INOVIO Reports Positive Interim Phase 2 VGX-3100 Results In Patients with HPV-associated Anal Dysplasia

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PLYMOUTH MEETING, Pa., March 26, 2020 /PRNewswire/ --INOVIO Pharmaceuticals, Inc. (NASDAQ: INO) today announced positive interim results from an open-label, Phase 2 study showing its lead DNA medicine candidate VGX-3100 to be safe and effective in treating men and women with anal dysplasia, also known as high grade squamous intraepithelial lesion (HSIL), a precancerous condition caused by high-risk human papillomavirus (HPV) types 16/18. Of the 20 subjects who had results at the time of data review, 50% (10 of 20 subjects) showed clearance of HPV-16/18 associated precancerous lesions and 75% (15 of 20 subjects) demonstrated an overall decrease in the number of lesions 6 months after the start of treatment. No cases of anal cancer have been observed in the trial. The results support the ability of VGX-3100 to effectively treat multiple HPV associated diseases and will be presented in the virtual session of the annual American Society for Colposcopy and Cervical Pathology (ASCCP) meeting titled: Preliminary Results of an Open-label Phase 2 Study of VGX-3100 for the Treatment of HPV16 and/or HPV-18 (HPV16/18) related Anal HSIL.

Anal dysplasia or anal HSIL, is an orphan disease that affects men and women in both immunocompetent and immunocompromised populations. Fewer than 1 in 5 people with HPV 16/18-associated precancerous dysplasia exhibit spontaneous resolution at one year. Without adequate treatment anal HSIL could progress to anal cancer. HPV 16/18 cause more than 90% of all anal cancer, which is now considered one the most rapidly rising causes of cancer incidence and mortality. According to the American Cancer Society, anal cancer will claim the lives of more than 1,300 people in the U.S. and 8,590 news cases (5,900 in women and 2,690 in men) will be diagnosed in 2020 and according to a study published November 2019 in theJournal of the National Cancer Institute, from 2001 to 2015 the overallincidenceof anal cancerincreased by 2.7% per year and mortality jumped by 3.1% each year

Prakash Bhuyan, M.D., Ph.D., INOVIO’s Vice President and Head of HPV Therapeutic Clinical Development said, “These initial proof-of-concept efficacy results show that VGX-3100 has the potential to enable the immune system
to clear HPV 16/18 HSIL that cause precancerous anal dysplasia and are consistent with the results of our VGX-3100 Phase 2b efficacy study in high-risk HPV-associated precancerous cervical dysplasia.”

Currently, the treatments for anal dysplasia are surgical excision, electro-cautery or laser therapy. Up to 50% of those treated with these invasive options experience disease recurrence within one year of treatment and nearly 70% experience recurrence within three years. Therefore, many patients with this condition need multiple invasive treatments.

VGX-3100 Safety and Efficacy Highlights for Anal Dysplasia

- The first 20 subjects on VGX-3100 demonstrated safety results consistent with the known safety profile of VGX-3100. There were no drug-related serious adverse events.
- 75% showed an overall decrease in the number of lesions 6 months after treatment and 50% of subjects showed no HPV-16/18 associated precancerous lesions
- 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

“These results are very encouraging and represent a potential important step forward in the treatment of precancerous anal dysplasia,” said Dr. Celine Bouchard, Gynecologist/Anoscopist at Centre Médical Santé Femme in Québec City, Canada, former Associate Clinical Professor in the Department of Obstetrics and Gynecology and Reproduction of Université Laval, and Coordinating Principal Investigator for the study. “Having a DNA medicine that can destroy and clear lesions without the burden of repetitive, multiple, and painful surgical or invasive treatments would change the standard of care and provide patients with a meaningful benefit. I look forward to continuing this research and learning more about the potential advantages of VGX-3100.”

About the Study

This open-label, multi-center Phase 2 study is designed to evaluate the safety and efficacy of VGX-3100 in adults with precancerous anal dysplasia caused by HPV-16 and/or HPV-18. Twenty three subjects who are human immunodeficiency virus (HIV) negative with histologically confirmed anal or anal/peri-anal high-grade squamous intraepithelial lesion (HSIL) associated with human papilloma virus (HPV)-16 and/or HPV-18 enrolled. One subject discontinued due to an unrelated adverse event. Twenty two received three doses of VGX-3100 administered by INOVIO’s CELLECTRA™ 5PSP smart device at Day 0, Week 4 and Week 12. Participants are scheduled to be followed to Week 88.

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 MERS and COVID-19 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

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 MERS and COVID-19. 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, Plumline 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:
Media: Jeff Richardson, 267-440-4211, jrichardson@inovio.com
Investors: Ben Matone, 484-362-0076, ben.matone@inovio.com


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