NEWS RELEASE

INOVIO Announces Positive Results from REVEAL 1, a Phase 3 Pivotal Trial Evaluating VGX-3100, its DNA-based HPV Immunotherapy for the Treatment of High-grade Precancerous Cervical Dysplasia Caused by HPV-16 and/or HPV-18

3/1/2021

Trial achieved primary and secondary efficacy endpoints among all evaluable subjects in the Phase 3 multi-center, randomized, double-blind, placebo-controlled trial

VGX-3100 is the first DNA medicine to achieve efficacy endpoints in a Phase 3 clinical trial

INOVIO also continues to partner with QIAGEN to develop a pre-treatment predictive biomarker with the goal of identifying women expected to respond to VGX-3100

PLYMOUTH MEETING, Pa., March 1, 2021 /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 HPV-associated diseases, today announced it met primary and secondary endpoints among all evaluable subjects for the REVEAL 1 trial. This trial is one of two ongoing pivotal, randomized, double-blind, multi-center, placebo-controlled, Phase 3 trials (REVEAL 1 and REVEAL 2) evaluating the safety, tolerability and efficacy of VGX-3100 to treat HPV-16/18-associated cervical high-grade squamous intraepithelial lesions (HSIL) using the company's proprietary CELLECTRA® 5PSP device.

The trial protocol-defined modified intention to treat (mITT) population (N=193) includes all subjects with endpoint data. For the primary endpoint of histopathological regression of HSIL combined with virologic clearance of HPV-16 and/or HPV-18 at week 36, the percentage of responders was 23.7% (31/131) in the treatment group, versus 11.3% (7/62) in the placebo group (p=0.022; 12.4% difference in percentage, 95%CI: 0.4,22.5), thus achieving statistical significance. All secondary efficacy endpoints were achieved. These endpoints were: a) regression of cervical HSIL to normal tissue combined with HPV-16/18 viral clearance, b) regression of cervical HSIL alone, c) regression of cervical HSIL to normal tissue, and d) HPV-16/18 viral clearance alone.

The trial protocol-defined intention to treat (ITT) population (N=201) includes all randomized subjects regardless of availability of endpoint data and defines those without endpoint data as non-responders. There were eight such subjects (seven in the treatment group, one in the placebo group). Including subjects with missing endpoint data, the percentage of subjects meeting the primary endpoint was 22.5% (31/138) in the treatment group, versus 11.1% (7/63) in the placebo group (p=0.029; 11.4% difference in percentage, 95%CI: -0.4,21.2), which was not statistically significant. All secondary endpoints were achieved except for regression of cervical HSIL alone (12.8% difference in percentage, 95%CI: -0.6,24.5). The reasons for missing endpoint data were: one subject was randomized but was never dosed, one withdrawal due to pregnancy, one withdrawal due to administration error, one withdrawal due to post-administration pain, one loss of follow-up due to COVID19-related travel restrictions, and three losses to follow up due to undetermined reasons. A pre-specified per-protocol (PP) analysis will also be performed upon trial completion.

There were no treatment-related serious adverse events and most adverse events were self-resolving and were considered to be mild to moderate, consistent with earlier clinical trials.

REVEAL 1 and REVEAL 2 are designed to assess and confirm the safety, tolerability, and efficacy of VGX-3100. INOVIO will continue to follow subjects in REVEAL 1 for safety and durability of response for 18 months following the last administration and REVEAL 2 is currently enrolling subjects. INOVIO expects to present REVEAL 1 findings at a scientific meeting this year.

Dr. J. Joseph Kim, President and CEO of INOVIO, said, "INOVIO is very proud to advance VGX-3100 as the first DNA medicine to achieve efficacy endpoints in a Phase 3 clinical trial in all evaluable subjects. We expect VGX-3100, if approved, to be an important therapeutic option for those impacted by HPV-16-/18-related disease. The REVEAL 1 efficacy and safety data also represent an important proof-of-platform for INOVIO's DNA medicines.

Dr. Mark Einstein, MD, MS, FACS, FACOG, Principal Coordinating Investigator for the REVEAL 1 trial, said, "There is a very significant need for a non-surgical therapeutic for young women suffering from HPV-associated cervical dysplasia. These results are very encouraging and show that we are headed in the right direction."

Dr. Prakash Bhuyan, MD, PhD, Senior Vice President and Head of HPV Therapeutic Clinical Development at INOVIO, said, "We thank the investigators, site personnel, and patients who made this research possible. We are excited to be developing a new therapeutic designed to advance women's health. Through our ongoing partnership with QIAGEN, we also plan to develop complementary a biomarker diagnostic test that would enable practitioners to more effectively identify women expected to respond to VGX-3100."

Biomarker Development

In the course of the REVEAL 1 and REVEAL 2 clinical trials, INOVIO continues to pursue development of a pre-treatment RNA-based biomarker blood test which could be used to identify prospective VGX-3100 patients who would be most likely to respond to the immunotherapy. INOVIO believes this will be an important element of VGX-3100 product and market development.

INOVIO announced in February that it is continuing its partnership with QIAGEN to co-develop an in-vitro diagnostic based on RNA sequencing technology to guide clinical decision-making for the use of VGX-3100 in cervical HSIL. This technology had previously been employed in a post-hoc assessment of VGX-3100 Phase 2 data by INOVIO, in which 85% of VGX-3100 treated subjects who had the biomarker experienced regression of HPV-16- and/or HPV-18-associated cervical HSIL.

VGX-3100 REVEAL 1 Phase 3 Cervical Dysplasia Trial Design & Highlights

- Trial participants included 201 women, 18 years of age or older, who have histologically-confirmed cervical HSIL associated with HPV-16 and/or HPV-18, but who were otherwise healthy.
  (**ClinicalTrials.gov** Identifier: NCT03185013)
- Participants received either VGX-3100 or placebo at 0, 4 and 12 weeks (randomized 2:1).
- Trial had 90% statistical power (two-sided 0.05 alpha-level) for the evaluation of the primary endpoint
- Results are based on the demonstration of having no evidence of HSIL associated with HPV-16 and/or HPV-18 from cervical biopsy samples and non-detectability of HPV-16 and/or HPV-18 using the cobas® HPV test from ThinPrep samples, at approximately 6 months following VGX-3100 or placebo administration.
- Based upon blinded aggregate data, the overall safety findings have been consistent with previously reported trials and considered generally safe and well tolerated.
- Data will continue to be collected until the end of the trial (week 88).

About High Grade Cervical Dysplasia (Cervical HSIL)

Cervical HSIL is the pre-cancerous condition of the cervix that immediately precedes the development of invasive cervical cancer. Cervical HSIL is caused by persistent infection with high risk-HPV, including HPV-16 and HPV-18, which collectively confer the highest risk for cervical HSIL development and cervical cancer development. Estimates of the incidence rate of cervical HSIL over recent years have indicated that up to 195,000 cases are diagnosed in the U.S. annually.

About VGX-3100

VGX-3100 is a DNA medicine in clinical trials for the treatment of three HPV-16-/18-related disease states – cervical dysplasia, vulvar dysplasia and anal dysplasia. The cervical dysplasia program is in late Phase 3 clinical trials

(REVEAL 1 and REVEAL 2). VGX-3100 is designed to utilize the patient's own immune system to clear HPV-16/18 virus and HPV-16-/18-associated high-grade precancerous lesions with the aim of reducing the risk of cancer.

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 COVID-19 and MERS for which programs are being developed with funding support from the U.S. Department of Defense and 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®. 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 is designed to ensure 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 3,000 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. INOVIO's lead immunotherapy candidate, VGX-3100, currently in Phase 3 trials for precancerous cervical dysplasia, cleared high-risk HPV-16 and/or HPV-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 infectious disease DNA vaccine development programs in coronaviruses associated with COVID-19 diseases and MERS, Lassa fever, Ebola, and HIV. 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**.

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This press release contains certain forward-looking statements relating to our business, including our plans to develop VGX-3100 for HPV-16/18-associated cervical high-grade squamous intraepithelial lesions, plans to present clinical data at an upcoming scientific meeting, the advantages and potential benefits of our DNA medicines platform, as well as VGX-3100 and our other product candidates, and our expectations regarding our research and development programs, including our plans for a collaboration with QIAGEN to develop an in-vitro diagnostic to guide clinical decision making for the use of VGX-3100. 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 product candidates, 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, 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.

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