NEWS RELEASE

# INOVIO Collaborates with GuardRX and Geneva University Hospitals for Heterologous Booster Clinical Trial of its Ebola DNA Vaccine Candidate, INO-4201

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Clinical trial evaluates INO-4201 as potential booster vaccine following initial vaccination with Ervebo, an FDA-approved Ebola vaccine

PLYMOUTH MEETING, Pa., Nov. 16, 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 that several volunteers have been dosed with its DNA-based, intradermal Ebola vaccine candidate, INO-4201, as part of a randomized, placebo-controlled, Phase 1b clinical trial (**NCT04906629**). The trial will assess whether INO-4201 can be used as a booster in healthy volunteers previously vaccinated with rVSV-ZEBOV (Ervebo®1), an FDA- and EMA-approved viral-based vector Ebola vaccine. It follows INOVIO's pre-clinical and Phase 1 trials which suggested to investigators that INO-4201 was well-tolerated and resulted in 100% seroconversion after two doses.

"We are excited to begin this Phase 1b trial with our intradermal DNA vaccine candidate INO-4201 as a potential Ebola booster vaccine," said Laurent Humeau, Ph.D., Chief Scientific Officer, INOVIO. "Due to the potential for anti-vector immunity after primary Ervebo vaccination, boosting with the same vaccine several years later may not be possible. INOVIO's DNA vaccine candidate INO-4201 has the potential to serve as a booster in the setting of prior Ervebo vaccination depending on its tolerability after multiple administrations. Furthermore, our DNA vaccine candidates could offer scalability and allow for room-temperature storage critical to transportation within tropical environments."

Investigators plan to recruit approximately 50 healthy volunteers to participate in the clinical trial. The trial will evaluate the safety, tolerability, and immunogenicity of INO-4201 in healthy adult volunteers who previously received a single intramuscular injection of rVSV-ZEBOV (Ervebo). Ervebo is approved by the U.S. Food and Drug Administration (FDA) for the prevention of disease caused by Zaire ebolavirus in individuals 18 years of age and

older as a single dose administration. Ervebo is a replication-competent, live, attenuated recombinant vesicular stomatitis virus (rVSV) -based vaccine.

Trial participants will be randomized to either INO-4201 or placebo (4:1 ratio) and will receive an intradermal injection followed by electroporation using INOVIO's CELLECTRA® 2000 smart delivery device. The primary outcome measures include the incidence of adverse events related to INO-4201 from day 0 to 14, and levels of antibodies that bind to Ebola virus surface glycoprotein antigen four weeks after injection.

The trial is being coordinated by GuardRX, a non-profit organization whose goal is to spur development of and access to life-saving therapeutics. Its sponsor is the Geneva University Hospitals, which conducted one of the first randomized trials testing the Ervebo vaccine in 2014. The trial is funded by the U.S. Defense Advanced Research Projects Agency (DARPA). The information herein does not necessarily reflect the position or the policy of the U.S. Government, and no official endorsement should be inferred.

Angela Huttner, M.D., Infectious Disease Consultant, Geneva University Hospitals, and the lead investigator of the study, said, "We are grateful to our volunteers for their critical role in the development of this vaccine, which we hope will be a key player in future Ebola Virus Disease prevention."

Dr. Gary Kobinger, microbiologist, GUARDRx ex-officio (President) and Board Member and Director of the Galveston National Laboratory at the University of Texas Medical Branch, said, "Stimulating long-term protection through affordable booster doses that have the most advantageous safety profiles has become a priority and this is what is being addressed in this study."

INO-4201 is composed of a precisely designed DNA plasmid that is injected intradermally followed by electroporation using a proprietary smart device, which delivers the DNA plasmid directly into cells in the body and is intended to produce a well-tolerated immune response. As one of the only nucleic acid-based vaccine candidates INO-4201 is stable at room temperature for more than a year, at 37°C for more than a month, has a five-year projected shelf life at normal refrigeration temperature and does not need to be frozen during transport or storage.

## About Ebola Virus Disease

The Ebola virus family includes four virus species that cause periodic outbreaks of a highly contagious and lethal human infectious disease – called Ebola Virus Disease (EVD) [US CDC (2021a)]. EVD is characterized by fatigue, vomiting, diarrhea, abdominal pain, severe hemorrhagic fever, and very often death [Feldmann et al New Eng J Med (2020)]. The EBV case fatality ratio (CFR) has averaged 60% to 65% across outbreaks [Nyakarahuka et al BMC Infect Dis (2016); Kawuki et al Pub Hlth (2021)]. The virus is transmitted from wild animals to people then easily spreads via human-to-human transmission. Disturbingly, new research suggests dormant Ebola virus in a previously

infected survivor could re-emerge up to nearly 5 years later and again allow human-to-human transmission [Keita et al Nature (Sept. 15, 2021)]. Since virus discovery, the worst Ebola outbreak was 2014-2016 in West Africa, including more than 28,000 cases, 11,000 deaths, and a few cases that traveled to the U.S. or Europe [WHO (2021)].

Ebola virus is classified as a Category A Priority Pathogen by the U.S. Centers for Disease Control and Prevention (CDC) [CDC (2021b)]. This designation indicates a national security risk, and the US FDA has an accelerated development approval pathway for vaccines against such pathogens. Also, the World Health Organization (WHO) continues to list Ebola Virus Disease as a priority for research and development in emergency contexts [WHO (2021b)] and coordinates planning to prevent and respond to Ebola epidemics [WHO (2016)]. (see references below)

## About INOVIO's DNA Medicines Platform

INOVIO has 15 DNA vaccine candidate clinical programs currently in development and focused on HPV-associated diseases, cancer, and infectious diseases, including programs for Middle East Respiratory Syndrome, Lassa Fever and COVID-19 being developed under grants from the Coalition for Epidemic Preparedness Innovations and the U.S. Department of Defense. Its DNA vaccine candidates are composed of precisely designed 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 vaccine candidates 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. 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 allows the vaccine candidate to be efficiently delivered directly into the body's cells, where it can go to work to drive an immune response. INOVIO's DNA vaccine candidates do not interfere with or change in any way an individual's own DNA. The anticipated advantages of INOVIO's platform are the relative speed at which DNA vaccines can be designed and manufactured; the stability of the candidates, which do not require freezing in storage and transport; and the robust immune response and tolerability that have been observed thus far in clinical trials.

More than 3,900 clinical trial participants have received INOVIO's investigational DNA medicines in more than 12,000 applications across a range of clinical trials.

## 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 company to have clinically demonstrated that a DNA vaccine candidate 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 therapeutic candidate VGX-3100 met primary and secondary endpoints for all evaluable subjects in REVEAL 1, the first of two, Phase 3 trials for precancerous cervical dysplasia, demonstrating ability to destroy and clear both high-grade cervical lesions and the underlying high-risk HPV-16/18. INOVIO is also evaluating INO-4800, a DNA vaccine candidate against COVID-19, in a Phase 2/3 clinical trial; the Phase 3 segment of which has received regulatory approvals to proceed in Colombia, Mexico, Brazil, Philippines, India, Thailand, and the United States. INOVIO's partners, Advaccine Biopharmaceuticals and International Vaccine Institute, are also evaluating INO-4800 in ongoing clinical trials in China and South Korea, respectively.

Partners and collaborators include Advaccine, ApolloBio Corporation, AstraZeneca, The Bill & Melinda Gates Foundation, Coalition for Epidemic Preparedness Innovations, Defense Advanced Research Projects Agency/Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense/Department of Defense, HIV Vaccines Trial Network, International Vaccine Institute, Kaneka Eurogentec, Medical CBRN Defense Consortium, 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. For more information, visit **www.inovio.com**.

## About GUARDRx

Established in 2018, Global Urgent and Advanced Research and Development (GUARD) executes preclinical and clinical development strategies on prophylactic and therapeutic products for neglected diseases. GUARD is a non-profit, non-governmental organization whose goal is to bring prophylactic and therapeutic products that do not have a traditional commercialization pathway. GUARD is committed to facilitating the availability of lifesaving products to the global community including in the event of an infectious disease emergency. GUARD expertise includes preclinical and clinical development of vaccines and therapeutics, regulatory submissions and production of cGMP material; humoral immune responses evaluation using tailored sensitive plate-based ELISA; establish & standardize new diagnostics protocols; submission to appropriate regulatory agencies for Therapeutic Products and Institutional Review Boards (IRBs); production of study final reports, and award data management.

GUARD's main objective is to accumulate clinical data packages within rigorous regulatory processes to support further clinical progression or long-term solutions to orphan diseases for the betterment of the global population. For more information, visit **www.guardrx.org**.

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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, including the planned initiation and conduct of preclinical studies and clinical trials and the availability and timing of data from those studies and trials, 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 pre-clinical 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, 2020, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 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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