NEWS RELEASE

# INOVIO's COVID-19 DNA Vaccine INO-4800 Provides Protection with Memory Immune Responses In Non-Human Primates Challenged with SARS-CoV-2 Virus

7/30/2020

- INO-4800 showed durable antibody and T cell responses in rhesus macaques for 4 months
- INO-4800 is the only vaccine to demonstrate long-term protection in non-human primates challenged with SARS-CoV-2 virus 13 weeks from vaccination
- Memory T and B cell responses resulted in reduced viral loads and faster viral clearance in macaques' lungs and nasal passages
- INO-4800 vaccination generated antibodies neutralizing both the earlier strain of virus as well as the mutant variant (D614G) that has emerged with greater infectivity, and now accounts for >80% of newly circulating virus
- No antibody-dependent enhanced disease events were reported

PLYMOUTH MEETING, Pa., July 30, 2020 /PRNewswire/ -- INOVIO (NASDAQ:INO), a biotechnology company focused on rapidly bringing to market precisely designed DNA medicines to treat and protect people from infectious diseases and cancer, today announced that its COVID-19 DNA vaccine INO-4800 targeting SARS-CoV-2 was effective in protecting non-human primates (NHPs; specifically rhesus macaques) from live virus challenge 13 weeks after the last vaccination. These protective results were mediated by memory T and B cell immune responses from INO-4800 vaccination.

These results, submitted to a peer-reviewed journal and also published today on the non-peer reviewed online preprint site **bioRxiv**, demonstrate that INO-4800 reduced viral load in both the lower lungs and nasal passages in macaques that received two doses of INO-4800 (1 mg) four weeks apart and then were challenged with live virus 13 weeks after the second dose (study week 17). The reduced viral loads following exposure to SARS-CoV-2 infection at this timeframe demonstrate an important durable impact mediated by INO-4800. This is the first time a vaccine protection in non-human primates was reported from memory immune responses as previously reported monkey vaccine challenge studies were conducted at the time near their peak immune responses (1-4 weeks from their last vaccination).

INO-4800-treated animals demonstrated seroconversion after a single vaccination, with protective neutralizing antibodies and T cells lasting in their blood more than four months after the initial dose. The antibody levels were similar to or greater than those seen in patients who have recovered from COVID-19, the infection caused by SARS-CoV-2, and the T cell responses were significantly higher than those from convalescent patients.

Dr. J. Joseph Kim, President and Chief Executive Officer of INOVIO, said, "All other previously reported NHP vaccine protection studies actually challenged the animals at the peak of their immune response. Our study demonstrates that INO-4800 could provide protection in a more real-world setting, where vaccine-generated memory immune responses protected NHPs for more than 3 months (13 weeks) from the last vaccination. Given the importance of protective antibody and T cell responses, this study gives us more confidence as we continue to advance INO-4800 in the clinic. We believe INO-4800 holds significant potential to help address this global public health crisis."

B cells are responsible for producing the antibodies that recognize SARS-CoV-2, while T cells play a role in killing the virally infected cells as well as supporting the B cell response. The published data support that immunization with INO-4800 limits active viral replication and has the potential to reduce severity of disease, as well as reduced viral shedding in the nasal cavity. In the study, researchers assessed the ability of INO-4800 to induce acute and memory T cell and B cell immune responses, including neutralizing antibody responses against both early virus as well as now-dominant G614 mutant variants. To INOVIO's knowledge, this is the first report of vaccine-induced responses driving immunity against G614 variants. A strong anamnestic or memory T and B cell responses were demonstrated following challenge with the live virus.

"As we eagerly anticipate initiating a Phase 2/3 efficacy trials this summer, an animal challenge is currently the closest thing we have to testing a vaccine's efficacy when confronting a live virus. We are very encouraged with the duration of protection that INO-4800 demonstrated in this NHP study and look forward to reassessing its impact on durability of response at 12 months out from our other ongoing non-human primate and animal challenge studies," said Dr. Kate Broderick, Ph.D., INOVIO's Senior Vice President, Research & Development.

"In addition to safety and efficacy, it is essential that any vaccine targeting SARS-CoV-2 generates a relevant durability of response," Dr. Broderick added. "A vaccine that only provides protection for a very short period of time is not going to realistically solve the problem of this pandemic."

A separate NHP study evaluating the durability of INO-4800 at 12 months after vaccination is currently under way. INO-4800 also has been selected by U.S. Operation Warp Speed for its COVID-19 non-human primate challenge study.

In May, the peer-reviewed journal Nature Communications published an INOVIO study ("Immunogenicity of a DNA

vaccine candidate for COVID-19") showing that vaccination with INO-4800 generated robust binding and neutralizing antibody and T cell responses in mice and guinea pigs. The study was funded by a grant from the Coalition for Epidemic Preparedness Innovations (CEPI).

## About INO-4800

INO-4800 is INOVIO's DNA vaccine candidate created to protect against the novel coronavirus SARS-CoV-2, which causes COVID-19. INO-4800 is currently in Phase 1 trials in the U.S. and a Phase 2/3 trial is planned for the summer. Interim Phase 1 results showed a favorable safety profile and strong immunogenicity, including antibody and T cell responses. The Phase 1 study recently expanded to include adults over the age of 65 with no age limit given the propensity for COVID-19 to severely impact the health of older people. INO-4800 also is in Phase 1/2 trials for COVID-19 in South Korea and China.

In animal studies, INO-4800 has demonstrated robust and durable T cell and B cell acute and memory responses in a non-human primate challenge study showing protective immune responses in both nasal passages and lungs. INO-4800 also was selected by U.S. Operation Warp Speed for its COVID-19 non-human primate challenge study.

INO-4800 was designed using INOVIO's proprietary DNA medicine platform rapidly after the publication of the genetic sequence of SARS-CoV-2. INOVIO has extensive experience working with coronaviruses and is the only company with a Phase 2 vaccine for a related coronavirus that causes Middle East Respiratory Syndrome (MERS).

INO-4800 is the only nucleic-acid based vaccine that is stable at room temperature for more than a year and does not need to be frozen in transport of storage, which are important factors when implementing mass immunizations.

## 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 demonstrated 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), GeneOne Life Science/VGXI, HIV Vaccines Trial Network, International Vaccine Institute (IVI), 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, 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**.

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 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. 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, our Quarterly Report on Form 10-Q for the quarter ended June 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-covid-19-dna-vaccine-ino-4800-provides-protection-with-memory-immune-responses-in-non-human-primates-challenged-with-sars-cov-2-virus-301103039.html**

SOURCE INOVIO Pharmaceuticals, Inc.