NEWS RELEASE

INOVIO Announces Promising Interim Results from Ongoing Proof-of-Concept Clinical Trial of DNA-Encoded Monoclonal Antibodies (DMAbs) for COVID-19

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- Long-lasting in vivo antibody production: DMAb levels remained stable for 72 weeks in all participants (n=24) who have reached that timepoint
- No anti-drug antibodies (ADA): no immune rejection of the DMAbs was detected across ~1,000 blood samples, unlike other gene-based antibody delivery approaches where ADA formation has been a challenge
- Well-tolerated: most common side effects were mild, temporary injection site reactions such as pain and redness; no serious adverse events (SAEs) related to study drug
- Effective target binding: expressed DMAbs successfully bound to the SARS-CoV-2 Spike protein receptor-binding domain (RBD), confirming functional activity through week 72

PLYMOUTH MEETING, Pa., March 13, 2025 /PRNewswire/ -- INOVIO (NASDAQ: INO), a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-related diseases, cancer, and infectious diseases, today announced promising interim results from an ongoing Phase 1 proof-of-concept trial evaluating DMAbs for COVID-19. In the trial, 100% (24/24) of participants who have reached week 72 maintained biologically relevant levels of DMAbs, confirming the durability of in vivo antibody production. Notably, no participant developed anti-drug antibodies (ADA), a common challenge observed in other gene-based delivery platforms, such as adeno-associated virus (AAV) mediated antibody expression. Additionally, the DMAbs were well tolerated, with the most common side effects being mild, temporary injection site reactions, such as pain and redness. The trial is being led by The Wistar Institute in collaboration with INOVIO, AstraZeneca, and clinical investigators at the Perelman School of Medicine at the University of Pennsylvania.

"This study provides the first clinical proof-of-concept that DNA-encoded monoclonal antibodies can be durably and tolerably expressed in humans," said David B. Weiner, Ph.D, Executive Vice President of The Wistar Institute and

lead investigator for the study. "These findings could represent a breakthrough as they demonstrate the potential of DMAb technology to overcome traditional monoclonal antibody production challenges, such as short half-life and anti-drug immune responses, making it a promising platform for a broad range of diseases. This technology has the potential to transform treatments for infectious diseases, as well as cancer and metabolic disorders by enabling long-term expression of therapeutic antibodies and other proteins."

"One of the biggest hurdles for gene-based antibody delivery has been the immune system's response to the vector or the antibody itself, leading to anti-drug antibodies that can limit how long a treatment will be effective," said Pablo Tebas, M.D., a professor of Infectious Diseases at Penn. "Our DNA-based approach has demonstrated sustained antibody expression without generating ADA. And because antibodies are remaining active for longer, our approach may be a potentially promising long-term solution for conditions requiring continuous therapeutic protein delivery."

INOVIO's Chief Scientific Officer, Laurent Humeau, Ph.D. added: "We believe these data highlight the potential to apply our DNA Medicines technology to deliver a broad spectrum of therapeutic proteins that could be used to treat diseases with missing or defective proteins. We'd like to thank our partners in advancing this important new technology and we look forward to working with them to complete this trial and on future research where we anticipate exploring broader applications of our technology for long-term therapeutic protein delivery."

A manuscript describing interim results from the trial has been uploaded to **Research Square** for early dissemination and is under peer review by a leading scientific journal for publication. The consortium plans to present interim results from the trial at upcoming scientific conferences in 2025.

About the Phase 1 Trial

The Phase 1 trial is the first clinical study to report using synthetic DNA technology to enable in vivo production of monoclonal antibodies directly from muscle cells. Participants received an intramuscular (IM) injection of synthetic DNA plasmids encoding AZD5396 and AZD8076 (derived from AstraZeneca's cilgavimab and tixagevimab) delivered via INOVIO's proprietary CELLECTRA 2000 electroporation (EP) device. This delivery method temporarily increases cell permeability, which is intended to facilitate efficient DNA uptake and enable sustained antibody production.

The study is an open-label, single center, dose-escalation trial. Enrollment began in May 2022 and was completed in March 2024. The most common side effects observed were temporary local injection site reactions, such as pain and erythema, associated with the administration of the study product. There were three SAEs all of which were considered unrelated to the study product.

Now in its third year, the trial is led by The Wistar Institute in collaboration with INOVIO, AstraZeneca, and clinical investigators at the University of Pennsylvania. It is funded by the Coronavirus Aid, Relief, and Economic Security

Act (CARES Act) and the Defense Advanced Research Projects Agency (DARPA).

About INOVIO's DNA Medicines Platform

INOVIO's DNA medicines platform has two innovative components: precisely designed DNA plasmids, delivered by INOVIO's proprietary investigational medical device, CELLECTRA®. INOVIO uses proprietary technology to design its DNA plasmids, which are small circular DNA molecules that work like software that the body's cells can download to produce specific proteins to target and fight disease. INOVIO's proprietary CELLECTRA® delivery devices are designed to optimally deliver its DNA medicines to the body's cells without requiring chemical adjuvants or lipid nanoparticles and without the risk of the anti-vector response historically seen with viral vector platforms.

About INOVIO

INOVIO is a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-related diseases, cancer, and infectious diseases. INOVIO's technology optimizes the design and delivery of innovative DNA medicines that teach the body to manufacture its own disease-fighting tools. For more information, visit **www.inovio.com**.

Forward-Looking Statements

This press release contains certain forward-looking statements relating to INOVIO's business, including the planned publication of data from clinical trials and the potential benefits of INOVIO's DMAb technology platform. 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 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, 2023, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, 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 the 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.

This project was supported by the Joint Program Executive Office for Chemical, Biological, Radiological and Nuclear Defense (JPEO-CBRND) Joint Project Lead for Enabling Biotechnologies (JPL CBRND EB) in collaboration with the Defense Health Agency (DHA) COVID funding initiative for (Phase 1, dose-escalation trial of the safety and pharmacokinetics of SARS-CoV-2 DNA-encoded monoclonal antibodies (DMAb) in healthy adults, The Wistar Institute, Inovio Pharmaceuticals, AstraZeneca, University of Pennsylvania, HR0011-21-9-0001) for this effort.

The views expressed in this press release reflect the views of the authors and do not necessarily reflect the position of the Department of the Army, Department of Defense, nor the United States Government. References to non-federal entities do not constitute or imply Department of Defense or Army endorsement of any company or organization.

Penn and Dr. Weiner have either received, or may receive in the future, financial consideration related to the licensing of certain Penn intellectual property to INOVIO. Dr. Weiner is a member of the Scientific Advisory Board and Board of Directors for INOVIO.

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