Inovio’s Cancer (INO-3112) Generates T Cell Immune Responses in Tumor Tissue in Patients with HPV

Inovio Pharmaceuticals, Inc. {NASDAQ: INO}, announced an interim data analysis showing that its INO-3112 cancer immunotherapy product generated antigen-specific CD8+ killer T-cell responses measured both in tumor tissue and in peripheral blood from subjects with head and neck cancer associated with human papillomavirus (HPV).

Inovio’s Cancer Immunotherapy (INO-3112) Generates T Cell Immune Responses in Tumor Tissue and Peripheral Blood in Patients with HPV-Associated Head and Neck Cancer

Four of five study subjects in treated group show progression free survival ranging from nine to 24 months to date in phase I/IIa clinical study

PLYMOUTH MEETING, Pa. – November 14, 2016 – **Inovio Pharmaceuticals, Inc. {NASDAQ: INO}**, today announced an interim data analysis showing that its INO-3112 cancer immunotherapy product generated antigen-specific CD8+ killer T-cell responses measured both in tumor tissue and in peripheral blood from subjects with head and neck cancer associated with human papillomavirus (HPV).

The immunology results show that INO-3112 treatment generated robust HPV16/18 specific CD8+ T cell responses in peripheral blood in four of five subjects who also showed increased T-cell activation in resected tumor tissue samples. These four subjects remained disease free in continuing follow-up that

ranged from nine to 24 months at the time of analysis. One subject with only minimal increases in T cell immune responses developed progressive disease at 11 months post start of the study. These results were presented November 12th at the 2016 Annual Meeting of the Society for Immunotherapy of Cancer (SITC) in National Harbor, Maryland.

Dr. J. Joseph Kim, Inovio's President and CEO, said, "*In immuno-oncology, it's all about the T cells. We now have evidence in cancer patients that our immunotherapy product can generate antigen-specific CD8+ killer T cell responses in the tumor, a major step forward towards an effective immunotherapy. This study gives us an important opportunity to evaluate a novel treatment approach using a DNA vaccine platform to increase immune activation by generating a robust in-vivo T cell response, especially in the tumor, and potentially decreasing tumor recurrence in HPV positive head and neck cancer patients*."

INO-3112, an active immunotherapy targeting HPV 16/18 combined with a DNA plasmid for IL-12 as an immune activator, is designed to activate patients' immune responses to specifically target and kill HPV associated tumors. This open label phase I/IIa study has fully enrolled twenty-two subjects with HPV-positive head and neck squamous cell carcinoma and is intended to assess the safety, tolerability, and immunogenicity of INO-3112 in two treatment groups.

Additionally, the study is evaluating the anti-tumor response and progression free survival of patients. The first group enrolled six subjects who were treated with INO-3112 before and after resection of their tumor. One subject withdrew consent after surgery, leaving five evaluable subjects in this

group. All of these subjects received one dose of INO-3112 (averaging 14 days and ranging 7 to 28 days) prior to definitive surgery plus three additional doses post-surgery. The second group enrolled sixteen subjects who received four doses of INO-3112 after at least two months following completion of definitive chemoradiation or surgery and adjuvant chemoradiation therapy.

This poster presentation provided immune response and disease free survival data from the first treatment group. CD8+ and FoxP3 T cell expression were evaluated in tumor samples obtained before and after surgery. In addition, ELISpot analysis was performed to determine the number of T cells capable of secreting IFN-γ in response to HPV antigen stimulation. Four of five subjects had robust T cell response as measured by blood ELISpot assay and the same four subjects also showed an average increase of 60% of CD8+ to FoxP3 ratio measured by immunohistochemistry post vaccination, demonstrating increased infiltration of CD8+ T cells as well as reduction of regulatory T cells measured by FoxP3 expression in tumor tissue. These four subjects remained disease free with follow-up ranging from nine to 24 months to date. One subject with only a marginal increase in ELISpot response magnitude to HPV and no increase in CD8+/FoxP3 ratio in tumor tissue post INO-3112 developed progressive disease at 11 months post-treatment.

Overall the characteristics of these immune response data mirrored those previously observed in a phase IIb clinical study of VGX-3100 for HPV-associated cervical dysplasia. In that study, strong CD8+ T cell immune responses were positively correlated with achievement of primary and secondary efficacy endpoints. VGX-3100 is the first therapy to demonstrate that activated killer T cells induced in the body

have the power to clear neoplastic lesions as well as the virus which caused the disease.

Inovio is continuing subject monitoring and comprehensive immune analyses for both cohorts of this study and expects multiple reports of additional data throughout 2017.

In August 2015, Inovio licensed INO-3112 to MedImmune, the global biologics research and development arm of AstraZeneca, for an upfront payment of $27.5 million, $700 million in potential development and commercial milestone payments, and royalties on INO-3112 product sales.

About HPV-Caused Head & Neck Cancer

Human papillomavirus (HPV) is the most common sexually transmitted disease in the United States, currently infecting about 79 million Americans. HPV is known to play a major role in the development of head and neck cancers, which include cancers of the oral cavity, oropharynx, nose/nasal passages and larynx. In 2016 an estimated 48,330 persons will get oral cavity or oropharyngeal cancer in the U.S. New cases of head and neck cancer occur nearly three times more often in men as in women. Incidence rates of head and neck cancers have been on the rise, especially HPV-associated oropharyngeal cancer in men, and are expected to continue growing.

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, The Wistar Institute, University of Pennsylvania, 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, please visit www.inovio.com

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