

INOVIO Receives FDA Feedback that Data from Completed Phase 1/2 Trial of INO-3107 Can Be Used to Submit a BLA Under Accelerated Approval Program

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- Previously planned Phase 3 trial no longer required to support Biological License Application (BLA) submission
- If approved, INO-3107 could potentially revolutionize treatment options for patients with Recurrent Respiratory Papillomatosis (RRP), a debilitating rare disease caused by human papillomavirus (HPV)
- INO-3107 could be the first DNA medicine available in the United States and the first commercial product for INOVIO

PLYMOUTH MEETING, Pa., Oct. 10, 2023 /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 that it has received feedback from the U.S. Food and Drug Administration (FDA) that data from its completed Phase 1/2 trial of INO-3107 for the treatment of RRP could support INOVIO's submission of a BLA for review under the FDA's accelerated approval program. The FDA also advised that the company's previously planned Phase 3 randomized, placebo-controlled trial would not be required to support this submission. INOVIO will be required to initiate a confirmatory trial prior to BLA submission for accelerated approval and satisfy all other FDA filing requirements. The design of the confirmatory trial has not yet been finalized. If approved, INO-3107 would be the first DNA medicine in the United States and the first INOVIO candidate to receive regulatory approval.

"Following the recent grant of Breakthrough Therapy Designation for INO-3107 for the treatment of RRP, we're grateful for the additional feedback from the FDA providing a potentially accelerated development pathway. We believe INO-3107 could become a game-changing treatment option for those suffering from RRP, a serious and often difficult-to-treat disease," said INOVIO's President and Chief Executive Officer, Dr. Jacqueline Shea. "We're now focused on streamlining our development plan to support submission of a BLA for accelerated approval. We would

like to thank the patients and investigators who have participated in our trials to date."

"I commend the FDA for recognizing the immense burden RRP puts on patients and the critical need for a better standard of care," said the President of the Recurrent Respiratory Papillomatosis Foundation, Kim McClellan. "I'm thrilled by the progress being made for RRP patients who are desperate for an alternative to surgery."

INOVIO's completed Phase 1/2 open-label, multicenter trial assessed INO-3107's safety, tolerability, immunogenicity, and efficacy in patients with HPV-6 and/or HPV-11-related RRP (NCT:04398433). The trial evaluated the reduction in the number of surgical interventions in the year following initial administration of INO-3107 compared to the year prior to treatment. Patients received four doses of INO-3107 on Day 0, and Weeks 3, 6, and 9. Overall, 81.3% (26/32) of patients in the trial 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 study (Day 0), patients could 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.

Data from this Phase 1/2 trial were presented earlier this year at scientific and medical conferences, including the 2023 Annual Meeting of the American Broncho-Esophageal Association (ABEA) in May and at the European Laryngological Association's Annual Meeting in June. Data from the trial was also published in May in the peer-reviewed journal, *The Laryngoscope*, under the title "Interim Results of a Phase 1/2 Open-Label Study of INO-3107 for HPV-6 and/or HPV-11-Associated RRP." *The Laryngoscope* is the official journal of the Triological Society (TRIO), the American Laryngological Association (ALA), and the ABEA.

INO-3107 is INOVIO's lead candidate and one of three clinical-stage DNA medicine candidates targeting HPV-related disease. INOVIO's DNA technology has been studied in twelve HPV-related trials, ranging from Phase 1 to Phase 3, involving more than 900 patients in 20 countries with a variety of HPV-related diseases, including RRP, HSIL (cervical, anal and vulvar) and head and neck cancers. Shared observations in these trials include the ability of DNA medicines to generate HPV antigen specific T cells and a persistent cellular memory response, viral clearance and lesion regression, and no anti-vector immune responses. All three HPV-related product candidates (INO-3107, INO-3112 and VGX-3100) have been well tolerated in these trials.

Updated Cash Guidance

INOVIO previously announced it expected its cash runway to fund the company's operations into the third quarter of 2025. The changes to the development plan for INO-3107 as a result of the FDA feedback announced today could affect that prior guidance. The company plans to provide updated cash guidance on its third quarter earnings call scheduled to take place in November.

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 because the underlying HPV infection has not been eradicated.

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. More recent pediatric epidemiology data cites a range of 0.5 - 0.7 per 100,000 new cases in children in the U.S. each year.

About INO-3107

INO-3107 is INOVIO's lead DNA medicine product candidate and is being developed as a potential treatment for RRP. INO-3107 is designed to elicit a targeted T cell response against HPV-6 and HPV-11, the HPV types responsible for causing RRP among other HPV-related diseases. These targeted T cells are designed to seek out and kill infected cells, with the aim of potentially preventing or slowing the growth of new papillomas. INO-3107 was designated a Breakthrough Therapy by the FDA in September 2023. INO-3107 received Orphan Drug designation from the European Commission in May 2023 and from the FDA in 2020.

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 CELLECTRA® delivery devices help ensure its DNA medicines enter the body's cells for optimal effect, without chemical adjuvants or nanoparticles and without the risk of the anti-vector response seen in 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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Forward-Looking Statements

This press release contains certain forward-looking statements relating to INOVIO's business, including its plans to develop and commercialize DNA medicines and its expectations regarding its research and development programs, including plans to initiate a confirmatory trial for INO-3107 instead of the previously-announced Phase 3 trial, expectations with respect to INO-3107, if approved, expectations that the updated development plan for INO-3107 may affect prior financial guidance, and plans for regulatory submissions. 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, product development programs and commercialization activities and outcomes, 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 medicines, INOVIO's ability to support its pipeline of DNA medicine products, the ability of INOVIO's collaborators to attain development and commercial milestones for products INOVIO licenses and product sales that will enable INOVIO to receive future payments and royalties, the adequacy of INOVIO's capital resources, the availability or potential availability of alternative therapies or treatments for the conditions targeted by INOVIO or its collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that INOVIO and its collaborators hope to develop, issues involving product liability, issues involving patents and whether they or licenses to them will provide INOVIO 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 INOVIO can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of INOVIO'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 INOVIO's Annual Report on Form 10-K for the year ended December 31, 2022, its Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, and other filings INOVIO makes from time to time with

the Securities and Exchange Commission. There can be no assurance that any product candidate in INOVIO's pipeline will be successfully developed, manufactured, or commercialized, that the results of clinical trials will be supportive of regulatory approvals required to market products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this release, and INOVIO undertakes no obligation to update or revise these statements, except as may be required by law.

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