INOVIO PHARMACEUTICALS, INC.
Form 10-K
March 18, 2013
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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, 2012

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.)
1787 SENTRY PARKWAY WEST BUILDING 18, SUITE 400 BLUE BELL, PENNSYLVANIA	19422
(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	NYSE MKT
(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, 2012 was approximately $56,096,682 based on $0.46, 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 179,921,237 as of March 8, 2013.

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 2012 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, 2012.

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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.

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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 engaged in the discovery and development of a new generation of vaccines and immune therapies, called synthetic vaccines, focused on cancers and infectious diseases. Our DNA-based SynCon® technology is designed to provide universal protection against known as well as new unmatched strains of pathogens such as influenza. These synthetic vaccines, in combination with our proprietary electroporation delivery, have been shown in humans to generate best-in-class immune responses with a favorable safety profile. Our preclinical development and clinical programs include cervical dysplasia/cancer (therapeutic), influenza (preventive), prostate cancer (therapeutic), leukemia (therapeutic), hepatitis C virus, hepatitis B virus, HIV, and malaria vaccines. Our partners and collaborators include University of Pennsylvania, Drexel University, National Microbiology Laboratory of the Public Health Agency of Canada, Program for Appropriate Technology in Health/Malaria Vaccine Initiative ("PATH" or "MVI"), National Institute of Allergy and Infectious Diseases ("NIAID"), Merck, ChronTech, University of Southampton, United States Military HIV Research Program ("USMHRP"), U.S. Army Medical Research Institute of Infectious Diseases ("USAMRIID"), HIV Vaccines Trial Network ("HVTN") and Department of Homeland Security ("DHS").

Industry Background

Historical Importance of Vaccines

We believe vaccines have 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. Our society has found that the only way to control or even eliminate infectious diseases is consistent, widespread use of vaccines.

Challenges Facing Vaccines

Despite the advances made to quality of life as a result of the development and use of vaccines over the past century, several significant challenges continue to exist. The technical limitations of conventional vaccine technology have constrained the development of new vaccines for other diseases. Development of vaccines based on conventional technology requires significant infrastructure in research and manufacturing, and can be time consuming. Safety risks associated with conventional vaccine approaches may offset their potential benefits, as the conventional vaccines we have depended upon employ either weakened or killed viruses or different parts of a virus as vaccines. Further,

conventional vaccines are still grown in eggs or cells and harvested over periods of weeks with very inefficient manufacturing processes.

In addition, it is important to note a changing dynamic in the broader vaccine marketplace. Traditionally, vaccines have been predominantly focused on the pediatric market, intended to protect children from diseases that could cause them serious harm or death. Today, there is a growing interest in vaccines against diseases that may affect adolescents and adults, which include both sexually transmitted diseases and infections that strike opportunistically, such as during pregnancy, in immuno-

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compromised individuals, and in the geriatric population. Furthermore, there is encouraging data from and ongoing development of immunotherapies against cancers.

Inovio's Solution

With our synthetic vaccine platform comprising our SynCon® vaccine design process and proprietary electroporation delivery technology, we have developed a preclinical and clinical stage pipeline of vaccines that we believe has the potential to be safer than traditional vaccines (our synthetic vaccines are non-live and non-replicating therefore they cannot cause the disease), have equivalent or stronger immune-stimulating power than traditional vaccines (live viruses being the best at eliciting strong immune responses), are showing the potential to be used against diseases for which conventional vaccine technology cannot be applied, and have added advantages with respect to development time and cost. Preclinical studies in animals and initial human clinical study data have demonstrated a favorable safety profile and best-in-class immune responses that suggest the potential efficacy of our approach.

The Next Generation of Vaccines: Synthetic Vaccines

Our synthetic vaccines are designed to prevent a disease (prophylactic vaccines) or treat an existing disease (therapeutic vaccines). Our synthetic vaccine consists of a DNA plasmid encoding a selected antigen(s) that is introduced into cells of humans or animals with the purpose of having those cells produce the antigen encoded by the DNA instructions and consequently inducing an immune response to the antigen. Production by these cells of the targeted antigenic protein(s) may trigger one or both of two immune responses: the production of antibodies, known as a humoral immune response, and/or the activation of T-cells, known as a cellular or cell-mediated immune response. These responses may then neutralize or eliminate infectious agents (e.g. viruses, bacteria, and other microorganisms) or abnormal cells (e.g. malignant tumor cells). Synthetic vaccines have several advantages over traditional vaccines in that they are non-pathogenic (meaning they cannot cause the disease), may be effective against diseases which cannot be controlled by traditional vaccines, and are relatively fast, easy and inexpensive to design and produce. Synthetic vaccines are stable under normal environmental conditions for extended periods of time. Another potentially major advantage of synthetic vaccines is their relatively short development cycle. For example, synthetic vaccines against newly identified viral agents may be developed within weeks or months, as opposed to the years often required to develop a traditional vaccine candidate. In the area of cancer, synthetic vaccines use a portion of the genetic code of a cancer antigen to cause a host to produce proteins of the antigen that may induce an immune response.

Inovio's SynCon® Vaccines

Our synthetic vaccines are designed to generate specific antibody and/or T-cell responses. Our SynCon® technology provides processes that employ bioinformatics, which combine extensive genetic data and sophisticated algorithms. Our design process is based on the genetic make-up of a common antigen(s) from multiple strains of a virus within a viral sub-type or taxonomic group (family) of pathogens such as HIV, HCV, human papillomavirus ("HPV"), influenza and other diseases. We synthetically create a new antigen that represents a consensus of the DNA make-up of these multiple strains of the desired pathogen target. This synthetic consensus DNA sequence does not exist in nature (and is consequently patentable). This unmatched antigen has been shown to nevertheless induce a powerful immune response in humans against that antigen, providing protection not only against multiple existing strains of the same sub-type that were used to develop this synthetic antigen but to also provide protection against newly emergent strains not used in designing the vaccine. Thus, the SynCon® technology allows us to develop universal vaccines against target pathogens. These SynCon® synthetic vaccine constructs may provide a solution to the genetic "shift" and "drift" that is typical of infectious diseases. SynCon® immunogens are able to elicit broad, diverse immune responses, which in theory are important to protect against variable pathogens such as influenza, dengue, HCV and HIV.

Technically speaking, SynCon® vaccine antigens are designed by aligning numerous primary sequences and choosing DNA-based triplets for the most common or important amino acid at each site. These antigens are further optimized for codon usage, improved mRNA stability, and enhanced leader sequences for ribosome loading. The DNA inserts are therefore optimized at the genetic level to give them high expression capability 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 synthetic vaccine to induce the desired immune response.

Preclinical studies have shown that immunization of mice and non-human primates using SynCon® synthetic vaccine constructs elicited an immune response against multiple, unmatched strains within specific sub-types of HIV, HCV, HPV, dengue, prostate cancer and influenza viruses. Vaccine candidates for all these diseases are being advanced through preclinical and clinical studies. Inovio has reported that its SynCon® vaccine for H5N1 influenza generated HAI titers against six unmatched strains of H5N1 (May 2012) and nine unmatched strains of H1N1 (September 2012).

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Electroporation Delivery Technology

Our synthetic vaccine candidates are being delivered into cells of the body 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. Most drugs and biologics must enter into a cell through a cell membrane in order to perform their intended function. However, gaining entry into a cell through the outer cell membrane can be a significant challenge. Electric pulse-induced permeabilization of the cellular membrane, generally referred to as electroporation, has the observable effect that there is a less restricted exchange of molecules between the cell exterior and interior—the benefit being that it allows and enhances the uptake of, for example, a biopharmaceutical agent previously injected into local tissue. The extent of membrane permeabilization depends upon various electrical, physical, chemical, and biological parameters.

The transient, reversible nature of this electrical permeabilization of membranes is the underlying basis of our electroporation systems, which are designed to harness this phenomenon by delivering controlled electrical pulses into tissue to facilitate the uptake of useful biopharmaceuticals. 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 themselves (believed to compromise their ability to provide protection). We believe electroporation provides a relatively straightforward, cost effective method for delivering DNA into cells with high efficiency and minimal complications (as compared to viral vectors) and, importantly, enabling clinically relevant levels of gene expression.

Products and Product Development

Independently and together with our licensees and collaborators, we are currently developing a number of synthetic vaccines for the prevention or treatment of cancer and chronic infectious diseases. The table below summarizes progress in our proprietary and collaborative product development programs as of December 31, 2012.

Inovio Synthetic Vaccine Development

		Development Status				
Product Area	Product Target and Indication(s)	Pre-Clinical	Phase I	Phase II	Phase III	Partner/Funding/Sponsor
Cancer	Prostate cancer (INO-5150)	X	P			Inovio
	Chronic and acute myeloid leukemia (CML/AML)	X	X	IP		Univ. of Southampton/LLR and CRUK
	Cervical dysplasia (CIN 2/3) (VGX-3100)	X	X	IP		Inovio
	hTERT expressing cancers	IP				Inovio
Infectious Disease	Avian influenza (VGX-3400x)	X	X			Inovio
	Universal influenza (INO-3510)	X	IP			NIH
	HCV	X	X	IP		ChronTech
	HCV	X	P			VGX International
	HBV	IP				Inovio
	HIV (preventive) (PENNVAX®-B)	X	X			NIH
	HIV (therapeutic) (PENNVAX®-B)	X	X			UPENN
	HIV (preventive) (PENNVAX®-G)	X	IP			US MHRP/NIH/NIAID
	HIV (preventive)	X	P			NIH/NIAID

(PENNVAX®-GP)			
Malaria	IP	P	PATH MVI
Biodefense targets	IP		USAMRIID

X = Completed
IP = In Progress
P = Planning

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Cancer Synthetic Vaccines

Cancer vaccines are medicines that belong to a class of substances known as biological response modifiers. Biological response modifiers work by stimulating or restoring the immune system's ability to fight infections and disease. There are two broad types of cancer vaccines:

- Preventive (or prophylactic) vaccines, which are intended to prevent cancer from developing in healthy people; and
- Treatment (or therapeutic) vaccines, which are intended to treat an existing cancer by strengthening the body's natural defenses against the cancer.

Two types of cancer preventive vaccines are available in the United States, and one cancer treatment vaccine has recently become available. The United States Food and Drug Administration (the "FDA") has approved two vaccines, Gardasil® and Cervarix® that protect against infection by the two types of HPV—types 16 and 18—that cause approximately 70 percent of all cases of cervical cancer worldwide. At least 17 other types of HPV are responsible for the remaining 30 percent of cervical cancer cases. HPV types 16 and/or 18 also cause some vaginal, vulvar, anal, penile, and oropharyngeal cancers.

In addition, Gardasil® protects against infection by two additional HPV types, 6 and 11, which are responsible for about 90 percent of all cases of genital warts in males and females but do not cause cervical cancer.

Cervarix®, manufactured by GlaxoSmithKline, is composed of virus-like particles (VLPs) made with proteins from HPV types 16 and 18. Cervarix® is approved for use in females ages 10 to 25 for the prevention of cervical cancer caused by HPV types 16 and 18.

Gardasil®, manufactured by Merck, is approved for use in females for the prevention of cervical cancer, and some vulvar and vaginal cancers, caused by HPV types 16 and 18 and for use in males and females for the prevention of genital warts caused by HPV types 6 and 11. The vaccine is approved for these uses in females and males ages 9 to 26.

The FDA has also approved a cancer preventive vaccine that protects against hepatitis B virus (HBV) infection. Chronic HBV infection can lead to liver cancer. The original HBV vaccine was approved in 1981, making it the first cancer preventive vaccine to be successfully developed and marketed. Today, most children in the United States are vaccinated against HBV shortly after birth.

In April 2010, the FDA approved the first cancer treatment vaccine. This vaccine, sipuleucel-T (Provenge®, manufactured by United States based Dendreon), is approved for use in some men with metastatic prostate cancer. It is designed to stimulate an immune response to prostatic acid phosphatase (PAP), an antigen present on most prostate cancers. In a clinical trial, sipuleucel-T increased the survival of men with a certain type of metastatic prostate cancer by about 4 months. Thanks to the success of Provenge®, the development of immune cell-based cancer treatments is expected to gain momentum.

Cervical Dysplasia/Cancer Therapeutic Vaccine-VGX-3100

HPV is the causative agent responsible for cervical cancer. At any given time, approximately 10% of women worldwide are infected with HPV. While roughly 70% of HPV infections are cleared by the body on its own, persistent HPV can lead to dysplasia, or premalignant changes in cells, of the cervix. Researchers have estimated the global prevalence of clinically pre-cancerous HPV infections at between 28 and 40 million. These HPV infections may lead to pre-malignant cervical dysplasia; persistent dysplasia may then progress to cancer. Every year, 510,000 cases of cervical cancer are diagnosed worldwide, and about half of the afflicted women, primarily in developing countries, die.

Preventive vaccines such as Gardasil® and Cervarix® are playing an important role in limiting new HPV infections. However, preventive vaccines cannot provide protection for 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. There is no viable therapeutic vaccine or drug to fight HPV, nor dysplasias and cancers caused by HPV. Current ablative or surgical procedures to remove cervical dysplasias and cancers are unappealing due to the potential psychological stress arising from the "watch-and-wait" period that precedes earlier dysplasia and the potential for disfigurement and negative impacts on childbirth.

In contrast to Gardasil® and Cervarix®, Inovio's VGX-3100 is a therapeutic vaccine, designed to raise immune responses against the E6 and E7 genes 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 cancerous cells. The goal of the vaccine is to stimulate the body's immune system to mount a T-cell response strong enough to cause the rejection of the E6/E7 infected or transformed cells from the body. The potential of such a vaccine would be to treat cervical cancers as well as pre-cancerous dysplasias, caused by these HPV types.

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We completed the Phase I study of our therapeutic cervical cancer vaccine (VGX-3100) in 2010. 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 includes:

- 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 vaccine-related serious adverse events (SAEs). Reported adverse events and injection site reactions were mild to moderate and required no treatment.

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 may lead to cervical cancer. The trial enrolled patients in three cohorts of six subjects each with synthetic vaccine 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 day 0, month 1 and month 3. 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 vaccine. 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 vaccinated 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 vaccinated 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 6 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.

While the phase I study targeted only safety and immunogenicity as endpoints and did not address clinical efficacy, several literature reports support the hypothesis that induction of tumor antigen specific T-cell responses is important in controlling cancer. Furthermore, there are examples of other cancer vaccine candidates targeting the E6 and/or E7 proteins achieving significant clinical efficacy in patients with cervical or vulvar intraepithelial neoplasia, yet the CTL responses achieved in such studies were lower than those observed in the current VGX-3100 study.

Furthermore, 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." This desirable effect may ultimately contribute to the regression or elimination of cervical dysplasia and cervical cancer. Furthermore, 91% of patients who developed T-cell responses showed the presence of CD8+ T-cells capable of this type of killing activity. Direct killing by CTLs was observed in all vaccinated 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 of a vaccine, i.e. the ability of a vaccine to induce an immune response. Antibodies were generated against all four antigens, as tested by the enzyme-linked immunosorbent assay (ELISA). In the 6 mg cohort, antibody responses were observed in five of six subjects (83%). Overall, 100% of the study participants (18 of 18) reported antibody positivity to at least two vaccine antigens, 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, cervical intraepithelial neoplasia (CIN) 2/3. The women in the study will receive either 6 mg of VGX-3100 or a placebo using the CELLECTRA® in vivo electroporation device at months 0, 1, and 3. In addition to safety, the study will also assess proof of concept efficacy by measuring regression of cervical lesions in the treated versus control subjects. Immunological responses will also be measured in this clinical study (ClinicalTrials.gov NCT01304524).

Prostate Cancer Therapeutic Vaccine-INO-5150

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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 218,000 new cases of prostate cancer and more than 32,000 deaths in 2010.

We previously collaborated with the UK's University of Southampton and Institute of Cancer Research in a study evaluating a DNA-based vaccine for prostate cancer delivered using our electroporation delivery technology. The published data (Low et al, Human Gene Therapy; Chudley et al, Cancer Immunology and Immunotherapy) from this Phase I/II study of a DNA-based vaccine encoding for human PSMA epitopes generated both antibody and T-cell immune responses in the 30 patients vaccinated in this study.

In January 2011, we announced the publication of a scientific paper in the journal Human Vaccines detailing potent immune responses in a preclinical study of our SynCon® vaccine 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 therapeutic vaccine.

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® vaccine evaluated in this study was generated by the creation of PSA and PSMA synthetic consensus immunogens based on human and macaque sequences, which enabled the amino acid sequences of the antigens to differ slightly from the native protein. In humans, this difference may help avoid self-tolerance and enable the generation of an anti-tumor immune response. Mice received two immunizations of highly optimized vaccine delivered by electroporation. Immunogenicity was evaluated one week after the second vaccination. 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 this pre-clinical study of the first SynCon® vaccine against a cancer target, this dual-antigen immunotherapy generated strong antibody and T-cell immune responses. Taken together with the previous preclinical and clinical data, the current published results support the advancement of this product into a Phase I clinical study. We are now advancing this program toward Phase I.

Leukemia Therapeutic Vaccine

Leukemia is a malignant disease (cancer) of the bone marrow and blood characterized by the uncontrolled accumulation of blood cells. Leukemia accounts for at least 300,000 new cases and 222,000 deaths worldwide each year. This high ratio of deaths-to-cases (74%) reflects the poor prognosis of leukemia in many parts of the world, where the somewhat complex treatment regimens are not available. Approximately 45,000 new cases of leukemia were diagnosed in 2008 in the US, with 20,000 deaths. This represents 3% of all cancers in the United States, and 30.4% of all blood cancers. It is estimated that approximately $3 billion is spent in the United States each year to treat leukemia.

There are five types of leukemia based on rate of development and types of blood cells affected. Two of these are being evaluated in the present study: 1) Acute myeloid leukemia (AML), a cancer of the myeloid line of blood cells, is characterized by rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with the production of normal blood cells. AML is the most common acute leukemia affecting adults and its incidence increases with age. Only about one-third of those between ages 18-60 who are diagnosed with AML can be cured. With conventional chemotherapy 70% of the patients in the group under study will relapse within 2 years and current therapy is devastating in older adults.

Chronic myeloid leukemia (CML) is a type of cancer that causes the body to produce large numbers of immature and mature white blood cells (myelocytes). Approximately 85% of patients with CML are in the chronic phase at the time of diagnosis. Ultimately, in the absence of curative treatment, the disease progresses to an accelerated phase where median survival is around 3-5 years. Chronic myeloid leukemia can occur at any age, but it more commonly affects middle-aged and older people.

In January 2011, we announced the regulatory approval of a Phase II clinical trial (WIN Trial) to treat leukemia utilizing our ELGEN 1000 electroporation delivery device. This open-label, multi-center clinical trial being run by the University of Southampton is evaluating a DNA vaccine to treat chronic myeloid leukemia and acute myeloid leukemia. Financial support for the trial is being provided by the UK research charity Leukaemia and Lymphoma Research (LLR) and by the Efficacy and Mechanisms Evaluation (EME) programme (which is funded by the UK Medical Research Council and managed by the UK National Institute for Health Research). The DNA vaccine was developed at the University of Southampton with funding from LLR and the charity Cancer Research UK.
Wilms' Tumor gene 1 (WT1) is highly associated with these types of cancer, which led the University of Southampton to design its leukemia therapeutic vaccine to target this antigen. Preclinical data from mice showed strong induction of

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antigen-specific CD8+ T cells and the ability to kill human tumor cells expressing WT1. There have been several prior clinical studies in humans using parts of the WT1 gene, notably as peptide vaccine candidates, demonstrating the production of modest levels of CD8+ T-cell responses and measurable clinical responses, although both effects were transient. This is the first study to combine DNA vaccination with WT1 antigens using electroporation delivery with the goal of stimulating high and durable levels of immune responses, which are considered critical for improving clinical outcomes.

The single dose level, Phase II study, called “WT1 immunity via DNA fusion gene vaccination in haematological malignancies by intramuscular injection followed by intramuscular electroporation,” led by Professor Ottensmeier of the University of Southhampton and Dr. Katy Rezvani of MD Anderson Cancer Center, Houston, TX, is designed to recruit two patient groups. One group is planned to recruit up to 37 CML patients and the other up to 37 AML patients. All participants receive six doses of two DNA vaccines (called p.DOM-WT1-37 and p.DOM-WT1-126) delivered at four week intervals. Vaccine responders may continue with booster vaccinations every three months out to 24 months. An additional 100-110 AML/CML patients will be enrolled across the two arms as non-vaccinated controls for comparison. The primary endpoints will be molecular response to a disease marker called BCR-ABL in CML patients and time to disease progression in AML patients. The study also monitors WT1 transcript levels, immune responses to the WT1 antigen, time to progression and overall survival, and two-year survival in the AML group. The trial is under way at hospitals in Southampton, London and Exeter. Regulatory approval to start this clinical study was provided by the UK Medicines and Healthcare Products Regulatory Authority (MHRA) and Gene Technology Advisory Committee (GTAC).

In December, 2012, we reported preliminary results of this Phase II clinical trial. Fourteen CML patients had been enrolled while another 13 unvaccinated CML patients were enrolled to serve as a control group. These interim results from eight patients showed robust vaccine-specific antibody responses in all vaccinated subjects evaluated to date. Furthermore, T cell immune responses, including those of the "killer T cells," were detected. Antibody and T cell responses are strong signals of the DNA vaccine's potential to treat the disease. The vaccine has been shown to be safe overall and well-tolerated in the trial subjects.

As a result of the favorable safety and immunogenicity profiles observed in the CML vaccinated group, the trial is now open to enroll the acute myeloid leukemia (AML) clinical trial arm.

Merck Collaboration: Cancer Vaccines

In May 2004, we announced a collaboration and license allowing Merck to use Inovio's earlier generation proprietary electroporation delivery technology in conjunction with certain DNA vaccines developed by Merck. Merck completed Phase I clinical studies for two DNA vaccines but has not reported results from these clinical studies. As part of this license agreement, Merck paid Inovio milestone payments and funded all clinical development costs. Further development of products by Merck under the collaboration and license agreement may lead to additional milestone payments and royalties payable to Inovio.

Infectious Disease Synthetic Vaccines

Hepatitis C Virus Therapeutic Vaccine

Hepatitis is a disease characterized by inflammation of the liver. HCV 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 70% - 90% of newly infected patients may progress to develop chronic infection. Of those with chronic liver disease, 5% - 20% may develop cirrhosis. About 5% of infected people may die from the consequences of long term infection (due to liver cancer or cirrhosis). Globally, an estimated 170 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 4.1 million (1.6%) Americans have been infected with HCV, of whom 3.2 million 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.

In January 2006, we signed an agreement with Sweden-based ChronTech (formerly called Tripep) to co-develop a therapeutic vaccine for HCV using electroporation. The vaccine is based on ChronTech's proprietary HCV antigen

construct and delivered to infected individuals using our MedPulser® DNA Delivery System.

In November 2009, we announced the completion of the Phase I clinical study with ChronTech of the ChronVac-C HCV DNA vaccine delivered using our electroporation technology. The study established the safety and tolerability of this therapy, with vaccine-induced immune responses and transient effects on the serum levels of HCV in these chronically infected patients providing proof-of-concept of DNA vaccines delivered using electroporation.

Post-study observation of subjects who completed the protocol and then entered into standard of care (SOC) treatment using interferon and ribavirin showed a complete and rapid viral response (four weeks) in 70% of those participants (5 of 7

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patients). Significantly, 83% of the participants (5 of 6 patients) who were monitored for an extended period of time continued to be free of the virus six months after they completed SOC. SOC treatment alone usually results in about 40-50% of patients reaching undetectable virus levels after six months of treatment.

In March 2011, we announced the initiation of a follow-on open label, single dose Phase II clinical study in collaboration with ChronTech of the ChronVac-C HCV DNA vaccine delivered using our electroporation technology in treatment naïve HCV infected individuals. In this study we are looking at the effect of treating patients with the HCV vaccine followed by standard of care versus a control group of HCV infected adults who only receive the standard of care. The therapy is being given two times, with four weeks in between, followed by combination drug (ribavirin and IFN-a) treatment after the final vaccine dose in treatment-naïve chronic HCV infected genotype-1a subjects (the target antigen is NS3/4a). This trial will assess the level of immune responses, levels of HCV viral load, and further assess the response to the delivery technology. The study will enroll a total of 32 subjects (20 receiving vaccine + drugs and 12 controls receiving drugs only). The vaccines and controls will be further separated by their IL-28 genotype status which has been recently shown to yield different response rates to standard of care therapy for HCV.

Additionally, 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 to advance our proprietary synthetic vaccine to treat HCV using our 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 vaccines designed to treat persons who are chronically infected with HCV and have not responded to currently available therapies.

Subsequent to year end we announced positive preclinical results from this proprietary HCV vaccine, which were published in Molecular Therapy. This synthetic multi-antigen DNA vaccine 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-ã (IFN-ã) induction, robust CD4 and CD8 T cell proliferation, and induction of polyfunctional T cells.

Under a 2011 development agreement, VGX International will fully fund IND-enabling, phase I, and phase II studies for this vaccine. The companies intend to initiate a phase I/IIa clinical study in the second half of 2013.

HIV Preventive and Therapeutic Vaccines

Since its discovery in 1981, AIDS has killed more than 25 million people. In 2005, the total number of HIV-infected people worldwide reached an estimated 38.6 million, with 4.1 million newly infected individuals. In 2005, the disease claimed approximately 3.1 million lives. UNAIDS estimates that 60,000 individuals were newly infected with HIV across the United States and Western Europe in 2005; bringing the number of HIV-infected people to approximately 1.75 million. Over half of these individuals live in the United States.

In 2005, the HIV market accounted for 1.8% of global pharmaceutical sales and 17% of total anti-infective sales. Although this is relatively small compared to other therapeutic areas, the HIV market has experienced strong growth. It generated $7.4 billion of sales in 2005 and experienced a compound annual growth rate of 13.3% from 2001-2005, making it one of the fastest growing infectious disease markets. In 2011, the global HIV market reported over $13 billion in sales, up from around $7.4 billion in 2005. Overall, while the growth rates are slowing down with better control of mother-to-child transmission and newer pre-exposure prophylaxes, the market is still forecasted to have a compound annual growth rate of 3.6% through 2017 and global sales for 2021 are estimated at $16.5 billion.

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 are necessary to stop the spread of disease and perhaps reduce the need for anti-retroviral treatment.

After many years of rapid development and introduction of new anti-retroviral drugs for treatment of HIV infection, the introduction of new drugs to the market for treatment of HIV infection appears to be waning. Available drugs, despite several limitations, have set a high standard that must be met in terms of efficacy. However, there is still a significant need for better HIV therapies and patents are beginning to expire on early HIV drugs. For example, zidovudine and other early antiretrovirals are already available as generic drugs. To maintain HIV-related revenue, as well as meet the needs of HIV-infected patients, pharmaceutical companies must develop new drugs with improved profiles, especially in terms of toxicity and more barriers to development of viral resistance. As a result, the medical and commercial needs are fueling continued interest in the development of new nucleosides (NRTIs), non-NRTIs, and protease inhibitors (PI) for treatment of HIV infection.

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Noting that many long-term survivors have high counts of killer CD8+ T cells, the HIV vaccine 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 altered to prevent viral replication. These vaccines have proven to not be effective. We believe a different approach is needed to develop an effective vaccine for HIV. 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 a vaccine may be able to combat spread of HIV and has spurred the development of newer vaccine candidates.

Our HIV vaccines consist of candidates for HIV prevention as well as therapy or treatment. Furthermore, our vaccines are differentiated according to the HIV subtypes prevalent in targeted region of the world. PENNVAX®-B is designed to target HIV clade B (most commonly found in the United States, North America, Australia and the European Union (EU). PENNVAX®-G is designed to target HIV clades A, C and D, which are more commonly found in Asia, Africa, Russia and South America. PENNVAX®-GP is based on optimized synthetic immunogens targeting the env, gag and pol antigens of HIV-1 global subtypes A and C.

In October 2009, along with the HVTN, we initiated a Phase I study (HVTN-080) of PENNVAX®-B (with and without a cytokine) delivered with electroporation using the CELLECTRA® delivery device in healthy, uninfected individuals. 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 vaccine, 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 vaccine in a majority of subjects. Overall, either CD4+ or CD8+ or both T-cell responses were observed against at least one of the vaccine antigens in 83.3% (30 of 36) of evaluated subjects after three vaccinations using electroporation. The response rate increased to 88.9% (24 of 27) of evaluated subjects after three vaccinations 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 vaccine in 80.8% of evaluated vaccine recipients (21 of 26).
- Significantly strong antigen-specific, CD8+ T-cell responses were also generated by the vaccine in 51.9% of evaluated vaccine 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 vaccinations, but without electroporation delivery, response rates in HVTN 080 with electroporation were significantly higher for both CD4+ responses (40.7%) ll responses out 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.
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PENNVAX®-B delivered using the CELLECTRA® intramuscular electroporation delivery device with or without IL-12 was safe and generally well tolerated. There were no vaccine-related serious adverse events. Reported adverse events and injection site reactions were mild to moderate and required no treatment.

A second clinical study testing PENNVAX®-B in a therapeutic setting, conducted in collaboration with the University of Pennsylvania, started in 2011. 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 vaccine delivered with its 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

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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.

In March 2012 we reported that there were no significant adverse events or vaccine related grade 3 or 4 adverse events noted in the study and the vaccine was found to be generally well tolerated. Reported injection site reactions were mild to moderate and did not require treatment to resolve.

T-cell responses were measured using a validated ELISpot assay at the U Penn Immunology Core Facility. Overall, significant vaccine-specific T-cell responses were observed in 75% (9 out of 12) of subjects against at least one of the three vaccine antigens (gag. pol, or env) following vaccination. Fifty percent of the subjects (6 out of 12) had strong vaccine induced antigen-specific responses above the pre-vaccination levels to at least two of the antigens. Importantly, the responses induced by vaccination 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 a therapeutic vaccine. These results are in stark contrast to previously reported studies with other DNA vaccines delivered without electroporation that yielded poor overall T cell immune responses.

We believe these positive interim results, which showed that a DNA vaccine was able to generate robust T cell immune responses in people chronically infected with HIV, demonstrate the potency of our synthetic vaccine technology platform and raise the potential for the development of therapeutic vaccines against HIV.

The valuable proof of concept data achieved with the PENNVAX®-B clinical studies has provided a strong and positive basis with which to advance our HIV vaccine 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 vaccines 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 synthetic vaccine, 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 of 80 subjects in three African countries (Kenya, Tanzania and Uganda).

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 preclinical optimization, immunogenicity and challenge studies in animal models, IND-enabling toxicology studies, cGMP (current good manufacturing practices) manufacturing of all components of the synthetic vaccine 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 will be conducted at the manufacturing facility of our affiliate, VGX International, Inc. (“VGX Int'l”).

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 vaccine candidate.

Avian Influenza (H5N1) Vaccine

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 lead to approximately 36,000 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

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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 620 people and resulted in 367 deaths (approximately 60% death rate) in 15 countries since 2003 (WHO, February 2013). 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.

Our VGX-3400X targets H5N1. The vaccine 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 universal flu vaccine 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 VGX International). 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 vaccine components. After cohort 3 samples were analyzed, 20 of 29 vaccinated subjects (69%) in all 3 cohorts developed strong CTL responses to at least one of the vaccine components. These positive T cell responses were measured up to seven months after the first vaccination. 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 vaccine 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® vaccines 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 vaccinations. Twenty-two participants received the ID booster vaccination.

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 vaccination was found to be generally safe and well tolerated.

HAI measurements from the blood of a vaccinated 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 vaccinated subjects generally associated with protection against influenza in humans.

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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 vaccinated subjects demonstrated high-titered 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 vaccine'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 vaccinated subjects (29%) displayed an HAI titer of 1:20 or higher against at least three different H5N1 viruses tested.
- In an unprecedented result, two vaccinated subjects demonstrated an HAI titer of 1:20 or higher against all six strains tested.

Hemagglutination inhibition (HAI) measurements from the blood of a vaccinated 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 vaccinated 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.

We are in the process of seeking additional grant funding to advance this program further.

Universal Influenza Vaccine

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 vaccine 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 vaccines able to provide broad protection against known as well as newly emerging, unknown seasonal and pandemic influenza strains.

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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 synthetic vaccines 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 vaccinated 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 vaccine elements that can target both pandemic (H5N1, H1N1) as well as seasonal influenza strains (H3N2, H1N1, influenza B).

Moreover, using our approach the vaccines 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 Inovio 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 synthetic 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 vaccine 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 synthetic vaccine's broad cross-reactive coverage, a significant percentage of subjects immunized with Inovio's SynCon® vaccine 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 vaccines generate an HAI titer of 1:40 or higher against the matched vaccine strain.

By design, Inovio's SynCon® universal flu vaccine is not matched to any single virus and was not matched to any of the strains tested in this study. The vaccine 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 is matched to the current H1N1 seasonal flu strain (A/California/07/09), those immunized with Inovio's vaccine 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.

This phase I study is ongoing, with additional results from a higher dose group expected in 2013. Inovio is also conducting optimization studies in animal models to further strengthen its H1N1 vaccine'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.

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In December 2012 we reported interim results of a phase I trial that showed that a single dose of our H1N1 universal SynCon® flu vaccine 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 is evaluating the ability of Inovio's SynCon® vaccine 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, 50 healthy elderly patients have been divided into three groups: one group of 20 subjects received a two-dose regimen of Inovio's H1N1 universal SynCon® flu vaccine 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® vaccine 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 are to assess the tolerability, safety, and immune responses of these different vaccination regimens. This first interim data reports on the last two arms in the influenza study. The phase I open label study is ongoing at the University of Manitoba in Winnipeg, Canada.

Serum samples from the vaccinated 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, vaccine-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. Vaccination with the H1N1 universal SynCon® flu vaccine 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.

Finally, on our path to develop a universal seasonal vaccine we are completing tests in animal models of our vaccine constructs for A/H3N2 and Type B influenza. Our goal is to develop vaccines 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 synthetic vaccines for influenza Type A H3N2 and Type B achieved protective antibody responses in immunized animals against multiple unmatched strains.

In the study of Inovio's SynCon® H3N2 vaccine, investigators immunized small animals (mice and guinea pigs) with a synthetic 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 vaccine 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 Inovio's SynCon® Type B vaccine, 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 vaccine 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.

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Malaria

Malaria continues to present a major healthcare challenge in the developing world and has been the focus of much attention by global public health agencies. It is a deadly disease that still kills more than 500,000 children under age 5 every year. Development of an effective vaccine against Plasmodium falciparum has been a challenge. The parasite undergoes several stages of development during its life cycle and presents different potential target antigens at each stage as it passes through its human and mosquito hosts.

Subsequent to year end, in January 2013 the PATH Malaria Vaccine Initiative (MVI) and Inovio announced a follow-on collaboration to advance malaria vaccine development and new vaccination delivery technologies. Researchers will test whether a novel vaccine approach that combines genetically engineered DNA with an electroporation delivery technology could induce an immune response in humans that protects against malaria parasite infection.

Our vaccine candidate targets the pre-erythrocytic stage of the parasite and focuses on induction of both humoral and cellular responses against multiple target antigens. This approach is intended to help prevent infection of liver cells and to further clear those cells that, despite the antibody response, become infected. By targeting the parasite during the first days after infection, this type of vaccine may prevent the onset of malaria symptoms and further inhibit spread of the disease.

This follow-on agreement for clinical development builds on a 2010 research and development collaboration between Inovio and MVI. Inovio researchers and their academic collaborators developed novel DNA plasmids targeting multiple malaria parasite antigens and conducted studies in rodents to demonstrate induction of broad immune responses. The success of these studies resulted in an expanded collaboration, in which further testing demonstrated potent T cell and antibody responses in other animal models.

The Phase 1/2a clinical trial, which will begin in 2014, will test Inovio's plasmid DNA and electroporation technology in approximately 30 individuals, as part of what is known as a challenge trial by controlled human malaria infection. Volunteers will be administered the DNA and then exposed to the malaria parasite through the bite of infected mosquitoes to see whether this approach prevents infection. If successful, this trial would provide valuable information that may further the development of a highly efficacious vaccine against malaria.

The clinical study will contain two study arms. The first study arm will include three antigens, two pre-erythrocytic (CSP and TRAP) and one blood stage (AMA-1), shown previously to protect against Plasmodium falciparum, the most deadly malaria strain. The second study arm will include two additional pre-erythrocytic-stage antigens (LSA-1 and CelTOS).

The focus on vaccines that deliver multiple antigens simultaneously is a leading approach to developing highly effective malaria vaccines. The Inovio platform is technically well suited to deliver multiple target antigens and has effectively demonstrated in preclinical studies an ability to induce potent immune responses to these antigens. This is one of a series of platforms MVI plans to evaluate for its capacity to induce immune responses that confer protection from malaria infection in the human challenge model.

Hepatitis B Virus

Although an effective preventive vaccine against hepatitis B virus (HBV) infection has existed for over three decades, HBV remains a major epidemic, especially among the people of Asian and African descent. One-third of the world's population has been infected with HBV, with 400 million people chronically infected with the virus and at risk of developing cirrhosis or liver cancer. Currently, the only therapies available for chronically infected individuals are interferon-a 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 third most common cancer and the most deadly, killing most patients within five years of diagnosis. About 600,000 new cases arise each year. One of the major causes and risk factors for liver cancer is infection by hepatitis B.

In November 2012 we announced data indicating that our synthetic HBV therapeutic vaccine generated strong T cell responses that eliminated targeted liver cells in mice. Results from this preclinical 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, Inovio developed a synthetic DNA vaccine 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

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electroporation, researchers first demonstrated that this vaccine 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 vaccination could also induce antigen-specific CD8 and CD4 T cells that produced both IFN-y and TNF-a in the liver, indicating a strong vaccine-induced T cell response was also present in the liver.

Furthermore, study researchers found the vaccine-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.

Cytomegalovirus

Cytomegalovirus (CMV) is a member of the herpes family of viruses that spreads from one person to another through the transfer of body fluids. CMV causes a wide variety of infection and illness in healthy adults, in those with compromised immune systems (such as HIV patients), and in pregnant women who can pass the infection to their unborn child (congenital CMV) and this cause infant death and congenital abnormalities. It is the most common viral infection in solid organ transplant recipients and is considered a causative factor in certain cancers, inflammatory diseases, and cardiovascular/pulmonary diseases. CMV infects over 95% of people in some developing countries. In the US, 50 - 80% of people become infected with CMV by the time they are 40 years old. CMV is the most common viral infection that infants are born with in the United States. The genetic complexity of CMV has inhibited the advancement of vaccines for this disease and, despite 50 years of research, this disease is a medical problem that has yet to see a vaccine or cure. The US Institute of Medicine and US National Vaccine Program offices have ranked CMV with the highest priority in terms of potential healthcare dollar savings and improvement in "quality adjusted life years." Although healthy people usually have few symptoms at the time of initial infection, after infection the virus remains in a latent state in the body for the rest of a person's life. The virus can then be transmitted and cause infection through organ donation, or latent virus can become reactivated and cause symptomatic disease.

In November 2012 we announced that our multiple synthetic vaccine constructs for cytomegalovirus (CMV) induced robust T cells in mice, demonstrating the potential for a SynCon® DNA vaccine to treat this disease. The results from this preclinical study appear in the peer-reviewed journal Human Vaccines & Immunotherapeutics in an article entitled "Vaccination with synthetic constructs expressing cytomegalovirus immunogens is highly T cell immunogenic in mice."

In this study, Inovio researchers first investigated a novel panel of ten CMV immunogens comprised of mainly surface-associated proteins based on promising prior clinical and preclinical data that had been previously shown to be important for inducing cellular immune responses in CMV infection. To maximize the potential for broadly-reactive immunity, Inovio researchers created SynCon® vaccines for each of the target proteins based on amino acid consensus sequences from multiple variant CMV clinical strains, and excluded those from potentially divergent, highly passaged lab-adapted strains.

Researchers observed that vaccination with each CMV construct was highly T cell immunogenic in preclinical proof-of-concept mice studies, generating robust and broad T cell responses as extensively analyzed by the T cell ELISPOT assay. Each antigen produced responses against at least four and as many as 28 different regions of the antigen and, importantly, responses from both CD8+ and CD4+ T cells were observed. This increased diversity and magnitude of cellular responses may be critical for effectively mitigating CMV infection and disease in the transplantation setting.

These data demonstrate that Inovio's next-generation SynCon® DNA vaccine technology is effective at inducing CD8+ T cell responses specific to CMV, in contrast to prior strategies that induced mainly CD4+-dominant responses. Additionally, a majority of epitopes identified for the gB, gH, and gL antigens also contained HLAs that have previously been reported to contribute to the suppression of viremia and amelioration of disease. Further ongoing work will determine how many of the 10 antigens will be selected and taken further for clinical development as well as assess the induction of antibody responses to prevent CMV infection.

Synthetic Vaccines 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 strain H5N1. 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

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

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 synthetic DNA vaccines 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 its 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.

Animal Health/Veterinary

VGX Animal Health, Inc. (VGX AH), a majority-owned subsidiary, is advancing the development and commercialization of LifeTide®, a plasmid-based growth hormone releasing hormone (GHRH) technology for swine. LifeTide® is one of only four DNA-based treatments approved for use in animals and is the only DNA-based agent delivered using electroporation that has been granted marketing approval (Australia and New Zealand). We are working on partnering and/or monetizing this program.

In September 2012 we announced that a study published in a leading peer-reviewed journal, the American Journal of Veterinary Research, showed that LifeTide® SW 1.0, an optimized version requiring only 20% of the dose of the licensed LifeTide® SW 5.0, demonstrated significant decreases in perinatal mortality rate, an increase in the number of pigs born alive, and an increase in the weight and number of pigs weaned compared with the control group. Additionally, there was a significant increase in the lifespan of the treated sows in the study. These findings provide further evidence of the potential of the plasmid-based GHRH technology to improve productivity and profitability for pig producers around the world.

VGX AH is also developing a GHRH-based treatment for cancer and anemia in dogs and cats.

We are developing a novel synthetic vaccine for foot-and-mouth disease (FMD) administered by our proprietary vaccine delivery technology. The FMD virus is one of the most infectious diseases affecting farm animals including cattle, swine, sheep and goats, and is a serious threat to global food safety. Once an area is exposed to FMD, livestock & dairy exports are ceased and herds are culled. For example, in a major FMD outbreak in the UK in 2001, more than 4 million animals were slaughtered, resulting in more than $10 billion (USD) in economic losses. In a current FMD epidemic in South Korea, more than 3.3 million animals, mostly swine, have been culled in an attempt to keep the disease from spreading. Today's FMD vaccines based on killed/inactivated viruses can actually cause FMD infection, so are only used regionally after an outbreak rather than for broad preemptive vaccination. Our synthetic DNA vaccine cannot cause the disease, providing a safe approach to potentially protect against FMD and reduce its serious impact on global food supply and commerce.

Because FMD can spread rapidly and beyond regional boundaries there is a need to develop vaccines that can simultaneously target different regional serotypes (subtypes) of FMD in a single vaccine. Our SynCon® vaccine constructs target four of the seven main FMD virus subtypes.

Due to the fear of inadvertent spread to farm animals, research with the live virus to test vaccine efficacy is heavily restricted to only a few government laboratories in the US. The investigators therefore developed a patented new proprietary

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neutralization assay (using a mock virus unrelated to FMD to assess the ability of the vaccine-induced antibodies to neutralize virus infection). In a follow-on investigation of the immune responses with the novel neutralization assay against the Asia strain, the vaccinated animals developed neutralizing antibody (NAb) titers averaging 90 after a single vaccination and increasing in magnitude to 191 after two vaccinations. For comparison, commercially available attenuated/killed FMD virus vaccines are able to protect swine with an NAb titer of 32-40. These results are the first report of a DNA vaccine producing high titers of neutralizing antibodies against FMD.

In a second large-animal study, sheep were vaccinated three times at 0, 5, and 10 weeks with a combination vaccine targeting either four subtypes (O, A, C, Asia), three subtypes (O, A, Asia), or a single subtype (Asia). The study investigators observed in the vaccinated animals high levels of seroconversion (production of antibodies specific to a particular antigen) and antibody titers (the actual level of antibody production; in this case, ranging from 1000 – 100,000) to all the vaccine subtypes after only one or two vaccinations. Importantly, the multi-subtype DNA vaccines targeting three or four subtypes simultaneously were able to induce equally strong levels of antibody titers compared to the single-subtype vaccines. Strong T-cell responses (cumulatively > 1,500 SFU/million PBMC), which would potentially play a role in treating the disease, were also noted against the four different subtype antigens.

In September 2011 we entered into a Cooperative Research and Development Agreement (CRADA) with the United States Department of Homeland Security (DHS) Science and Technology Directorate Plum Island Animal Disease Center. This collaboration will evaluate the efficacy of our SynCon® vaccines for FMD in important animal models including cattle, sheep, and pigs.

Additional Applications of Our Electroporation Delivery Technology

In addition to using our technology for human drug and vaccine delivery, it can be used for research to validate new drug targets, to generate monoclonal antibodies, deliver siRNA and other molecules. The use of our technology for research increases general awareness for the technology and may facilitate its transition into clinical development for these other applications. In addition, we believe there may be a benefit to exploring future potential applications for our technology in the area of gene therapy to treat genetic disorders.

We continue to pursue limited opportunities in the areas of stem cells, ex-vivo applications and RNAi, where collaborators would provide the majority of required development resources.

Our Electroporation Delivery Technology

Choice of Tissue for DNA Delivery

Skeletal muscle has been a core focus for delivery of DNA-based vaccines 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 vaccination, 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 preclinical and preliminary clinical evidence that intramuscular electroporation-based DNA delivery will be effective for a number of vaccines, 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 immunocompetent (able to recognize antigens and mount an immune response to them).
Our Electroporation Systems

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Existing generations of 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 recently unveiled our new CELLECTRA®-SP series of hand-held, cordless electroporation devices. The new CELLECTRA®-SP devices 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 cGMP and are ready for use 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. The device is intended to be used in combination with a DNA plasmid-based vaccine.

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 vaccination 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 vaccine and tissue for delivery (skin or muscle).

Elgen™ System

The Elgen™ DNA Delivery System is designed primarily for muscle delivery. It consists of a computer-controlled, motorized two needle delivery device that injects DNA and delivers electroporation pulses through one pair of needles. An earlier prototype version of this experimental system is currently under evaluation in our clinical trial for a prostate cancer vaccine at the University of Southampton in the U.K.

MedPulser® DNA Delivery System

The MedPulser® DNA Delivery System (DDS) was developed to optimize the delivery of DNA into muscle cells. The pulse is designed specifically for DNA delivery with a low strength electrical field. The applicator has a four needle-electrode array consisting of opposite pairs. They are available in a range of configurations to meet the requirements of a variety of applications.

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 vaccine was coded to produce) of “naked” DNA vaccines by 100-fold or more compared to delivery of naked DNA vaccines via conventional injection alone. Delivery of our SynCon® vaccines 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 for 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 minimally invasive surface electroporation (SEP) device that sits on the surface of the skin and uses a virtually undetectable scratch to facilitate delivery of the vaccine. 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 vaccine 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 October 2012 in the peer-reviewed journal, Human Gene Therapy, in a paper 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) new needle-free, contactless electroporation technology for vaccine 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

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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.

Collaborations and Licensing Agreements

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 March 24, 2010, we entered into a Collaboration and License Agreement (the "Agreement") with VGX International ("VGX Int'l"). Under the Agreement, we granted VGX Int'l 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 the license granted to VGX Int'l, 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 VGX Int'l 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 VGX Int'l right to terminate without cause upon prior written notice.

In October 2011, we entered into a product development collaboration agreement with VGX Int'l to co-develop our SynCon® therapeutic vaccines for hepatitis B and C infections. Under the terms of the agreement, VGX Int'l will receive marketing rights for these vaccines in Asia, excluding Japan, and in return will 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 January 2010, we announced that we expanded our existing license agreement with the University of Pennsylvania, adding exclusive worldwide licenses for technology and intellectual property for novel synthetic vaccines against pandemic influenza, Chikungunya, and FMD. The amendment also encompassed new chemokine and cytokine molecular adjuvant technologies. 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. Under the terms of the original license agreement 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. These prior and most recent agreements and amendments provide for royalty payments, based on future sales, to the University of Pennsylvania.

In July 2011, we further expanded our license agreement with the University of Pennsylvania, adding exclusive worldwide licenses for technology and intellectual property for novel synthetic vaccines 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 again expanded our license agreement with the University of Pennsylvania (UPenn), adding worldwide rights to technology and intellectual property for novel synthetic 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 March 2009, we announced an agreement with the PATH Malaria Vaccine Initiative (MVI) to evaluate in a preclinical feasibility study our SynCon® vaccine development platform. More specifically, this collaboration was to design and test synthetic vaccine candidates using target antigens from Plasmodium species and deliver them intradermally using the CELLECTRA® electroporation device. The first program was completed in February 2010. In September 2010, MVI agreed to provide follow-on funding to continue evaluation and development of our malaria synthetic vaccine candidate in non-human primates.

In the prior MVI-funded feasibility study, our malaria vaccine candidate induced broad-based immunity to four pre-erythrocytic malaria antigens. In the subsequent non-human primate study, our SynCon® vaccine constructs, which target sporozoites and the liver stage of the parasite, demonstrated potent T cell and antibody.

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Subsequent to year end, in January 2013 we announced a follow-on collaboration with the PATH Malaria Vaccine Initiative (MVI) focused on initiating human studies to assess whether a DNA vaccine(s) delivered using electroporation can induce an immune response in humans that protects against malaria parasite infection.

In May 2004, we announced a collaboration and license allowing Merck to use Inovio's earlier generation proprietary electroporation delivery technology in conjunction with certain DNA vaccines developed by Merck. Merck completed Phase I clinical studies for two DNA vaccines but has not reported results from these clinical studies. As part of this license agreement, Merck paid Inovio milestone payments and funded all clinical development costs. Further development of products by Merck under the collaboration and license agreement may lead to additional milestone payments and royalties payable to Inovio.

Market

We anticipate that over the next several years a number of key demographic and technological factors should accelerate growth in the market for vaccines and medical therapies to prevent and treat infectious diseases and cancer, particularly in our product categories. These factors include the following:

- Rise in emerging infectious diseases and the threat of pandemics. The attention received by the pandemic potential of avian influenza has mobilized cross-border agencies including governments, world health organizations and private and public corporations to develop effective vaccination and therapeutics strategies. Our candidate vaccines for avian influenza, Chikungunya and dengue are among those intended to serve these needs.
- Increased consumer awareness. In areas such as cervical cancer, increased consumer awareness related to HPV infection, the primary cause of cervical cancer, has led to renewed efforts for developing effective therapies. The current vaccines for cervical cancer prevention (Gardasil® and Cervarix®), while being effective measures for prevention in the unexposed population, are ineffective in people infected with HPV.
- Large unmet need. In areas such as HIV and HCV (prevention and therapy) there is a large unmet need with no vaccine options on the market. With the exit of several players in the recent years from the HIV vaccine development area, if our vaccines prove successful we believe we are positioned to obtain a significant market position.

We believe there is a significant unmet clinical need to develop more efficacious vaccines that stimulate cellular immunity (i.e. can induce T-cell responses) and can be applied to diseases such as cancer, hepatitis C or HIV infection. For these applications, our scientists believe that synthetic vaccines may offer an improvement over conventional vaccination. Our scientists believe that electroporation of DNA is critical to maximizing the efficiency of DNA vaccination and meeting unmet clinical needs for therapeutic vaccines, which some industry analysts consider to be a multi-billion dollar market opportunity.

Competition

We are aware of several development-stage and established enterprises, including major pharmaceutical and biotechnology firms, which are actively engaged in infectious disease and cancer vaccine 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. We may also experience competition from companies that have acquired or may acquire technologies from companies, universities and other research institutions. As these companies develop their technologies, they may develop proprietary technologies which may materially and adversely affect our business.

In addition, a number of companies are developing products to address the same diseases that we are targeting. For example, Sanofi-Aventis, Novartis, Inc., MedImmune, GlaxoSmithKline, CSL (in collaboration with Merck), and others have products or development programs for influenza. Merck and GlaxoSmithKline have commercialized preventive vaccines against HPV to protect against cervical cancer; Advaxis has a therapeutic cervical dysplasia/cancer product in Phase II trials. Much of the development for our HIV and malaria vaccines is being done by government and non-government organizations such as the NIH and Bill & Melinda Gates Foundation.

We compete with companies that are developing DNA delivery technologies, such as viral delivery systems, lipid-based systems, or electroporation technology with an aim to carry out in vivo gene delivery for the treatment of various diseases. Currently there are five key DNA delivery technologies: viral, lipids, naked DNA, “gene gun” 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 vaccines.

Viral DNA Delivery

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This technology utilizes a virus as a carrier to deliver genetic material into target cells. The method is very efficient for delivering vaccine antigens and has the advantage of mimicking real viral infection so that the recipient will mount a broad immune response against the vaccine. 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 the cost of vaccines 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 vaccine antigens. Since the DNA is dry coated, excellent stability of the vaccine 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 vaccine 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 vaccines. 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.

“Naked” DNA Delivery

The simplest DNA delivery mode is the injection of “naked” plasmid DNA into target tissue, usually skeletal muscle. This method is safe and economical but inefficient in terms of cell transfection, the process of transferring DNA into a cell across the outer cell membrane. Unfortunately, it is the least effective way of delivering DNA since only an extremely small fraction (approximately one out of twenty million) of the DNA molecules are taken up by the cells. While the method may have provided some utility for the field of gene therapy, a number of clinical studies over the last decade have shown that the method is inadequate for delivering DNA vaccines into large animals and humans.

“Naked” DNA Delivery With Electroporation

When naked DNA injection is followed by electroporation of the target tissue, transfection is significantly greater with resultant gene expression generally enhanced a 1000-fold. This increase makes many DNA vaccine candidates potentially feasible without unduly compromising safety or cost.

In December 2004, the first patient was treated using our electroporation system to deliver a plasmid DNA-based therapeutic vaccine and we have initiated, together with partners, additional Phase I and Phase II clinical trials using our electroporation technology to deliver preventive and therapeutic synthetic vaccines. To date our scientists have not observed any serious adverse events that can be attributed to the use of electroporation in these clinical studies.

We believe that the greatest obstacle to making synthetic vaccines a reality has been the lack of safe, efficient and economical 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 synthetic vaccines.
- 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,

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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 preclinical 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 preclinical 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, preclinical studies, and clinical trials in addition to detailed chemistry, manufacturing and control information.

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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 preclinical 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 VGX Int'l

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We acquired an equity interest in VGX Int'l in 2005. As of December 31, 2012 we owned 16.1% of the outstanding capital stock of VGX Int'l and VGX Int'l owned 294,360 shares of our common stock. None of our current officers, directors, or key employees beneficially owns, directly or indirectly, any securities of VGX Int'l. In June 2011, Bryan Kim, a former member of VGX Int'l's Board of Directors and former President and Chief Executive Officer of VGX Int'l, terminated his employment with the Company as Vice President of Asian Operations.

In 2008 we sold our manufacturing operations (including patent rights to certain manufacturing technology) to VGXI, Inc, a wholly-owned United States subsidiary of VGX Int'l. 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 clinical trials. The price of the plasmids we purchase from VGXI, Inc. is determined by us and VGX Int'l 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 VGX Int'l and its subsidiary as our most favored supplier for DNA plasmids and VGX Int'l 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 VGX Int'l or its subsidiary to manufacture DNA plasmids for us, we must first offer such manufacturing work to VGX Int'l or its subsidiary.

We have also entered into license and collaboration agreements pursuant to which we have granted VGX Int'l exclusive rights to certain of our product candidates in certain jurisdictions. For example, VGX Int'l has exclusive rights in countries in Asia including Korea to our VGX-3400X for treatment of the avian flu and our hepatitis B and Hepatitis C programs. In exchange for these rights, VGX Int'l shares the development costs for some of our product candidates.

For the years ended December 31, 2012 and 2011, we recognized revenue from VGX Int'l of $577,000 and $411,000, respectively, which consisted of licensing, collaborative research and development arrangements and other fees. Operating expenses related to VGX Int'l for the years ended December 31, 2012 and 2011 were $871,000 and $5.3 million, respectively, relating to biologics manufacturing. At December 31, 2012 and 2011 we had an accounts receivable balance of $36,000 and $20,000, respectively, from VGX Int'l and its subsidiaries.

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 March 8, 2013, our patent portfolio included over 68 issued United States patents and 214 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.
- 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.
- International publication WO2009/099716, entitled, "Novel Vaccines Against Multiple Subtypes Of Dengue Virus."

- US Pat. No. 8,133,723, entitled, “Novel Vaccines Against Multiple Subtypes Of Influenza.”
- International publication WO2009/073330, entitled, “Novel Vaccines Against Multiple Subtypes Of Influenza Virus.”

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- International publication WO2010/0050939, entitled, “IMPROVED HCV VACCINES AND METHODS FOR USING THE SAME”
- International publication WO2010/044919, 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. 7173116, entitled, “NUCLEIC ACID FORMULATIONS FOR GENE DELIVERY AND METHODS OF USE”

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. 6,110,161 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.

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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 years ended December 31, 2012 and 2011 we derived 69% and 80% 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 synthetic vaccines. 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 $18.0 million in 2012 and $20.0 million in 2011.

Corporate History and Headquarters

We were originally incorporated on June 29, 1983, under the laws of California as Biotechnologies & Experimental Research, Inc. The entity changed its corporate name to BTX, Inc. on December 10, 1991, and Genetronics, Inc. on February 8, 1994. On April 14, 1994, the board of directors approved a share exchange agreement with Consolidated United Safety Technologies Inc. On September 2, 1997, we listed on the Toronto Stock Exchange as Genetronics Biomedical Ltd, under the laws of British Columbia, Canada, which wholly owned Genetronics, Inc. On June 15, 2001, we completed a change in jurisdiction of incorporation from British Columbia, Canada, to the state of Delaware and became Genetronics Biomedical Corporation, a Delaware corporation. On January 17, 2003, Genetronics voluntarily de-listed from the Toronto Stock Exchange. On March 31, 2005, our corporate name changed from Genetronics Biomedical Corporation to Inovio Biomedical Corporation. On June 1, 2009, we completed the acquisition of VGX Pharmaceuticals, Inc. ("VGX"), a privately-held company, 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 by and among Inovio, Inovio's wholly-owned subsidiary Inovio Acquisition, LLC and VGX (the "Merger"). Upon the closing of the Merger, Inovio Acquisition, LLC assumed all of VGX's business, properties and assets and assumed its obligations, changed its name to VGX Pharmaceuticals, LLC, and remains a wholly-owned subsidiary of the Company, utilizing a single, integrated management team with Inovio. On May 14, 2010, the entity changed its corporate name to Inovio Pharmaceuticals, Inc. We conduct our business through our United States wholly-owned subsidiaries, Genetronics, Inc. and VGX Pharmaceuticals, LLC.

Our principal executive offices are located at 1787 Sentry Parkway West, Blue Bell, Pennsylvania 19422, and the telephone number is (267) 440-4200.

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).

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We will provide any of the foregoing information without charge upon request to Peter Kies, 11494 Sorrento Valley Road Suite A, 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 8, 2013, we employed 53 people on a full-time basis and 6 people under consulting and project employment agreements. Of the combined total, 41 were in product research, which includes research and development, quality assurance, clinical, engineering, and manufacturing, and 18 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, 2012 our accumulated deficit was approximately $229.8 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 2014. 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 are 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

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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.

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

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 Merck. The amount and timing of resources applied by our collaborators are largely outside of our control.

Wyeth terminated one of our existing collaboration agreements. If any of our other 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, 2012, the NIAID and VGX Int'l accounted for approximately 69% and 14%, 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

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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

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our applications approvable. If any of these outcomes occur, we may be forced to abandon one or more of our applications for approval, which might significantly harm our business and prospects.

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

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

Clinical testing is expensive and can take many years to complete, and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of 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