

INOVIO Interim Results of an Open-Label Phase 2 Trial of VGX-3100 Show Efficacy Against HPV-associated Vulvar Dysplasia

3/30/2020

PLYMOUTH MEETING, Pa., March 30, 2020 /PRNewswire/ -- INOVIO Pharmaceuticals, Inc. (NASDAQ: INO) today reported interim results from an open-label Phase 2 trial designed to evaluate the safety and efficacy of VGX-3100 in women with vulvar dysplasia, also known as high grade squamous intraepithelial lesion (HSIL), a precancerous condition caused by high-risk human papillomavirus (HPV) types 16 and/or 18. A total of 22 subjects have received all 4 doses and will be evaluated to the end of the study. INOVIO is reporting interim data on the 10 subjects who have completed their primary endpoint evaluation at six months following treatment with VGX-3100. Based upon the available results, 80% (8 out of 10 subjects) had a reduction (2 cm² on average) in qualifying lesion area (average 60% reduction) of which 20% (2 of 10) completely resolved their vulvar HSIL and had no virus detectable in the healed area, 6 months following treatment.

Trial results will be presented from April 1st through April 2nd at the annual American Society for Colposcopy and Cervical Pathology (ASCCP) meeting as a virtual session titled: "Preliminary Results of an Open-Label Phase 2 Study of VGX-3100 for the Treatment of HPV-16 and/or HPV-18 (HPV-16/18) Related Vulvar HSIL." Safety results were consistent with the known safety profile of VGX-3100. There were no drug-related serious adverse events. No cases of carcinoma have been observed.

Vulvar HSIL is an orphan condition that usually requires surgery, which has significant physical and psychosocial impacts (e.g. severe pain, disfigurement, sexual dysfunction). The success of such surgery is marginal, as the recurrence rate of high grade vulvar pre-cancer is approximately 30 to 50% three years post-treatment. Overall less than 5% of women with vulvar HSIL exhibit spontaneous resolution. Without adequate treatment vulvar HSIL can progress to vulvar cancer which is projected to claim approximately 1350 lives in the US in 2020 alone.

Dr. Prakash Bhuyan, MD PhD, Vice President and Head of Clinical Development of HPV Therapeutics for INOVIO said: "INOVIO is developing VGX-3100 as a comprehensive treatment for HPV precancerous diseases. These proof-

of-concept data take us one step closer to a better approach to treat vulvar precancer and improve women's health."

Dr. Robert Edwards, MD, Milton Lawrence McCall Professor and Chair, Department of Obstetrics, Gynecology & Reproductive Sciences, University of Pittsburgh and Principal Coordinating Investigator for the trial said: "This novel platform allows effective immune stimulations in the face of long standing viral induced precancer for this highly morbid disease. Many of these patients face years or sequential surgical resections and markedly impaired sexually function, apprehension about cancer risk, and some cases invasive cancer requiring highly morbid therapy."

VGX-3100 Safety and Efficacy Highlights for Vulvar Dysplasia

- Safety results are consistent with the known safety profile of VGX-3100. There were no drug-related serious adverse events.
- 80% (8 of 10 subjects) showed an overall decrease in the lesion area six months after treatment and 20% (2 of 10 of subjects) completely resolved their vulvar HSIL, which compares to a spontaneous regression of 1.5% to 5%.
- Results further support proof of concept for DNA medicines as also demonstrated in prior VGX-3100 Phase 2b study in high-risk HPV-associated precancerous cervical dysplasia.
- Less than 5% of women with vulvar HSIL exhibit spontaneous resolution.
- The success of surgery for vulvar HSIL is marginal, as the recurrence rate of high grade vulvar pre-cancer is approximately 30 to 50% three years post-treatment.

About Vulvar Dysplasia (HSIL)

If left untreated vulvar pre-cancers can progress to invasive cancer of the vulva. Approximately 27,000 cases of HPV-related vulvar pre-cancers occur in the U.S. each year with a similar number of estimated cases in Europe each year. HPV-16 and/or HPV-18 are involved in about 80% of HPV-related vulvar pre-cancers cases in the U.S. and Europe. Once vulvar pre-cancers develop, spontaneous regression (i.e. natural resolution of the lesion) is rare and occurs in 1.5% to 5% of cases. An estimated 6,000 new cases of vulvar cancer occur in the U.S. each year with about 50% to 80% of those being HPV-associated.

About the Study

This open-label, randomized, multi-center Phase 2 study is designed to evaluate the safety and efficacy of VGX-3100 in adult women 18 and older, with precancerous vulvar dysplasia caused by HPV-16 and/or HPV-18. The key efficacy measures being evaluated are resolution of HSIL, non-detectability of HPV 16/18, and the decrease in lesion area. 33 women received 4 doses of VGX-3100 at Weeks 0, 4, 12, and 24, of whom 8 subjects also received topical

imiquimod, which was being evaluated as an adjunctive treatment. Enrollment into the imiquimod arm was halted due to having no meaningful improvement upon the efficacy of VGX-3100 alone. Efficacy at 6 months following VGX-3100 treatment will be reported for all participants with available data, 22 of whom received VGX-3100 alone. Three participants have discontinued due to reasons of moving (1 subject) and electing for earlier surgery (2 subjects). The trial will follow treated participants for up to 1 year after the 4th dose.

About INOVIO's HPV-Associated DNA Medicines Clinical Programs

This study builds on significant clinical benefits demonstrated with INOVIO's HPV-associated DNA medicines in multiple clinical trials. Specifically, VGX-3100 in a Phase 2 proof-of-concept trial for cervical dysplasia demonstrated a complete response in 43 out of 107 patients in regression of high-grade cervical lesions and elimination of the underlying HPV infection. Additionally, two out of four metastatic HPV-associated head and neck cancer patients treated with MEDI0457 and a PD-1 check point inhibitors in a Phase 1 study experienced a long-term complete response for more two years and counting. Lastly, a pilot study of INOVIO's DNA medicine INO-3107 in recurrent respiratory papillomatosis (RRP) resulted in two out of two patients delaying surgery due to lack of tumor recurrence.

About VGX-3100

VGX-3100 is a DNA medicine under Phase 3 investigation for the treatment of HPV-16 and HPV-18 infection and precancerous lesions of the cervix. INOVIO is in open-label Phase 2 clinical trials evaluating its efficacy for treating HPV-related vulvar and anal dysplasia (HSIL). VGX-3100 has the potential to be the first approved treatment for HPV infection of the cervix and the first non-surgical treatment for precancerous cervical lesions. It works by stimulating a specific immune response to HPV-16 and HPV-18, which targets the infection and causes destruction of precancerous cells. In a randomized, double-blind, placebo-controlled phase 2b study in 167 adult women with histologically documented HPV-16/18 cervical dysplasia (CIN2/3 or HSIL), treatment with VGX-3100 resulted in a statistically significantly greater regression of cervical dysplasia and clearance of HPV-16/18 infection vs. placebo. The most common side effect was injection site pain, and no serious adverse events were reported. VGX-3100 utilizes the patient's own immune system to clear HPV-16 and HPV-18 infection and precancerous lesions without the increased risks associated with surgery, such as loss of reproductive health and negative psychosocial impacts.

About INOVIO's DNA Medicines

INOVIO has 15 DNA medicine clinical programs currently in development focused on HPV-associated diseases, cancer, and infectious diseases, including coronaviruses associated MERS and COVID-19 diseases under grants from the Coalition for Epidemic Preparedness Innovations (CEPI). DNA medicines are composed of optimized DNA plasmids, which are small circles of double-stranded DNA that are synthesized or reorganized by a computer

sequencing technology and designed to produce a specific immune response in the body.

INOVIO's DNA medicines deliver optimized plasmids directly into cells intramuscularly or intradermally using INOVIO's proprietary hand-held smart device called CELLECTRA®. CELLECTRA® uses a brief electrical pulse to open small pores in the cell reversibly to allow the plasmids to enter, overcoming a key limitation of other DNA and mRNA approaches. Once inside the cell, the plasmids are used by the cell's own machinery to generate specific coded antigens, which then stimulate an immune response. Administration with the CELLECTRA device ensures that the DNA medicine is delivered directly into the body's cells, where it can go to work immediately mounting an immune response. INOVIO's DNA medicines do not interfere with or change in any way an individual's own DNA. The advantages of INOVIO's DNA medicine platform are how fast DNA medicines can be constructed and manufactured, the stability of the products which do not require freezing in storage and transport, and the robust immune response, safety profile and tolerability that have been demonstrated in clinical trials.

With more than 2,000 patients receiving INOVIO investigational DNA medicines in more than 6,000 applications across a range of clinical trials, INOVIO has a strong track record of rapidly generating DNA medicine candidates to meet urgent global health needs.

About INOVIO Pharmaceuticals, Inc.

INOVIO is a biotechnology company focused on rapidly bringing to market precisely designed DNA medicines to treat, cure, and protect people from diseases associated with HPV, cancer, and infectious diseases. INOVIO is the first and only company to have clinically demonstrated that a DNA medicine can be delivered directly into cells in the body via a proprietary smart device to produce a robust and tolerable immune response. Specifically, INOVIO's lead candidate VGX-3100, currently in Phase 3 trials for precancerous cervical dysplasia, demonstrated it destroyed and cleared high-risk HPV 16 and 18 in a Phase 2b clinical trial. High-risk HPV is responsible for 70% of cervical cancer, 90% of anal cancer, and 69% of vulvar cancer. Also in development are programs targeting HPV-related cancers and a rare HPV-related disease: recurrent respiratory papillomatosis (RRP); non-HPV-related cancers glioblastoma multiforme (GBM) and prostate cancer; as well as externally funded infectious disease DNA vaccine development programs in Zika, Lassa fever, Ebola, HIV, and coronaviruses associated MERS and COVID-19 diseases. Partners and collaborators include Advaccine, ApolloBio Corporation, AstraZeneca, The Bill & Melinda Gates Foundation, Coalition for Epidemic Preparedness Innovations (CEPI), Defense Advanced Research Projects Agency, GeneOne Life Science, HIV Vaccines Trial Network, Medical CBRN Defense Consortium (MCDC), National Cancer Institute, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Plumblin Life Sciences, Regeneron, Roche/Genentech, University of Pennsylvania, Walter Reed Army Institute of Research, and The Wistar Institute. INOVIO also is a proud recipient of 2020 Women on Boards "W" designation recognizing companies with more than 20% women on their board of directors. For more information, visit www.inovio.com.

This press release contains certain forward-looking statements relating to our business, including our plans to develop DNA medicines, our expectations regarding our research and development programs, as well as commercialization activities, including the planned initiation and conduct of clinical trials, the availability and timing of data from those trials and our commercialization strategy and tactics. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including uncertainties inherent in pre-clinical studies, clinical trials, product development programs and commercialization activities and outcomes, the availability of funding to support continuing research and studies in an effort to prove safety and efficacy of electroporation technology as a delivery mechanism or develop viable DNA medicines, our ability to support our pipeline of DNA medicine products, the ability of our collaborators to attain development and commercial milestones for products we license and product sales that will enable us to receive future payments and royalties, the adequacy of our capital resources, the availability or potential availability of alternative therapies or treatments for the conditions targeted by us or our collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that we and our collaborators hope to develop, issues involving product liability, issues involving patents and whether they or licenses to them will provide us with meaningful protection from others using the covered technologies, whether such proprietary rights are enforceable or defensible or infringe or allegedly infringe on rights of others or can withstand claims of invalidity and whether we can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of our technology by potential corporate or other partners or collaborators, capital market conditions, the impact of government healthcare proposals and other factors set forth in our Annual Report on Form 10-K for the year ended December 31, 2019 and other filings we make from time to time with the Securities and Exchange Commission. There can be no assurance that any product candidate in our pipeline will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this release, and we undertake no obligation to update or revise these statements, except as may be required by law.

CONTACTS:

Investors: Ben Matone, 484-362-0076, ben.matone@inovio.com

Media: Jeff Richardson, 267-440-4211, jrichardson@inovio.com

View original content:<http://www.prnewswire.com/news-releases/inovio-interim-results-of-an-open-label-phase-2-trial-of-vgx-3100-show-efficacy-against-hpv-associated-vulvar-dysplasia-301031393.html>

SOURCE INOVIO Pharmaceuticals, Inc.