



NEWS RELEASE

# Inovio's dMAb™ PD-1 Checkpoint Inhibitors Demonstrate Higher and More Prolonged Expression Compared to Native Pembrolizumab and Nivolumab Sequences In Preclinical Studies

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PD-1 DNA-encoded monoclonal antibodies (dMAbs) highlighted in a paper published in cancer journal *Oncotarget* PLYMOUTH MEETING, Pa., Jan. 15, 2019 /PRNewswire/ -- Inovio Pharmaceuticals, Inc. (NASDAQ: INO) announced today the successful development of optimized DNA-encoded monoclonal antibodies (dMAbs™) targeting the immune checkpoint molecule PD-1. The breakthrough preclinical data demonstrated that a single injection of synthetic designer dMAb versions of pembrolizumab (KEYTRUDA®) or nivolumab (OPDIVO®) sequences targeting PD-1 protein can be robustly redeveloped to be expressed directly in vivo in mice for up to several months. Furthermore, Inovio's proprietary sequence optimization of the molecular design of these therapeutics resulted in significantly improved expression compared to the original KEYTRUDA and OPDIVO native sequences while maintaining identical binding capabilities.

These published dMAb results demonstrate the potential of advancing of a new generation of checkpoint inhibitors with multiple benefits including: 1) simplifying the patient regimen for checkpoint blockade therapy - converting 90-minute intravenous infusions administered every three weeks with currently marketed protein-based mAbs into a single local injection of dMAbs, 2) possibly resulting in more consistency of expression in vivo providing improved benefits for the patient, and 3) through simple additional modifications and simplified dMAb combination formulations, engender further improved functions rapidly providing additional clinical benefit. The PD-1 dMAb results were published in the recent edition of *Oncotarget* in an article entitled, "Simplifying checkpoint inhibitor delivery through in vivo generation of synthetic DNA-encoded monoclonal antibodies (dMAbs)," by Inovio's collaborators at The Wistar Institute.

Dr. J. Joseph Kim, Inovio's President and CEO, said, "We are rapidly pioneering a potentially breakthrough class of medicines – dMAbs – produced directly in the human body. PD-1/PD-L1 targeting checkpoint inhibitor mAb products represent some of the most important advancements in immuno-oncology today. We look forward to advancing our PD-1 targeting dMAb products as potentially better versions of blockbusters KEYTRUDA and OPDIVO – with whole new sets of IP behind them – through corporate partnerships,

external funding and collaborations."

Inovio recently initiated the first human study of its dMAb technology. In addition to demonstrating safety and tolerability, the Phase 1 dose-escalation study of INO-A002 (for preventing or treating Zika virus infection) will assess initially the level of the body's production of the Zika dMAb over several doses. Using direct delivery into the body, the genetic instructions provided by the designed synthetic dMAbs delivered locally by the CELLECTRA® platform, instruct the body's cells to become a customized patient specific factory which manufactures their own therapeutic antibody products, enabling a major leap in antibody technology.

Traditional monoclonal antibodies represent the largest segment of pharmaceutical markets today, accounting for more than \$100 billion in pharmaceutical sales each year, with treatments spanning cancer, infectious diseases, inflammation and cardiovascular diseases. With its synthetic design and in-patient production, dMAb products represent a disruptive entrant to this important class of pharmaceuticals. Inovio and its collaborators have already received over \$60 million in non-dilutive grant funding to advance its dMAb platform in the last few years. There is a significant interest in dMAb's as a disruptive entrant to a highly profitable overall mAb market as well as its unique applicability for rapid responses against emerging global infectious disease threats and for addressing critical vaccine limitations.

In the past few years Inovio and collaborators have published multiple impactful papers consistently demonstrating potent preclinical data from the dMAb platform, with therapeutic displays spanning protection against deadly infections to eliminating cancers and lowering life-threatening levels of cholesterol. In this regard dMAbs offer unique features for rapid production, deployment and advancement of new mAb-like biologics, with much increased efficiency. In addition, the dMAb's constructed in vivo likely have additional advantages such as expression profiles, as well as patient specific glycosylation, and unlike traditional mAb approaches, there is no reliance on in vivo tissue culture and costly or time consuming production systems. Inovio has previously published successful animal testing of dMAbs targeting the immune checkpoint molecule CTLA-4 (Duperret et al. Cancer Res. 2018). The preclinical study demonstrated that highly optimized dMAbs targeting mouse CTLA-4 protein can be robustly expressed in vivo, and can drive therapeutic anti-tumor immune responses in established disease models. Importantly, Inovio's dMAb constructs for anti-human CTLA-4 antibodies ipilimumab and tremelimumab, achieved high levels and prolonged expression for months from a single delivery. Inovio has multiple patents awarded in this space including the first two patents from the U.S. patent office covering this specific dMAb technology granted last quarter.

KEYTRUDA® is a registered trademark of Merck & Co. (MRK); OPDIVO® is a registered trademark of Bristol-Myers Squibb Company (BMY).

## About Inovio's DNA-based Monoclonal Antibody Platform

Traditional monoclonal antibodies are manufactured outside the body in bioreactors, typically requiring costly large-scale manufacturing facility development and laborious production. Inovio's disruptive dMAb technology has the potential to overcome these limitations by virtue of their simplified design using novel plasmid vectors and unique formulations allowing for rapidity of

development, product stability, ease of manufacturing and deployability, ultimately all resulting in increases in cost effectiveness, providing potential new avenues for treating a range of diseases. These dMAbs are delivered directly into cells of the body using CELLECTRA® and the encoded monoclonal antibody is then produced by the locally transfected cells. Previously published studies show that a single administration of a highly optimized DNA-encoded monoclonal antibody targeting Ebola virus produced a high level of expression of the antibody in the bloodstream of mice that was protective against lethal animal challenge; Additional studies similarly reported data showing that dMAb products against flu, chikungunya and dengue protected animals against lethal challenge. In addition the team has reported delivery of dMAbs that impact prostate as well as breast and ovarian cancers in animals.

## About Inovio Pharmaceuticals, Inc.

Inovio is a late-stage biotechnology company focused on the discovery, development, and commercialization of DNA immunotherapies that transform the treatment of cancer and infectious diseases. Inovio's proprietary platform technology applies next-generation antigen sequencing and DNA delivery to activate potent immune responses to targeted diseases. The technology functions exclusively in vivo, and has been demonstrated to consistently activate robust and fully functional T cell and antibody responses against targeted cancers and pathogens. Inovio is the only immunotherapy company that has reported generating T cells whose killing capacity correlates with relevant clinical outcomes. Inovio's most advanced clinical program, VGX-3100, is in Phase 3 for the treatment of HPV-related cervical pre-cancer. Also in development are Phase 2 immuno-oncology programs targeting head and neck cancer, bladder cancer, and glioblastoma, as well as platform development programs for hepatitis B, Zika, Ebola, MERS, and HIV. Partners and collaborators include MedImmune, Regeneron, Roche/Genentech, ApolloBio Corporation, The Bill & Melinda Gates Foundation, The Wistar Institute, University of Pennsylvania, Parker Institute for Cancer Immunotherapy, CEPI, DARPA, GeneOne Life Science, Plumblin Life Sciences, Drexel University, NIH, HIV Vaccines Trial Network, National Cancer Institute, U.S. Military HIV Research Program, and Laval University. For more information, visit [www.inovio.com](http://www.inovio.com).

This press release contains certain forward-looking statements relating to our business, including our plans to develop electroporation-based drug and gene delivery technologies and DNA vaccines, our expectations regarding our research and development programs, including the planned initiation and conduct of clinical trials and the availability and timing of data from those 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 and product development programs, 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 vaccines, our ability to support our pipeline of SynCon® active immunotherapy and vaccine 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, 2017, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018 and other regulatory filings we make from time to time. 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 licensed 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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