assets	474,568	402,075
Total assets	$131,785,097	$88,287,207
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued expenses	$6,383,170	$5,444,508
Accounts payable and accrued expenses due to affiliated entity	28,407	522,255
Accrued clinical trial expenses	2,007,432	1,446,180
Common stock warrants	2,022,729	19,540,583
Deferred revenue	3,187,223	1,624,388
Deferred revenue from affiliated entity	394,791	388,542
Total current liabilities	14,023,752	28,966,456
Deferred revenue, net of current portion	173,779	1,997,333
Deferred revenue from affiliated entity, net of current portion	836,694	1,211,694
Deferred rent	4,709,229	3,013,263
Deferred tax liabilities	504,049	195,778
Total liabilities	20,247,503	35,384,524
Commitments and contingencies		
Inovio Pharmaceuticals, Inc. stockholders' equity:		
Preferred stock—par value $0.001; Authorized shares: 10,000,000, issued and outstanding shares: 23 at December 31, 2014 and 26 at December 31, 2013	—	—
Common stock—par value $0.001; Authorized shares: 600,000,000 at December 31, 2014 and December 31, 2013, issued and outstanding: 60,741,082 at December 31, 2014 and 52,576,390 at December 31, 2013	60,741	52,577
Additional paid-in capital	443,327,915	348,267,389
Accumulated deficit	(331,910,290)	(295,788,577)
Accumulated other comprehensive loss	(251,390)	(76,365)
Total Inovio Pharmaceuticals, Inc. stockholders' equity	111,226,976	52,455,024
Non-controlling interest	310,618	447,659
Total stockholders' equity	111,537,594	52,902,683
Total liabilities and stockholders' equity	$131,785,097	$88,287,207

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,		
	2014	2013	2012
Revenues:			
Revenue under collaborative research and development arrangements	$7,416,568	$9,239,547	$82,536
Revenue under collaborative research and development arrangements with affiliated entity	479,464	425,000	577,467
Grants and miscellaneous revenue	2,560,734	3,802,799	3,458,649
Total revenues	10,456,766	13,467,346	4,118,652
Operating expenses:			
Research and development	34,095,039	21,368,604	17,984,825
General and administrative	15,857,688	13,643,074	10,778,359
Gain on sale of assets	—	(2,000,000)	(1,151,000)
Total operating expenses	49,952,727	33,011,678	27,612,184
Loss from operations	(39,495,961)	(19,544,332)	(23,493,532)
Other income (expense):			
Interest and other income, net	331,461	132,214	166,113
Change in fair value of common stock warrants	348,143	(45,632,669)	1,982,620
Gain (Loss) on investment in affiliated entity	2,676,224	(1,038,745)	1,631,819
Net loss	(36,140,133)	(66,083,532)	(19,712,980)
Net loss attributable to non-controlling interest	18,420	55,084	44,025
Net loss attributable to Inovio Pharmaceuticals, Inc.	$(36,121,713)	$(66,028,448)	$(19,668,955)
Net loss per common share attributable to Inovio Pharmaceuticals, Inc. stockholders			
Basic	$(0.61)	$(1.43)	$(0.58)
Diluted	$(0.64)	$(1.43)	$(0.58)
Weighted average number of common shares outstanding used in per share calculations:			
Basic	59,127,349	46,087,773	34,127,312
Diluted	59,408,252	46,087,773	34,127,312

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,		
	2014	2013	2012
Net loss	$(36,140,133)	$(66,083,532)	$(19,712,980)
Other comprehensive income (loss):			
Foreign currency translation adjustments	(1,689)	118	1,984
Unrealized (loss) gain on short-term investments	(173,336)	(149,845)	35,985
Comprehensive loss	$(36,315,158)	$(66,233,259)	$(19,675,011)
Comprehensive loss attributable to non-controlling interest	18,420	55,084	44,025
Comprehensive loss attributable to Inovio Pharmaceuticals, Inc.	$(36,296,738)	$(66,178,175)	$(19,630,986)

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	Number of shares	Amount					
Balance at December 31, 2011	26	33,742,282	$33,743	$257,336,932	$(210,091,174)	$ 35,393	$546,768	$47,861,662
Issuance of common stock for cash, net of financing costs of $164,695	—	2,336,153	2,336	5,322,805	—	—	—	5,325,141
Stock-based compensation	—	—	—	1,345,613	—	—	—	1,345,613
Net loss attributable to common stockholders	—	—	—	—	(19,668,955)	—	(44,025)	(19,712,980)
Unrealized gain on short-term investments	—	—	—	—	—	35,985	—	35,985
Foreign currency translation adjustments	—	—	—	—	—	1,984	—	1,984
Balance at December 31, 2012	26	36,078,435	$36,079	$264,005,350	$(229,760,129)	$ 73,362	$502,743	$34,857,405
Issuance of common stock and warrants for cash, net of financing costs of $783,000	—	6,844,317	6,844	14,267,975	—	—	—	14,274,819
Fair value of common stock warrants issued in connection with equity financing	—	—	—	(5,968,244)	—	—	—	(5,968,244)
Issuance of common stock for cash, net of financing costs of $585,000	—	3,925,167	3,925	18,920,931	—	—	—	18,924,856
Exercise of stock options and warrants for cash	—	5,712,439	5,713	19,802,519	—	—	—	19,808,232

Cashless exercise of warrants	—	16,032	16	(16)	—	—	—	—
Change in classification of warrants from liability to equity due to exercise	—	——	—	35,370,529	—	—	—	35,370,529
Stock-based compensation	—	——	—	1,868,345	—	—	—	1,868,345
Net loss attributable to common stockholders	—	——	—	—	(66,028,448)	—	(55,084)	(66,083,532)
Unrealized loss on short-term investments	—	——	—	—	—	(149,845)	—	(149,845)
Foreign currency translation adjustments	—	——	—	—	—	118	—	118
Balance at December 31, 2013	26	—52,576,390	$52,577	$348,267,389	$(295,788,577)	$(76,365)	$447,659	$52,902,683
Issuance of shares related to reverse stock split	—	—6,378	6	57,181	—	—	—	57,187
Issuance of common stock for cash, net of financing costs of $4.0 million	—	—5,452,725	5,453	59,203,729	—	—	—	59,209,182
Conversions of preferred stock to common stock	(3)	—1,103	1	(1)	—	—	—	—
Acquisition of non-controlling interest	—	——	—	118,621	—	—	(118,621)	—
Exercise of stock options and warrants for cash	—	—2,689,868	2,689	13,249,854	—	—	—	13,252,543
Cashless exercise of warrants	—	—14,618	15	(15)	—	—	—	—
Change in classification of warrants from liability to equity due to exercise	—	——	—	17,002,211	—	—	—	17,002,211
Stock-based compensation	—	——	—	5,428,946	—	—	—	5,428,946

Net loss attributable to common stockholders	—	____