



INOVIO and Advaccine Receive Regulatory Allowance for Two Heterologous Prime-Boost Clinical Trials in China Using INO-4800, INOVIO's COVID-19 DNA Vaccine Candidate

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Announcement builds on INOVIO's expanded partnership with Advaccine for INNOVATE, a global efficacy Phase 3 trial for INO-4800

INO-4800's Phase 1 and 2 trial data, combined with recent findings that showed robust T cell level response against the delta variant, position it well for both primary vaccination and boosting

PLYMOUTH MEETING, Pa. and SUZHOU, China, Aug. 9, 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 it has received regulatory allowance for two clinical trials investigating heterologous boosting with INO-4800, its DNA vaccine candidate for COVID-19, through partner and trial-sponsor Advaccine Biopharmaceuticals Suzhou Co., Ltd.

("Advaccine") together with Sinovac Biotechnology ("Sinovac"). The studies will evaluate the safety, tolerability and immunogenicity of heterologous prime-boost sequential immunizations using INO-4800 and CoronaVac®, an inactivated COVID-19 vaccine developed by Sinovac and validated by the World Health Organization (WHO) for emergency use.

China's Center for Drug Evaluation of the National Medical Products Administration has allowed the initiation of two Advaccine-sponsored open-label, positive-control trials to evaluate the safety, tolerability, and immunogenicity of mixed boosted regimens. Both studies, which will be conducted in China, are anticipated to begin this fall and will involve healthy adult subjects 18 years of age or older.

The companies completed cross prime-boost pre-clinical animal tests using INO-4800 and CoronaVac®, demonstrating that the prime-boost strategy can stimulate high-level of antigen specific binding antibodies, neutralizing antibodies by both live-virus neutralization assay and hACE2 receptor blocking assay, and antigen-specific T cell immune responses.

Dr. J. Joseph Kim, President and CEO of INOVIO, said, "With the increased challenge of the highly contagious delta variant and other variants of concern around the world, our work with Advaccine and Sinovac is more important than ever. We are especially proud to expand on our partnership with Advaccine to explore heterologous prime-boosting using INO-4800 to protect more people in the continued fight against COVID-19. If approved, we believe INO-4800 will be well-positioned to serve the vaccine needs of the global community as both a primary and a booster vaccine due to its tolerability, balanced cross-reactive immune responses, and strong thermostability profile that does not require cold or ultra-cold-chain transport."

Dr. Bin Wang, Founder and Chairman of Advaccine, said, "The development of heterologous prime-boost strategies for COVID-19 vaccines with different mechanisms of action is an important research direction in the field of vaccine applications. It provides an efficient solution to synergistically enhance the immunogenicity of vaccines, a key factor to fight against the current increase in global COVID-19 cases and variants of concern. We look forward to partnering with INOVIO and Sinovac on this important effort building on our pre-clinical work, which found that prime-boosting brings the advantages of two different vaccine applications to produce an even stronger and more balanced immune response."

INOVIO previously **announced** the expansion of its partnership with Advaccine to jointly conduct the global Phase 3 segment of the ongoing Phase 2/3 trial called INNOVATE ([INOVIO INO-4800 Vaccine Trial for Efficacy](#)). The global INNOVATE Phase 3 efficacy segment is being prepared in multiple countries with an initial focus on Latin America, Asia and Africa. The primary endpoint will be virologically confirmed COVID-19 cases. The 2.0 mg dose was selected from the Phase 2 segment, where INO-4800 was shown to be generally well-tolerated and immunogenic across all adult age groups.

Recent analysis using clinical samples showed that INO-4800 maintained a robust T cell level against the delta variant, when compared to T-cell responses from the original wildtype strain, further demonstrating INO-4800's ability to generate CD8 T cells, which INOVIO believes will be crucial in mitigating against rising variants such as delta. This data complements the Phase 1 and 2 trial data for INO-4800, which highlighted key advantages across INOVIO's DNA medicines platform – specifically, the ability to induce a balanced immune response that includes engagement of both T cells and B cells.

In parallel with INO-4800, INOVIO is also developing a novel, pan-COVID, second-generation vaccine candidate, INO-4802, which is designed to protect against current and future variants of concern. In May 2021, INOVIO published a manuscript in **BioRxiv** that demonstrated cross-reactive immune responses against current and emerging viral variants using INO-4802 as either a first-line vaccine or potentially as a booster for individuals previously immunized with various wildtype strain-matched vaccines. Specifically, INO-4802 induced potent neutralizing antibodies and T cell responses against the original wildtype strain as well as against alpha, beta, gamma, and delta

variants in pre-clinical models.

About INO-4800

INO-4800 is INOVIO's DNA vaccine candidate against SARS-CoV-2, the novel coronavirus that causes COVID-19. INOVIO has extensive experience working with coronaviruses. The company recently **dosed** its first participant in a Phase 2 trial for INO-4700, its DNA vaccine candidate for the prevention of Middle East Respiratory Syndrome (MERS), a coronavirus that is 100 times deadlier than COVID-19.

Composed of a precisely designed DNA plasmid, INO-4800 is injected intradermally followed by electroporation using a proprietary smart device delivering the DNA plasmid directly into cells in the body and is intended to produce a well-tolerated immune response. INO-4800 is the only nucleic-acid based vaccine that is stable at room temperature for more than a year, at 37o 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 – all of which Inovio believes are important considerations for mass immunizations.

About INOVIO's DNA Medicines Platform

INOVIO has 15 DNA medicine 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. DNA medicines 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 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. 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 the relative speed at which 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, 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 the 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 met primary and secondary endpoints for all evaluable subjects in REVEAL 1, in 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 and 18. INOVIO is also evaluating INO-4800, a DNA vaccine candidate against COVID-19, in a Phase 2 clinical trial in the U.S., as well as Phase 2 trials in China and South Korea. 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, Plumblin 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.

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This press release contains certain forward-looking statements relating to our business, including our plans to develop and commercialize DNA medicines, our expectations regarding our research and development programs, including the planned initiation and conduct of pre-clinical 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 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 March 31, 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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