

New Retrospective Data Shows Half of RRP Patients Treated with INO-3107 Achieved a Complete Response When Evaluated 2 and 3 Years Following Initial Phase 1/2 Trial

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- Data from a retrospective trial evaluating the longer-term benefit of INO-3107 to patients with Recurrent Respiratory Papillomatosis (RRP) involved in a Phase 1/2 trial showed the number of patients who met the criteria for a Complete Response (CR) increased to 50% by the end of year 2 and to 54% in year 3, compared to 28% by the end of the initial 52-week trial
- 95% of patients in the retrospective trial (RRP-002) maintained or enhanced their original Overall Response Rate (ORR) reported in the Phase 1/2 trial (RRP-001) by the end of year 2; 86% of patients maintained or enhanced ORR into year 3
- New durability data will help inform re-dosing strategy focused on long-term elimination or reduction in the need for surgery to treat RRP disease
- INOVIO plans to present data at future scientific conferences and submit for publication in peer-reviewed journals

PLYMOUTH MEETING, Pa., Dec. 3, 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 data from a retrospective trial showing that the number of RRP patients meeting the criteria for a Complete Response increased to 50% by the end of the second year following initial treatment with INO-3107 in a previously reported Phase 1/2 52-week trial where the Complete Response rate was 28%. In year three, the Complete Response rate had risen to 54%. In the retrospective trial, 95% of patients maintained or enhanced their original Overall Response Rate two years following initial treatment with INO-3107. In year three, 86% of patients had maintained or enhanced their initial response to INO-3107.

"These new data provide further support that INO-3107 has the potential to provide RRP patients with a durable,

non-surgical therapeutic option in treating this chronic disease," said Dr. Michael Sumner, INOVIO's Chief Medical Officer. "These results are particularly meaningful because patients tell us that reducing the number of surgeries is of utmost importance. The durability data will help inform future research to establish re-dosing schedules that could further maintain or enhance clinical response for patients across the disease spectrum. We plan to share these data with the FDA as part of our BLA package targeted for submission in mid-2025."

"Viewed in the context of our recently presented immunology data, these promising durability results are consistent with the mechanism of action for INO-3107, including establishment of a memory T cell response that could drive continued antiviral activity resulting in a further reduction or potential elimination of surgical interventions in RRP patients," said Dr. Jacqueline Shea, INOVIO's President and Chief Executive Officer. "We believe INO-3107's profile supports its potential to become the preferred product by healthcare providers and patients, if approved. We plan to publish and present these new durability data at upcoming scientific conferences and in medical publications."

Durability of Response to Treatment with INO-3107

In a retrospective trial (RRP-002), INOVIO investigated the long-term clinical and safety response of 28* of the 32 patients treated with INO-3107 in a previously reported 52-week Phase 1/2 trial (RRP-001). The retrospective trial collected patient data for nearly three years (median time of follow-up 1,025 days) following initial treatment in RRP-001. Twenty-one of the 23 patients who achieved the criteria for Overall Response Rate (ORR; Complete Response + Partial Response) in RRP-001 agreed to participate in the retrospective study. Of these, 20 of 21 patients (95%) maintained or improved upon their initial response by the end of year two, and 18 of the 21 patients (86%) did so in year three. All data presented is from the modified intent-to-treat dataset, defined as subjects who received at least one dose of INO-3107.** Complete Responses (CR) were defined as requiring no surgeries and a Partial Response (PR) was defined as greater than or equal to 50% reduction in the number of surgeries compared to the year prior to treatment, but less than a 100% reduction in surgeries.

The number of patients treated with INO-3107 who met the CR criteria increased to 50% by the end of year two. This compares to the initial CR rate of 28% observed at the end of the 52-week period in RRP-001. In year three of the retrospective trial, the number of patients with a CR increased to 54%.

No treatment-emergent serious adverse events were identified during the retrospective trial.

Phase 1/2 Trial (RRP-001) – Overall Clinical Benefit (Previously Reported)

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# of Patients	CR	PR	ORR (CR+PR)
32*	28% (9/32)	44% (14/32)	72% (23/32)

Retrospective Trial (RRP-002) – Long-Term Maintenance of Patients in ORR Group

# of Patients	ORR at end of Year 2	ORR in Year 3 (median 295 days)
21	95% (20/21)	86% (18/21)

Retrospective Trial (RRP-002) – Change in CR

Met CR Criteria at Year 1	Met CR Criteria at end of Year 2	Met CR Criteria in Year 3 (median 295 days)
28% (9/32)	50% (14/28)	54% (15/28)

*Four of the original 32 patients were not able to be consented in the retrospective trial.

**The number of patients treated with INO-3107 who met the CR criteria increased to 55% by the end of year two in the per protocol population. In year three, the number of patients with a CR was 52% per protocol.

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 an investigational DNA medicine designed to elicit an antigen-specific T cell response against both HPV-6 and HPV-11 proteins. These targeted T cells 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-

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 (Complete Response) 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, with trial participants experiencing mostly low-grade (Grade 1) treatment-emergent adverse effects such as injection site pain and fatigue. Like other DNA medicines, INO-3107 has shown 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 anticipated to allow INO-3107 to maintain T cell response and overall efficacy, which could make it an important therapeutic option for a majority of RRP patients.

The FDA previously granted INO-3107 Orphan Drug designation and Breakthrough Therapy designation and has advised INOVIO that it can submit a biologics license application under the FDA's accelerated approval program using data from INOVIO's already completed Phase 1/2 trial. The European Commission granted INO-3107 Orphan Drug designation. In addition, INOVIO has CE-marked its CELLECTRA® delivery device in the EU, which allows INOVIO to commercialize the device in the EU and other geographies that recognize CE-marking. 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.

Forward-Looking Statements

This press release contains certain forward-looking statements relating to our business, including our plans to develop and commercialize DNA medicines and expectations regarding our research and development programs, including timelines and prospects for regulatory approval, expectations regarding INO-3107's ability to maintain T cell response and overall efficacy, as well as benefits for patients. 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, our ability to support our pipeline of DNA medicine 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 us or collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that we and our collaborators hope to develop, issues involving product liability, issues involving patents and whether they or licenses to them will provide us 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 we can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of our 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, 2023, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2024, and other filings we make from time to time with the Securities and Exchange Commission. There can be no assurance that any product candidate in our 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 we undertake no obligation to update or revise these statements, except as may be required by law.

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