NEWS RELEASE

INOVIO's VGX-3100 Demonstrates Positive Phase 2 Efficacy In Treatment of Precancerous Anal Dysplasia Caused by HPV-16/18

12/9/2020

DNA immunotherapy candidate VGX-3100 demonstrated resolution of HPV-16/18-associated precancerous anal lesions in 50% of treated patients six months after treatment

Current standard of care for anal dysplasia typically requires surgical excision, electro-cautery or laser therapy, and without adequate treatment can progress to anal cancer

PLYMOUTH MEETING, Pa., Dec. 9, 2020 /PRNewswire/ -- INOVIO (NASDAQ:INO), a biotechnology company focused on bringing to market precisely designed DNA medicines to treat and protect people from infectious diseases, cancer and diseases associated with HPV, today announced positive Phase 2 efficacy results demonstrating that DNA medicine VGX-3100, the company's lead immunotherapy asset, showed resolution of HPV-16/18-associated precancerous anal lesions (HSIL) in 50% (11 of 22) of subjects six months following the start of treatment. The open label, single arm trial also showed VGX-3100 to be safe and well-tolerated in treating men and women with HPV-16-/18-associated anal dysplasia. INOVIO plans to pursue a registrational Phase 3 clinical trial for HPV-16-/18-associated anal dysplasia as well as to apply for rare and orphan disease designation for this indication in 2021.

Dr. Céline Bouchard, Gynecologist and Anoscopist at Centre Médical Santé Femme in Québec City, Canada and Coordinating Principal Investigator for the Phase 2 trial, said, "Results of this trial are very promising and may offer a safe and efficacious new therapeutic option for patients suffering from this debilitating condition."

VGX-3100 Phase 2 Anal Dysplasia Trial Highlights

- Enrolled 23 men and women 18 years of age or older. One subject discontinuation occurred due to an event related to a pre-existing condition of depression.
- Trial participants were men and women between 29 and 76 years of age at entry and other than having high grade anal squamous intraepithelial lesions were otherwise healthy.
- The relative proportion of anal dysplasia severity at baseline was skewed toward the more severe condition of

AIN-3 disease (78% [18/23] of subjects). Subjects had a median of 4 lesions (range 2-7).

- Results are based on the demonstration of having no evidence of dysplasia from anal biopsy samples as assessed by two independent pathologists and non-detectability of HPV-16 or HPV-18 from lesion tissue using PCR-based testing, at six months following VGX-3100 administration.
- Efficacy endpoints were measured six months post-treatment. Safety will continue to be assessed for 18 months following the last dose.
- The most observed adverse event was injection site pain, the majority of which were mild to moderate.
- No discontinuations occurred due to treatment-related adverse events
- No treatment-emergent serious adverse events have been observed.
- No cases of anal cancer have been observed in the trial.

For more information about the Phase 2 trial, please visit **www.clinicaltrials.gov** (search identifier NCT03499795).

Prakash Bhuyan, M.D., Ph.D., Senior Vice President and Head of HPV Therapeutic Clinical Development at INOVIO, said, "Anal dysplasia is a rare disease that is typically treated via surgical excision, electro-cautery or laser therapy, with up to 50% of patients experiencing disease recurrence within one year of surgical treatment. We are encouraged by these positive results from our Phase 2 trial and look forward to continuing our work in Phase 3 trials to develop a systemic DNA-based immunotherapy that leverages our DNA medicines platform in order to improve the current standard of care."

INOVIO also has an ongoing partnership with the AIDS Malignancy Consortium (AMC) to evaluate VGX-3100 in HIV-positive adult men and women. This ongoing open-label, multi-center Phase 2 study is designed to evaluate the safety and efficacy of VGX-3100 administered by intramuscular (IM) injection with CELLECTRA® delivery system in adult men and women who are HIV-positive with anal HSIL associated with HPV-16 and/or HPV-18. For additional information about the AMC-partnered study, please visit **www.clinicaltrials.gov** (search identifier NCT03603808).

About Anal Dysplasia

Anal dysplasia is a rare disease that affects men and women in both immunocompetent and immunocompromised populations. Fewer than 1 in 5 people with HPV-16- or HPV-18-associated precancerous dysplasia exhibit spontaneous resolution at one year. Without adequate treatment, anal dysplasia can 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. According to a study published November 2019 in the Journal of the National Cancer Institute, from 2001 to 2015 the overall incidence of anal cancer increased by 2.7% per year and mortality jumped by 3.1% each year.

About VGX-3100

VGX-3100 is a DNA medicine in clinical trials for the treatment of three HPV-16/18 related disease states – anal dysplasia, vulvar dysplasia and cervical dysplasia. The cervical dysplasia program is in late Phase 3 clinical trials (REVEAL1 and REVEAL2). VGX-3100 is designed to utilize the patient's own immune system to clear HPV-16/18-associated high-grade precancerous lesions with the aim of reducing the risk of cancer.

About INOVIO's HPV-Associated DNA Medicines Clinical Programs

This Phase 2 clinical trial 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 inhibitor in a Phase 1 trial experienced a long-term complete response for more two years and counting. Lastly, a pilot study of INOVIO's DNA medicine INO-3107 in HPV-caused recurrent respiratory papillomatosis (RRP) resulted in two out of two patients delaying surgery due to lack of tumor recurrence.

About INOVIO's DNA Medicines Platform

INOVIO has 15 DNA medicine clinical programs currently in development focused on HPV-associated diseases, cancer, and infectious diseases, including coronaviruses associated with MERS and COVID-19 diseases being developed under grants from the Coalition for Epidemic Preparedness Innovations (CEPI) and the U.S. Department of Defense. 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®. The CELLECTRA device uses a brief electrical pulse to reversibly open small pores in the cell to allow the plasmids to enter, overcoming a key limitation of other DNA and other nucleic acid approaches, such as mRNA. Once inside the cell, the DNA plasmids enable the cell to produce the targeted antigen. The antigen is processed naturally in the cell and triggers the desired T cell and antibody-mediated immune responses. Administration with the CELLECTRA device ensures that the DNA medicine is efficiently delivered directly into the body's cells, where it can go to work to drive 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 designed 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 observed in clinical trials.

With more than 2,000 patients receiving INOVIO investigational DNA medicines in more than 7,000 applications across a range of clinical trials, INOVIO has a strong track record of rapidly generating DNA medicine candidates with potential 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 and protect people from infectious diseases, cancer, and diseases associated with HPV. 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, 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, 91% 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 with 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 (DARPA)/Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND)/Department of Defense (DOD), HIV Vaccines Trial Network, International Vaccine Institute (IVI), Kaneka Eurogentec, Medical CBRN Defense Consortium (MCDC), National Cancer Institute, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Ology Bioservices, the Parker Institute for Cancer Immunotherapy, Plumbline Life Sciences, Regeneron, Richter-Helm BioLogics, Thermo Fisher Scientific, 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**.

CONTACTS:

Media: Jeff Richardson, 267-440-4211, **jrichardson@inovio.com**
Investors: Ben Matone, 484-362-0076, **ben.matone@inovio.com**

This press release contains certain forward-looking statements relating to our business, including our plans to develop and manufacture DNA medicines, our expectations regarding our research and development programs, and our ability to successfully manufacture and produce large quantities of our product candidates if they receive

regulatory approval. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including uncertainties inherent in preclinical studies, clinical trials, product development programs and commercialization activities and outcomes, our ability to secure sufficient manufacturing capacity to mass produce our product candidates, 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, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2020 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.

View original content:**http://www.prnewswire.com/news-releases/inovios-vgx-3100-demonstrates-positive-phase-2-efficacy-in-treatment-of-precancerous-anal-dysplasia-caused-by-hpv-1618-301189067.html**

SOURCE INOVIO Pharmaceuticals, Inc.