



NEWS RELEASE

Inovio's DNA-based Monoclonal Antibody and DNA Vaccine Provide 100% Protection Against Lethal Chikungunya Virus Challenge in Preclinical Study

2016-03-22

Ability of unique dMAb and DNA vaccine combination to induce rapid short-term and long-term protection has broad implications for infectious disease prevention and control

PLYMOUTH MEETING, Pa., March 22, 2016 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) announced today that its novel dMAb antibody and DNA vaccine targeting the chikungunya virus (CHIKV) provided 100% protection against a lethal virus challenge in mice. This breakthrough data was published in the latest issue of *The Journal of Infectious Diseases* in a paper, "Rapid and long-term immunity elicited by DNA encoded antibody prophylaxis and DNA vaccination against Chikungunya virus," prepared by Inovio authors and their academic collaborators. While conventional vaccine and marketed monoclonal antibody technologies have shown limited ability to provide an effective solution to CHIKV to date, Inovio's DNA vaccine and dMAb products show potential, separately and in combination, to offer immediate and long term protection to large populations from CHIKV infection.

Over the years, CHIKV outbreaks have occurred in Africa, Asia, Europe, and throughout the Indian and Pacific Oceans, with local transmission in over 43 countries infecting millions of people. In late 2013, CHIKV was found for the first time in the Americas on islands in the Caribbean and spreading to other parts of the western hemisphere, including the United States. Along with a dramatic increase in cases and geographic spread of CHIKV infection and disease there has been a reported increase in morbidity and mortality, suggesting increased virulence. The concern for even greater potential global outbreaks underscores the need for targeted anti-viral interventions.

Inovio previously published that its SynCon® DNA vaccine for CHIKV provided durable 100% protection in mice. In this study, a single intramuscular injection of a DNA plasmid encoding a monoclonal antibody targeting CHIKV protected mice from a lethal dose of the virus. The protection expressed by these dMAb antibodies was very rapid, with 100% survival in mice challenged with lethal enhanced CHIKV disease as early as two days after dMAb product administration. In comparison, vaccine-driven protection can take weeks to months to reach peak efficacy levels, but providing better long term protection compared to a dMAb product. Inovio's

study demonstrates that its CHIKV dMAb antibody and DNA vaccine could be used as an ideal combination to provide both rapid short-term as well as long-term protection.

Dr. J. Joseph Kim, Inovio's President & CEO, said, "This study is significant for two reasons. First, this is our third published study (two previous in HIV and dengue) demonstrating the protective efficacy of our dMAb products. Inovio is rapidly building its dMAb product development program targeting cancer and infectious diseases. Notably, DARPA is providing us over \$56 million to specifically develop dMAb products against influenza, antibiotic-resistant bacteria, and Ebola.

"Second, this study demonstrates that Inovio's dMAb products and DNA vaccines could be a powerful combination to provide robust immediate and long term protection not only for CHIKV but also other infectious diseases. Inovio is the only organization to report such results in any disease by using a DNA-based monoclonal antibody, with published preclinical data in dengue as well, and we now are creating Zika, MERS, and Ebola dMAb products. Our MERS and Ebola vaccines are in phase I clinical studies and we will advance our Zika vaccine to phase I before year end. We also aim to test further combinations."

Chikungunya does not often result in death, but the symptoms can be severe and disabling and include extreme pain, headache, muscle pain, joint swelling, or rash. The chikungunya virus is carried by the same mosquito species which carry Zika, dengue and West Nile virus (WNV). Inovio previously published robust immunogenicity and challenge protection data for its SynCon® CHIKV, dengue, and WNV vaccine candidates. Inovio's chikungunya program builds on its extensive preclinical development experience with various mosquito-borne viruses.

Paper Abstract

Background: Vaccination and passive antibody therapies are critical for controlling infectious diseases. Passive antibody administration has limitations including the necessity for purification and the delivery of multiple injections required for efficacy. Vaccination is associated with a lag phase before generation of immunity. Novel approaches reported here utilize the benefits of both methods for the rapid generation of effective immunity.

Methods: An antibody-based prophylaxis/therapy entailing the electroporation-mediated delivery of synthetic plasmids, encoding biologically active anti-Chikungunya virus envelope mAb (designated dMAb), was designed and evaluated for anti-viral efficacy as well as for the ability to overcome shortcomings inherent with conventional active vaccination by a novel passive immune-based strategy.

Results: One intramuscular injection of the CHIKV-dMAb produced antibodies in vivo more rapidly than active vaccination with a CHIKV-DNA vaccine. This dMAb neutralized diverse CHIKV clinical isolates and protected mice from viral challenge. Combinations of both afford rapid as well as long-lived protection.

Conclusions: We report that a DNA based dMAb strategy induces rapid protection against an emerging viral infection, which can be combined with DNA vaccination providing a uniquely both short term and long-term protection against this emerging infectious disease. These studies have implications for pathogen treatment and control strategies.

About Inovio's dMAb Technology

Unlike conventional monoclonal technology, which involves constructing protein-based antibodies and manufacturing them in cell culture in a complex and costly process, Inovio's patent-protected DNA-based monoclonal antibody technology encodes the DNA sequence for a specific monoclonal antibody in a highly optimized plasmid, which would be delivered directly into a subject's arm using electroporation. Cells in the body would then produce the encoded monoclonal antibody molecules, with intended functional activity including high antigen-binding and neutralization capabilities against the targeted disease. Monoclonal antibodies offer the benefit of inducing a rapid onset of the immune response. The current monoclonal antibody product market is well over \$50 billion. Overall, Inovio's dMAb technology may provide clear advantages over conventional monoclonal antibody technology, including faster development, easier product manufacturing, and more favorable pharmacokinetics.

About Inovio Pharmaceuticals, Inc.

Inovio is taking immunotherapy to the next level in the fight against cancer and infectious diseases. We are the only immunotherapy company that has reported generating T cells in vivo in high quantity that are fully functional and whose killing capacity correlates with relevant clinical outcomes with a favorable safety profile. With an expanding portfolio of immune therapies, the company is advancing a growing preclinical and clinical stage product pipeline. Partners and collaborators include MedImmune, Roche, The Wistar Institute, University of Pennsylvania, DARPA, GeneOne Life Science, Drexel University, NIH, HIV Vaccines Trial Network, National Cancer Institute, U.S. Military HIV Research Program, and University of Manitoba. 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 and our capital resources. 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 (including, but not limited to, the fact that pre-clinical and clinical results referenced in this release may not be indicative of results achievable in other trials or for other indications, that the studies or trials may not be successful or achieve the results desired, including safety and efficacy for VGX-3100 and INO-3112, that pre-clinical studies and clinical trials may not commence or be completed in the time periods anticipated, that results from one study may not necessarily be reflected or supported by the results of other similar studies and that results from an animal study may not be indicative of results achievable in human studies), 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 broad pipeline of SynCon® active immune therapy and vaccine products, our ability to advance our portfolio of immune-oncology products independently, 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 the company or its collaborators, including alternatives that may be more efficacious or cost-effective than any therapy or treatment that the company and its collaborators hope to develop, our ability to

enter into partnerships in conjunction with our research and development programs, evaluation of potential opportunities, issues involving product liability, issues involving patents and whether they or licenses to them will provide the company 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 the company can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of the company's 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, 2015, and other regulatory filings from time to time. There can be no assurance that any product in Inovio's pipeline will be successfully developed or manufactured, that final results of clinical studies 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.

CONTACTS:

Investors: Bernie Hertel, Inovio Pharmaceuticals, 858-410-3101, bhertel@inovio.com

Media: Jeff Richardson, Inovio Pharmaceuticals, 267-440-4211, jrichardson@inovio.com

Source: Inovio Pharmaceuticals