



NEWS RELEASE

Inovio Begins Phase 3 Clinical Trial of VGX-3100 for the Treatment of HPV-Related Cervical Pre-Cancer

2017-06-08

FDA removes clinical hold on phase 3; Inovio to immediately begin recruiting subjects

PLYMOUTH MEETING, Pa., June 08, 2017 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) today announced that it has commenced its phase 3 clinical program to evaluate the efficacy of Inovio's DNA-based immunotherapy, VGX-3100, to treat cervical dysplasia caused by human papillomavirus (HPV). Inovio's study will assess the efficacy of VGX-3100 in regressing cervical HSIL (high-grade squamous intraepithelial lesions), a direct precursor to cervical cancer, and eliminating the HPV infection that causes these lesions. The pivotal data from this program will support the potential licensure of VGX-3100 as the first immunotherapy for this disease.

Inovio satisfied the FDA's request for information relating to its CELLECTRA® SPSP delivery device, resulting in the FDA removing the clinical hold on this program. Inovio plans to immediately begin recruiting patients for the phase 3 trial.

Inovio's phase 3 program, named REVEAL (Randomized Evaluation of VGX-3100 and Electroporation for the Treatment of Cervical HSIL), will consist of a primary study (REVEAL 1) and confirmatory study (REVEAL 2), as per FDA general guidance for phase 3 programs, to be conducted in parallel. The studies will each enroll 198 patients in more than 100 study centers globally. Mark Einstein, MD, MS, FACS, FACOG, Professor and Chair Department of Obstetrics, Gynecology and Women's Health Assistant Dean, Clinical Research Unit, Rutgers New Jersey Medical School, is Principal Investigator for the studies.

The REVEAL studies are prospective, randomized (2:1), double-blind, placebo-controlled trials evaluating adult women with HPV 16/18 positive biopsy-proven cervical HSIL, otherwise known as cervical intraepithelial neoplasia (CIN) 2 or 3. The primary endpoint is regression of cervical HSIL AND virologic clearance of HPV-16 and/or HPV-18 in the cervix. The studies will evaluate cervical tissue changes at approximately 9 months after beginning a three dose regimen of VGX-3100 administered at months 0, 1, and 3. Secondary endpoints include safety; tolerability; regression of CIN 2/3 to CIN 1 or normal; virologic clearance of HPV; efficacy measured by non-progression to cancer; and clearance of HPV from non-cervical anatomic locations.

VGX-3100 has the potential to be the first treatment for HPV infection of the cervix and the first non-surgical treatment for pre-

cancerous cervical lesions. VGX-3100 stimulates a specific immune response to HPV-16 and HPV-18, targeting the infection and destroying pre-cancerous cells. There are no treatments available for HPV infection and surgery is the only approved treatment for cervical HSIL. While surgery is effective at removing dysplastic lesions, it does not treat the underlying HPV infection and carries increased risk of cervical incompetence and pre-term birth, which can result in fetal morbidity and mortality. VGX-3100 demonstrated in a phase 2b study (**published** in The Lancet) its ability to clear HPV-16 and HPV-18 infection and pre-cancerous lesions.

Dr. Mark Bagarazzi, Inovio's Chief Medical Officer, said, "Despite the availability of preventive HPV vaccines for over a decade, HPV-related cervical HSIL and cancers remain a widely prevalent problem. Unfortunately, current treatments are invasive and do not address the underlying HPV infection. VGX-3100 has the potential to be a first-in-class HPV-specific immunotherapy offering women the prospect of preventing cervical cancer without undergoing an invasive surgical procedure that may compromise their reproductive health. We are pleased to be able to immediately begin recruiting patients at the first 15 sites by the end of this month."

Dr. J. Joseph Kim, Inovio's President and CEO, said, "Initiating our REVEAL phase 3 program marks a milestone for Inovio, for the next generation of DNA-based immunotherapies, and for women's health. Combining this first phase 3 program with our previously announced phase 2 clinical trial of VGX-3100 for HPV-related vulvar neoplasia and our checkpoint inhibitor-based combination study with MedImmune/AstraZeneca targeting HPV associated cancers, Inovio is well positioned to comprehensively treat HPV-associated diseases across the continuum of HPV infection through to cancer in both men and women. Adding our recently announced collaborative immuno-oncology combination studies with Regeneron and Genentech, 2017 is a transformative year that is laying the foundation for multiple opportunities for important efficacy data."

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's DNA Immunotherapy Technology Platform

Inovio is advancing the medical potential of a unique class of immunotherapy technology. Its DNA-based platform, which is the foundation for all of Inovio's products, including VGX-3100, is unique in its ability to leverage the body's naturally existing mechanisms to generate robust, highly targeted immune responses to prevent and treat disease – and to do so in the body without harmful side effects. Its SynCon® immunotherapy design and CELLECTRA® delivery transform novel genetic blueprints into functional antibody and killer T cell responses. Inovio was the first to report the activation – in the body – of significant, antigen-specific functional T cells correlated to statistically significant efficacy in a placebo-controlled, randomized, double-blind phase 2b clinical trial (HPV-related pre-cancer), with a very favorable safety profile. These data were published in *The Lancet* and independently described as a “major breakthrough” in the field by U.S. National Cancer Institute scientists. Inovio has achieved significant antigen-specific immune responses against multiple diseases and is advancing a growing pipeline of cancer and infectious disease immunotherapies and vaccines.

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, Regeneron Pharmaceuticals, Genentech, GeneOne Life Science, Plumblin Life Sciences, ApolloBio Corporation, The Wistar Institute, Laval University, University of Pennsylvania, Drexel University, DARPA, NIH, HIV Vaccines Trial Network, National Cancer Institute, 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 conduct phase 3 clinical trials for VGX-3100 for the treatment of cervical dysplasia caused by HPV, a phase 2 clinical trial of VGX-3100 for HPV-related vulvar neoplasia and other immuno-oncology combination studies. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including the availability and timing of data from ongoing clinical trials, uncertainties inherent in the completion of ongoing clinical trials and the initiation of future clinical trials, whether the results of earlier clinical

trials will be indicative of the results of future trials, expectations for regulatory approvals, the availability of funding to support continuing research and studies, 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 and other factors discussed in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the U.S. Securities and Exchange Commission (SEC) on March 15, 2017, our Form 10-Q for the quarter ended March 31, 2017, filed with the SEC on May 10, 2017, and other filings that Inovio makes with the SEC from time to time. There can be no assurance that any product candidate in Inovio's pipeline will be successfully developed or manufactured, 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: Bernie Hertel, Inovio Pharmaceuticals, 858-410-3101, bhertel@inovio.com

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

Source: Inovio Pharmaceuticals