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

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

FORM 10-K

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

OR

¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM TO

COMMISSION FILE NO. 001-14888

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

DELAWARE	33-0969592
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
660 W. GERMANTOWN PIKE, SUITE 100 PLYMOUTH MEETING, PENNSYLVANIA	19462
(Address of principal executive offices)	(Zip Code)

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

SECURITIES REGISTERED PURSUANT TO SECTION 12(B) OF THE ACT:	
COMMON STOCK, $0.001 PAR VALUE	NASDAQ
(Title of Class)	(Name of Each Exchange on Which Registered)

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No x
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x
Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨
Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of Registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer x

Non-accelerated filer ¨ (Do not check if a smaller reporting company) Smaller reporting company ¨
Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No x
The aggregate market value of the voting and non-voting common equity (which consists solely of shares of Common Stock) held by non-affiliates of the Registrant as of June 30, 2014 was approximately $614,635,315 based on $10.81, the closing price on that date of the Registrant's Common Stock on the NYSE MKT.
The number of shares outstanding of the Registrant's Common Stock, $0.001 par value, was 60,741,082 as of March 9, 2015.

DOCUMENTS INCORPORATED BY REFERENCE
Portions of the registrant's definitive proxy statement to be filed with the Commission pursuant to Regulation 14A in connection with the registrant's 2015 Annual Meeting of Stockholders (the "Proxy Statement') are incorporated by reference into Part III of this Report. Such Proxy Statement will be filed with the Commission not later than 120 days after the conclusion of the registrant's fiscal year ended December 31, 2014.

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

PART I

ITEM 1. BUSINESS

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

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

Overview

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

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

Industry Background

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

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

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

Inovio's Solution

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

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

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

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

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

The SynCon sequences are further optimized at the DNA level for codon usage, improved mRNA stability, and are provided with enhanced leader sequences for ribosome loading. The DNA inserts are therefore optimized at the genetic level to give them high expression capability particularly in human cells. We believe these design capabilities allow us to better target appropriate immune system mechanisms and produce a higher level of the coded antigen to enhance the overall ability of the immunotherapy to induce the desired immune response.

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

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

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

Electroporation Delivery Technology

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

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

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

Products and Product Development

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

Inovio SynCon® Immunotherapy Development

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

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

X = Completed
IP = In Progress
P = Planning

Cancer Vaccines/Immunotherapies

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

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

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