



NEWS RELEASE

Inovio's Further Analysis of VGX-3100 Phase 2b Data Reveals Immune Correlates and Biomarker Signatures That Predicted Clinical Efficacy

2017-11-29

Inovio continues to investigate pre-treatment biomarkers which could identify patients most likely to respond to treatment with VGX-3100, increasing absolute efficacy of the product

PLYMOUTH MEETING, Pa., Nov. 29, 2017 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) today announced that post-hoc analysis of data generated from its phase 2b trial of VGX-3100 identified immune correlates and biomarker signatures predictive of treatment success. VGX-3100, Inovio's lead product now in a pivotal phase 3 trial, would be the first non-surgical treatment for HPV-associated high grade cervical dysplasia (squamous intraepithelial lesions or HSIL) which frequently progresses to cancer.

Details of the new biomarker and immunologic data are highlighted in the peer-reviewed journal Clinical Cancer Research in the article, "Clinical and Immunologic Biomarkers for Histologic Regression of High-grade Cervical Dysplasia and Clearance of HPV-16 and HPV-18 after Immunotherapy," by Inovio and its academic collaborators.

In this paper, Inovio has identified biomarker signatures which predicted success of VGX-3100 treatment as early as two weeks after the completion of treatment which was a full 22 weeks prior to the formal efficacy assessment. The company believes these biomarkers will aid physicians in guiding patient care during VGX-3100 treatment, and is pursuing the confirmation of these predictions in its phase 3 program. Inovio is also researching pre-treatment biomarkers which could identify patients most likely to respond to treatment with VGX-3100, increasing absolute efficacy of the product.

Dr. J. Joseph Kim, President and CEO, said: "Inovio will transform the treatment of HPV-associated disease with the first immunotherapies to treat both pre-cancer and cancer caused by HPV which infects more than 70% of sexually active adults. Today's advancement in discovering a successful treatment biomarker moves us closer to that goal."

Inovio previously reported that VGX-3100 eliminated high grade dysplasia in 50% of women in its phase 2b randomized, placebo-controlled trial. In 80% of the women whose high grade dysplasia was eliminated, the HPV infection was also cleared by VGX-3100.

Further data analysis revealed that the combination of HPV typing and cervical cytology (Pap smear) following dosing was predictive for both elimination of the high grade dysplasia and clearance of HPV.

Overall, Inovio is well positioned to comprehensively treat HPV-associated diseases across the continuum of HPV infection, from pre-cancerous conditions through to cancer in both women and men, with VGX-3100 -- already the most advanced product for treating these diseases.

- Inovio's phase 3 clinical program to evaluate the efficacy of VGX-3100 to treat high grade cervical dysplasia caused by HPV is enrolling as scheduled with over 35 clinical sites open. By the end of the year, the company expects to open approximately 50 sites in at least six countries. The pivotal data from this program will support the licensure application of VGX-3100.
- Extending its HPV franchise, Inovio is enrolling women into a phase 2 trial at more than 10 sites to evaluate the efficacy of VGX-3100 in women with high-grade vulvar dysplasia, another disease caused by HPV with a high unmet medical need.
- And, in 2018, Inovio will initiate a phase 2 "proof-of-concept" study for the treatment of high grade anal neoplasia, also caused by HPV with limited treatment options.

In this paper, Inovio has revealed immune responses in the phase 2b trial that were significantly associated with treatment success with VGX-3100 that had not been previously reported. Analysis of data from patient blood samples showed that when focusing on immune responses specific for the HPV type patients were infected with, a significant increase was seen in killer T cells that expressed perforin – a protein known to be a key mediator in killer T cell function. These significant increases were noted only in patients who clinically responded to VGX-3100 and were present at week 14 of treatment, which is 22 weeks prior to the efficacy assessment. Cervical tissue samples from these same patients also showed an influx of immune cells that expressed perforin after treatment, further strengthening the association between the induction of perforin by VGX-3100 and clinical response. This understanding of the immune mechanism of action could also aid in the advancement of Inovio's broader immunotherapy product pipeline.

About HPV and Cervical HSIL

HPV is the most common sexually transmitted infection, with over 14 million new infections annually. While many of these are transient infections, persistent high-risk infections can cause the formation of pre-cancerous lesions. Left untreated, women diagnosed with cervical HSIL are at increased risk of developing cervical cancer. HPV types 16 and 18 are responsible for 70% of cervical cancers, with more than 400,000 new cases of HPV 16/18 cervical HSIL annually in the US and Europe. Cervical cancer is a major global health problem, causing 260,000 deaths annually. While cervical HSIL and cervical cancer are the most well-known HPV related diseases, HPV is also a major cause of HSIL and cancer in the entire anogenital region and oropharynx. Currently there are no treatments available for HPV infection and surgery is the only approved treatment for cervical HSIL. While surgery is effective at removing lesions, it does not treat the underlying HPV infection and it carries increased risk of cervical incompetence and pre-term

birth, which can result in fetal morbidity and mortality.

About VGX-3100

VGX-3100 is a DNA-based immunotherapy under investigation for the treatment of HPV-16 and HPV-18 infection and pre-cancerous lesions of the cervix (phase 3) and vulva (phase 2). VGX-3100 has the potential to be the first approved treatment for HPV infection of the cervix and the first non-surgical treatment for pre-cancerous cervical lesions. VGX-3100 works by stimulating a specific immune response to HPV-16 and HPV-18, which targets the infection and causes destruction of pre-cancerous cells. In a randomized, double-blind, placebo-controlled phase 2b study in 167 adult women with histologically documented HPV-16/18 cervical HSIL (CIN2/3), treatment with VGX-3100 resulted in a statistically significantly greater decrease in cervical HSIL and clearance of HPV infection vs. placebo. The most common side effect was injection site pain, and no serious adverse events were reported. VGX-3100 utilizes the patient's own immune system to clear HPV-16 and HPV-18 infection and pre-cancerous lesions without the increased risks associated with surgery, such as loss of reproductive health and negative psychosocial impacts.

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 immunotherapies, the company is advancing a growing preclinical and clinical stage product pipeline. Partners and collaborators include or have included MedImmune, Regeneron, Genentech, The Wistar Institute, University of Pennsylvania, DARPA, GeneOne Life Science, Plumblin Life Sciences, ApolloBio Corporation, Drexel University, National Microbiology Laboratory of the Public Health Agency of Canada, NIH, HIV Vaccines Trial Network, NIAID, U.S. Army Medical Research Institute of Infectious Diseases and U.S. Military HIV Research Program. 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, and the sufficiency of 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, 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 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, 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, 2016, our Form 10-Q for the period ended September 30, 2017, and other regulatory filings we make from time to time. There can be no assurance that any product candidate in Inovio's 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. In addition, the forward-looking statements included in this press release represent Inovio's views as of the date hereof. Inovio anticipates that subsequent events and developments may cause its views to change. However, while Inovio may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing Inovio's views as of any date subsequent to the date of this release.

CONTACTS:

Investors/Media: Jeff Richardson, Inovio Pharmaceuticals, 267-440-4211, [**jrichardson@inovio.com**](mailto:jrichardson@inovio.com)

Source: Inovio Pharmaceuticals, Inc.