

INOVIO Announces New Data at Scientific Conferences for Lead Candidate, INO-3107, as a Potential Treatment for RRP

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- American Association for Cancer Research (AACR) Special Conference: Tumor Immunology and Immunotherapy: New immunology data showed ability of INO-3107 to induce an antigen-specific T cell response against HPV-6 and HPV-11 and drive recruitment of T cells into airway tissues and papilloma
- International Society of Vaccines Conference: Full safety and efficacy data from Phase 1/2 clinical study in patients with Recurrent Respiratory Papillomatosis (RRP) indicated that INO-3107 was well tolerated and immunogenic; 81% of patients in the trial required fewer surgeries post-treatment when compared to baseline

PLYMOUTH MEETING, Pa., Oct. 21, 2024 /PRNewswire/ -- INOVIO (NASDAQ:INO), a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-related diseases, cancer, and infectious diseases, today announced the presentation of new data at scientific conferences for its lead candidate, INO-3107, for which the company is preparing a Biologics License Application for targeted submission in mid-2025 under the U.S. Food and Drug Administration's Accelerated Approval Pathway Program.

At AACR's Tumor and Immunology Conference on October 19, INOVIO presented new immunology data demonstrating the ability of INO-3107 to induce antigen-specific T cell responses against HPV-6 and HPV-11 and drive recruitment of those T cells into airway tissues and papilloma of RRP patients, which could ultimately slow or eliminate papilloma regrowth. Additionally, INOVIO will tomorrow present its full safety and efficacy data set for the Phase 1/2 trial for INO-3107 at the International Society of Vaccines Conference. In the trial, INO-3107 was found to be well tolerated and immunogenic. Of the 32 patients in the trial, 26 patients, or 81%, experienced a decrease in the number of surgical interventions in the year after treatment when compared to the year before treatment.

"The new immunology data support the proposed mechanism of action of INO-3107 which is to generate an immune response that can seek out and eliminate HPV-6 and HPV-11 infected cells that are the underlying cause of

papilloma growth," said Dr. Matthew Morrow, INOVIO's Vice President of Translational Science. "Our analysis shows that INO-3107 induced significant clonal T cell expansion in the blood, including antigen-specific killer T cells. Investigators also observed T cell infiltration into airway tissue, which is positively associated with clinical response."

"The collective story these data sets provide is compelling. Over 81% of patients who received INO-3107 required fewer surgical procedures compared to baseline, a result that is further supported by the new immunology data demonstrating the ability of INO-3107 to stimulate the immune system and generate antigen-specific T cells that travel to the airways and could eliminate the underlying disease," said Dr. Jacqueline Shea, INOVIO's President and Chief Executive Officer. "We believe these data continue to demonstrate that INO-3107 has the potential to significantly improve the lives of patients living with RRP and become the preferred choice for the broadest number of RRP patients and healthcare providers."

Summary of Data Presented at Conferences

AACR Special Conference in Cancer Research: Tumor Immunology and Immunotherapy

Abstract: Reduction in Surgical Interventions for the Treatment of Recurrent Respiratory Papillomatosis by INO-3107 is Associated with Enriched Macrophage, Dendritic cell and T cell Signatures in Patient Airways

New Immunology data for INO-3107 demonstrated:

- Induction of T cell responses specifically for HPV-6 and HPV-11
- Expansion of antigen specific, clonal T cell populations in peripheral blood
- Induction of inflammatory responses in papilloma and airway tissue, including:
 - Interferon, cytokine and chemokine signaling
 - Adaptive and innate immune cell infiltration, with emphasis on T cells
- Cytotoxic signatures of infiltrated T cells in papilloma/airway tissue, providing direct evidence of increased overall T cell infiltration compared to pre-treatment
- Clinical activity not impacted by immunosuppressive papilloma microenvironment

International Society of Vaccines Conference

Abstract: Clinical Assessment of Adjuvant Immunotherapy, INO-3107, in Adult Patients with Recurrent respiratory papillomatosis (RRP)

Clinical Results of Phase 1/2 Study with INO-3107 in Adult RRP Patients

In the trial, the overall clinical response (OCR) was 81%, with 26 of the 32 enrolled patients experiencing a decrease in the number of surgical interventions in the year after INO-3107 administration compared to the prior year, including 28% (9/32) that required no surgical intervention (i.e., complete response or "CR") during or after the

dosing window. Further, 44% (14/32) of patients had a partial response ("PR"), measured by a reduction of at least 50%, but less than 100%, in the number of surgeries when compared to the prior year. The overall response rate (ORR) of patients (CR+PR) was therefore 72% (23/32).

Other key data points presented include:

- INO-3107 was well tolerated and immunogenic in the 32 patients enrolled
 - 41% (13/32) of patients reported a treatment-related Adverse Event (AE)
 - Most frequent treatment-related AE's reported were injection site pain (31%) and fatigue (9%)
 - No treatment-related AEs greater than Grade 2 severity were reported
- Modified Derkay-Pransky severity scores improved from baseline to the end of 52-week trial
- INO-3107 induced durable cellular responses and generated T cells against HPV-6 and HPV-11

The abstracts from the poster and presentations are available on the INOVIO events page: [tbd link]

About RRP

RRP is a debilitating and rare disease caused primarily by HPV-6 and/or HPV-11. RRP is characterized by the development of small, wart-like growths, or papillomas, in the respiratory tract. While papillomas are generally benign, they can cause severe, life-threatening airway obstruction and respiratory complications. RRP can also significantly affect quality of life for patients by affecting the voice box, limiting the ability to speak effectively. Surgery to remove papillomas is the standard of care for RRP; however, the papillomas often grow back. INOVIO's market research to date with patients and healthcare professionals indicates that a reduction of even one surgery matters, because every surgery poses a significant risk of causing permanent damage to the vocal cords. The most widely cited U.S. epidemiology data published in 1995 estimated that there were 14,000 active cases and about 1.8 per 100,000 new cases in adults each year.

About INO-3107

INO-3107 is a DNA immunotherapy designed to elicit an antigen-specific T cell response against both HPV-6 and HPV-11 proteins. These targeted T cells are designed to seek out and kill HPV-6 and HPV-11 infected cells, with the aim of potentially preventing or slowing the growth of new papillomas. In a Phase 1/2 clinical trial conducted with INO-3107, 81.3% (26/32) of patients had a decrease in surgical interventions in the year after INO-3107 administration compared to the prior year, including 28.1% (9/32) that required no surgical intervention during or after the dosing window. Patients in the trial had a median range of 4 surgeries (2-8) in the year prior to dosing. After dosing, there was a median decrease of 3 surgical interventions (95% confidence interval -3, -2). At the outset of the trial (Day 0), patients had a clinically warranted procedure to have RRP tissue surgically removed, but any surgery performed after Day 0 during the dosing window was counted against the efficacy endpoint. Treatment with INO-3107 generated a strong immune response in the trial, inducing activated CD4 T cells and activated CD8 T

cells with lytic potential. T-cell responses were also observed at Week 52, indicating a persistent cellular memory response. INO-3107 was well tolerated by participants in the trial, resulting in mostly low-grade (Grade 1) treatment-emergent adverse effects such as injection site pain and fatigue. Like other DNA medicines, INO-3107 has demonstrated the ability to generate antigen-specific T cells that is not affected by anti-vector immunity impacting immunogenicity, either before administration or after the first dose unlike other T-cell generating platforms such as viral vectors. This feature of DNA medicines is expected to allow INO-3107 to maintain T cell response and overall efficacy, which would make it an important therapeutic option for a majority of RRP patients.

The FDA granted INO-3107 Orphan Drug designation and Breakthrough Therapy designation, and advised INOVIO that it could submit its BLA under the accelerated approval program using data from its already completed Phase 1/2 trial. The European Commission granted INO-3107 Orphan Drug designation and assigned INOVIO's delivery device CELLECTRA® a CE marking, a regulatory standard that certifies that a product has met European Union's safety, health, and environmental standards. The United Kingdom awarded INO-3107 the Innovation Passport. This designation serves as the entry point to the Innovative Licensing and Access Pathway (ILAP), which aims to accelerate time to market and facilitate patient access to medicines.

About INOVIO's DNA Medicines Platform

INOVIO's DNA medicines platform has two innovative components: precisely designed DNA plasmids, delivered by INOVIO's proprietary investigational medical device, CELLECTRA®. INOVIO uses proprietary technology to design its DNA plasmids, which are small circular DNA molecules that work like software the body's cells can download to produce specific proteins to target and fight disease. INOVIO's proprietary CELLECTRA® delivery devices are designed to optimally deliver its DNA medicines to the body's cells without requiring chemical adjuvants or lipid nanoparticles and without the risk of the anti-vector response historically seen with viral vector platforms.

About INOVIO

INOVIO is a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-related diseases, cancer, and infectious diseases. INOVIO's technology optimizes the design and delivery of innovative DNA medicines that teach the body to manufacture its own disease-fighting tools. For more information, visit www.inovio.com.

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