NEWS RELEASE

INOVIO Announces Positive Preliminary Results from Second Cohort of Phase 1/2 Trial with INO-3107 for the Treatment of Recurrent Respiratory Papillomatosis

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- 10 of 11 patients (91%) had a reduction in number of surgical interventions, measured from Day 0 to one year following initial treatment; 4 of the 10 patients did not need any surgery

- Treatment with INO-3107 achieved statistical significance based on clinical endpoint of reduction in overall number of surgical interventions compared with previous year

- INO-3107 was well-tolerated and immunogenic, with efficacy and safety results for second cohort consistent with first cohort

- Patients in second cohort were administered INO-3107 using the exploratory side port needle

PLYMOUTH MEETING, Pa., Feb. 16, 2023 /PRNewswire/ -- INOVIO (NASDAQ: INO), a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-associated diseases, cancer, and infectious diseases, today announced positive preliminary results from the second cohort of its Phase 1/2 clinical trial evaluating INO-3107 for the treatment of HPV 6 and HPV 11-associated Recurrent Respiratory Papillomatosis (RRP) in adults. In the second cohort of 11 patients who were administered INO-3107 via the exploratory side port needle, 10 of the 11 patients (91%) saw a reduction in surgical interventions in the year following initial treatment, with measurement beginning at Day 0, the start of trial therapy. Of these 10 patients, four did not require surgery. There was a statistically significant median decrease of three surgical interventions when comparing the year following treatment to the year prior. In the year prior to treatment, the number of surgical interventions for these 11 patients ranged between 2 and 8, and the median was 5. INO-3107 was well-tolerated and immunogenic among patients in the second cohort. The safety and efficacy results for the second

cohort were consistent with results announced for the first cohort in October 2022.

"These results from the second cohort confirm previous data that show INO-3107 is well-tolerated, immunogenic and has the potential to improve patients' lives by reducing the need for painful surgery," said Dr. Jeffrey Skolnik, INOVIO's Senior Vice President of Clinical Development. "We will continue to engage with regulators regarding our development plans for INO-3107 and look forward to publishing and presenting our findings from the complete data set soon."

"Many patients with RRP need years of repeated surgeries with no end in sight," said Dr. Ted Mau, Principal Investigator and laryngologist at University of Texas Southwestern Medical Center. "A treatment that results in fewer surgeries – or even no surgery – would be transformational for patients and their families."

"We are pleased with the results from the second cohort, which are consistent with the positive data from the first cohort," said INOVIO's President and Chief Executive Officer, Dr. Jacqueline Shea. "We are focused on advancing our most promising candidates and achieving our broader strategic vision of delivering on the potential of DNA medicines for patients."

About the Trial

INO-3107 was evaluated in a Phase 1/2 open-label, multicenter trial to assess its safety, tolerability, immunogenicity, and efficacy in 32 patients with HPV 6 and/or HPV 11-associated RRP **(NCT:04398433)**. The first cohort included 21 patients - the second included 11. In the first cohort, patients were dosed with a standard needle, while in the second, an exploratory side port needle was used to deliver INO-3107. INOVIO plans to use the standard needle in the next trial involving INO-3107. In both cohorts, the proprietary CELLECTRA® electroporation device was used. 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.

In both cohorts, patients received four doses of INO-3107 on Day 0, and Weeks 3, 6, and 9. 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. Per protocol, a surgical intervention was defined as any removal of papilloma tissues, whether in hospital or in the clinic, using either general or local anesthesia, with any modality of removal.

Second Cohort Preliminary Results (11 Patients)

The results for the second cohort (n=11) achieved statistical significance based on the clinical endpoint of a reduction in the number of surgical interventions in the year following initial administration of INO-3107 compared

with the year prior to treatment; there was a median decrease of three surgical interventions (95% confidence interval 1, 4). In addition, 10 of 11 (90.9%) patients showed a decrease in surgical interventions in the year following initial administration of INO-3107 relative to the number of surgeries in the year prior to the trial. Of these 10 patients, four required no surgical intervention during the trial period. In the year prior to treatment, the range of surgical interventions for these 11 patients was 2 to 8 and the median was 5.

Treatment with INO-3107 induced cellular responses against both HPV 6 and HPV 11, inducing both activated CD4 and activated lytic CD8 T cells. T cell responses were also observed at Week 52, which was 43 weeks after final treatment with INO-3107, indicating a persistent cellular memory response.

INO-3107 was well-tolerated in the trial, with all 11 patients completing the trial follow-up. Treatment-emergent adverse events (TEAE) observed in the trial were generally low-grade, with five patients (46%) experiencing at least one TEAE; four patients (36%) reported at least one related TEAE, all of which were Grade 1 or 2. The only adverse events reported by more than one patient were injection site pain (two patients) and headache (two patients).

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 incidence of RRP is estimated to be 4.3 cases per 100,000 children and 1.8 cases per 100,000 adults. RRP is often a life-long disease, with patients undergoing numerous surgeries during their lifetimes to control their RRP.

About INO-3107

INO-3107 is INOVIO's clinical-stage DNA medicine product candidate 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-associated diseases. These targeted T cells are designed to seek out and kill infected cells, with the aim of regression of existing papillomas and clearance or reduction of the levels of the virus to potentially prevent or slow the growth of new papillomas. INO-3107 **received** Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) in July 2020. For more information about our HPV franchise, please visit **https://ir.inovio.com/events-and-presentations/default.aspx**

About INOVIO

INOVIO is a biotechnology company focused on developing and commercializing DNA medicines to help treat and protect people from HPV-associated diseases, cancer, and infectious diseases. INOVIO's DNA medicines in development are delivered using its investigational proprietary smart device, CELLECTRA®, to produce immune responses against targeted pathogens and cancers. For more information, visit **www.inovio.com**.

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Forward-Looking Statements

This press release contains certain forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995 relating to our business, such as our expectations regarding our research and development programs, including the planned publication of data from clinical trials, plans to engage with regulators regarding development plans for INO-3107 and plans to use the standard needle in the next INO-3107 trial. 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, 2021, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, 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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