NEWS RELEASE

Inovio Further Demonstrates Potency of its DNA-Encoded Monoclonal Antibody (dMAb™) Platform in Three Preclinical Publications and Prepares for First Clinical Trial in Early 2019

2018-11-26

PLYMOUTH MEETING, Pa. , Nov. 26, 2018 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ: INO) announced today that three recent published studies of its DNA-Encoded monoclonal antibody (dMAb™) technology showed impressive results in treating cardiovascular disease and in preventing infection from the Ebola virus and Lyme disease-causing bacteria in preclinical models. Leveraging several recent published positive preclinical data, Inovio plans to initiate a first clinical study of an infectious disease treatment dMAb product early next year with full external funding.

Traditional monoclonal antibodies represent the largest segment of pharmaceutical markets today, accounting for more than $50 billion in pharmaceutical sales each year, with treatments spanning from cancer and infectious diseases to inflammation and cardiovascular diseases. With its synthetic design and in-patient production, Inovio's dMAb products could provide new, disruptive entrants to this important class of drugs. When delivered directly into the body, the genetic instructions provided by the DNA plasmid enables the patient's own cells to become the factory which manufactures the therapeutic antibody products. Inovio has received over $60 million in non-dilutive grant funding to advance its dMAb platform in the last few years. Additional support for Inovio's dMAb platform recently came from the Bill & Melinda Gates Foundation which invested $2.2 million to advance Inovio's dMAb platform and to support the development of next-generation clinical delivery devices for dMAbs. In this regard, there is a significant interest in Inovio dMAbs' high applicability for rapidly responding to emerging global infectious disease threats and addressing critical vaccine limitations.

In the first of the three published studies, Inovio applied its dMAb technology against cardiovascular disease in a preclinical study directed against PCSK9, a protein key to regulating cholesterol levels in the bloodstream. Elevated, low-density lipoprotein cholesterol (LDL-C) is a major risk factor for cardiovascular disease, the leading cause of death in the U.S. and worldwide. Statins are effective and widely used cholesterol-lowering medications, but have been associated with a number of side effects that have prompted development of alternative treatment strategies, including monoclonal antibodies targeting the PSCK9 protein that result in reduced degradation of LDL-C receptors on liver cells and increased cholesterol clearance from blood circulation. Several PCSK9

inhibitors in the form of monoclonal antibodies have already been approved for use, including Repatha® (evolocumab) by Amgen and PRALUENT® (alirocumab) by Regeneron/Sanofi. Both of these products are dosed as injections every 2 weeks or 4 weeks. They target and inactivate PCSK9, dramatically reducing the amount of harmful LDL cholesterol circulating in the bloodstream.

Impressively, a single intramuscular administration of Inovio's dMAb drove robust anti-PCSK9 antibody expression within days and for up to two months, resulting in a substantial increase in the presence of LDL-C receptors on liver cells. This in turn resulted in a significant decrease in total cholesterol and non-high-density lipoprotein cholesterol (non-HDL-C), two important parameter for evaluating cardiovascular risk, opening the door for further development of this approach as a simple, less frequent and cost-effective therapy. These results were reported in a paper published in Molecular Therapy, by Inovio researchers and their academic collaborators.

The second study, published in the journal Cell Reports, demonstrated that Inovio's anti-Ebola dMAb product protected all animals from a lethal Ebola virus challenge. In fact, results showed that dMAbs were expressed over a wide window of time and offered complete and long-term protection against this lethal virus challenge. These studies were funded by a $45 million grant from DARPA to Inovio and collaborators to develop both dMAb-based therapy and DNA vaccines against Ebola.

The third dMAb study showed it can block transmission of the bacteria that causes Lyme disease in mice. These results, published on-line in the Journal of Infectious Diseases , represent the first demonstration using dMAbs that block transmission of the Lyme disease-causing bacteria (Borrelia) in animal models. In the study, plasmid DNA-encoded anti-OspA monoclonal antibodies inoculated in mice achieved a very high serum antibody concentration of >6 µg/mL. Among mice injected with the wildtype dMAb or the protein control wildtype MAb, about 75% in each group were protected against an acute challenge by Borrelia-infected ticks. Interestingly, when the dMAb was further optimized with SynCon sequence engineering, the protection level increased even further to 92%, fully demonstrating the power of Inovio's dMAb approach. These results are also important because there is no marketed vaccine against Lyme disease.

In the arena of global infectious diseases, Inovio's dMAb platform has many advantages over a conventional vaccine approach, including immediate protection with an antibody of known specificity and concentration, and independence from the age-dependent responses to active immunization. While a traditional protein antibody delivery is an attractive approach for intervention against pathogens, the expense of bioprocessing and cold chain requirements limit this approach for dissemination to global populations.

Dr. Laurent Humeau , Inovio's Chief Scientific Officer, said, "We are truly excited about these findings that support the flexibility and versatility of our dMAb platform as a next generation approach that can be optimized for a wide host of applications. Just in the past 18 months Inovio has published 10 impactful papers consistently demonstrating potent preclinical data from its dMAb platform, with therapeutic displays spanning protection against deadly infections to eliminating cancers and lowering life-threatening levels of cholesterol. Inovio's dMAbs offer unique features that could remove the difficult and costly issues surrounding the manufacture of monoclonal antibody drugs. In addition, we also published the first of our own dMAb checkpoint inhibitors with anti-cancer effects;

and the U.S. patent office just granted the first two patents covering our dMAb technology last quarter. Inovio plans to develop a pipeline of multiple dMAb products through corporate partnerships, external funding and collaborations, starting with advancing our first dMAb product into clinical testing early next year."

Inovio's recently published dMAb results can be found in the peer-reviewed journals below:

- Molecular Therapy -- "Development of Novel DNA-encoded PCSK9 Monoclonal Antibodies as Lipid-lowering Therapeutics."
- Cell Reports -- "In Vivo-delivered Synthetic Human dMAbs Protect Against Ebola Virus Infection in a Mouse Model."
- The Journal of Infectious Diseases – "Anti-OspA DNA-Encoded Monoclonal Antibody Prevents Transmission of Spirochetes in Tick Challenge Providing Sterilizing Immunity in Mice."

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, rapidity of development, product stability, ease of manufacturing and deployability, and cost effectiveness, thereby providing potential new avenues for treating a range of diseases. Another significant advancement seen in Inovio dMAb technologies is that the optimized genes for a desired monoclonal antibody is encoded in a DNA plasmid, which is produced using very cost effective and highly scalable fermentation techniques. These plasmids are delivered directly into cells of the body using electroporation and the encoded monoclonal antibody is then directly produced by these cells. Previously published studies show that a single administration of a highly optimized DNA-based monoclonal antibody targeting HIV virus produced a high level of expression of the antibody in the bloodstream of mice; Inovio similarly reported data showing that dMAb products against flu, Ebola, chikungunya and dengue protected animals against lethal challenge.

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 in 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, Plumbline 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** .

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.

CONTACTS:
Investors: Ben Matone , 484-362-0076, **ben.matone@inovio.com**
Media: Jeff Richardson , 267-440-4211, **jrichardson@inovio.com**

Source: Inovio Pharmaceuticals, Inc.