INOVIO

Corporate Presentation

November 2025

Forward-Looking Statements

This presentation includes statements that are, or may be deemed, “forward-looking statements,” within the meaning of Section 27A of the Securities Act of 1933, as amended. All statements, other than statements of historical facts, included in this presentation regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as “may,” “might,” “will,” “objective,” “intend,” “should,” “could,” “can,” “would,” “expect,” “believe,” “anticipate,” “project,” “target,” “design,” “estimate,” “predict,” “opportunity,” “proposition,” “strategy,” “potential,” “plan” or the negative of these terms and similar expressions intended to identify forward-looking statements.

You should not place undue reliance on these forward-looking statements. Forward-looking statements include, but are not limited to, statements about: the timing and success of preclinical studies and clinical trials; the ability to obtain and maintain regulatory approval of our product candidates; our request for priority review by the FDA of our BLA submission for INO-3107 and our expectation that the FDA will accept the submission by the end of 2025; the scope, progress, expansion and costs of developing and commercializing our product candidates; our expectations regarding the amount and timing of our expenses and revenue; the sufficiency of our cash resources, plans for the use of our cash resources and needs for additional financing; our ability to adequately manufacture our product candidates; our ability to obtain and maintain intellectual property protection for our product candidates; our expectations regarding competition; the size and growth of the potential markets for our product candidates and the ability to serve those markets; the rate and degree of market acceptance of any of our product candidates; our anticipated growth strategies; the anticipated trends and challenges in our business and the market in which we operate; our ability to establish and maintain development partnerships; our ability to attract or retain key personnel; our expectations regarding federal, state and foreign regulatory requirements; regulatory developments in the United States and foreign countries and other factors that are described in the “Risk Factors” and “Management's Discussion and Analysis of Financial Condition and Results of Operations” sections of our Annual Report on Form 10-Q for the quarter ended September 30, 2025, which has been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov.

In addition, the forward-looking statements included in this presentation represent INOVIO's views as of the date hereof. INOVIO anticipates that subsequent events and developments may cause its views to change. However, while INOVIO may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing INOVIO's views as of any date subsequent to the date of this presentation.

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Company Highlights

- Focused on developing and commercializing DNA medicines to treat and protect people from HPV-related diseases, cancer, and infectious diseases
- Registrational-stage lead program INO-3107 for treatment of Recurrent Respiratory Papillomatosis (RRP)
  - Rolling submission for Biologics License Application (BLA) completed on 10/30/25 seeking accelerated approval, with a goal of FDA acceptance by YE2025. Potential PDUFA date mid-2026, if Priority Review granted
  - Potential launch/revenue generation in 2026, if approved
  - Granted Orphan Drug and Breakthrough Therapy designations in US; Orphan Drug in EU
  - Significant market opportunity, potential to become preferred product based on efficacy and tolerability profile observed to date and a patient-centric treatment regimen
- Established commercial-scale manufacturing for plasmids; device manufacturing in-house
- Deep clinical pipeline of therapeutic and vaccine candidates with multiple potential near- and mid-term catalysts
  - Next-gen therapeutics and vaccines in earlier stage development poised to further unlock potential of DNA medicine technology
- **$50.8 M** in cash, cash equivalents & short-term investments as of 9/30/25
  - $26.5M in net proceeds from November 2025 offering

Progressing Strategy to Unlock the Promise of DNA Medicine

NEAR TERM

Working to Deliver INO-3107 to Patients

- BLA file acceptance expected by EOY, potential PDUFA date in mid-2026
- Potential to be preferred first-line treatment
  - Efficacy
  - Tolerability
  - Simple & patient-centric treatment regimen
- 1st DNA Medicine in U.S. if approved

MID TERM

Advancing Diversified Clinical Pipeline

- 8 additional clinical-stage candidates*
  - INO-3112: targeting HPV-related throat cancer
  - INO-5401: targeting glioblastoma
  - DMAb: 1st proof-of-concept clinical data announced

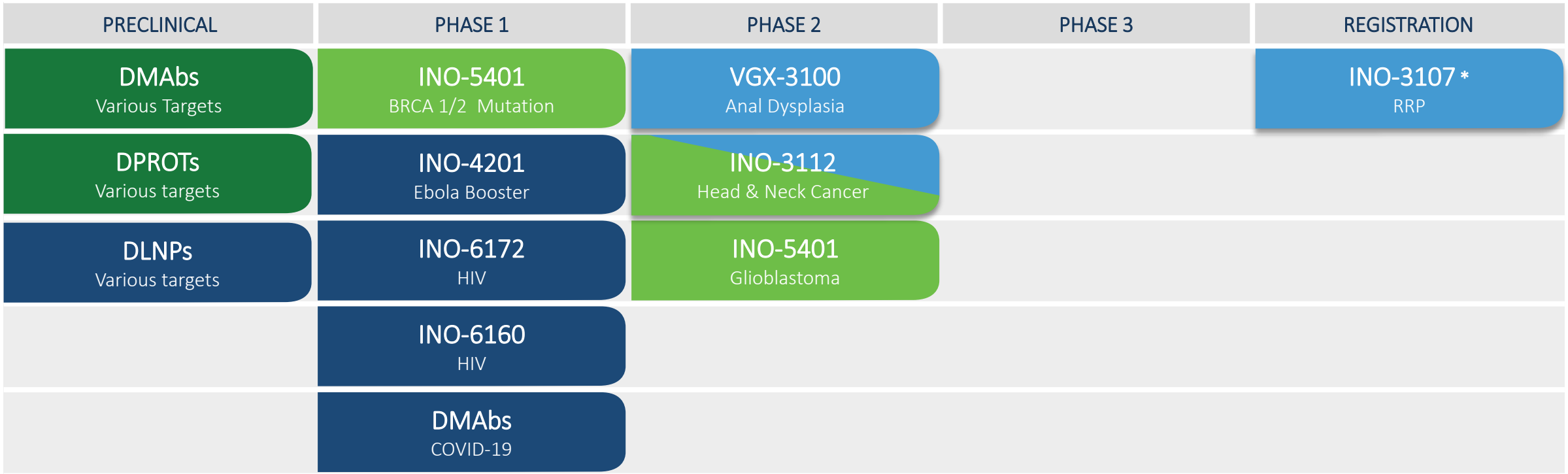
*Wholly-owned & in collaboration with 3rd parties

NEXTGEN

Innovating NextGen DNA Medicines

- DMAbs:
  - Applicable to diseases that can be targeted with mAbs & other proteins
  - Potential to overcome traditional mAb limitations
- DPROTs: targeting protein replacement diseases
- DLNPs: vaccines targeting COVID-19 and other diseases such as HIV
- Cancer therapeutics

INOVIO Pipeline



*Rolling submission of BLA completed in October 2025, seeking accelerated approval from FDA ** VGX-3100 to Apollo Bio for China

DNA Medicine Platform

Harnessing the power of in vivo protein production

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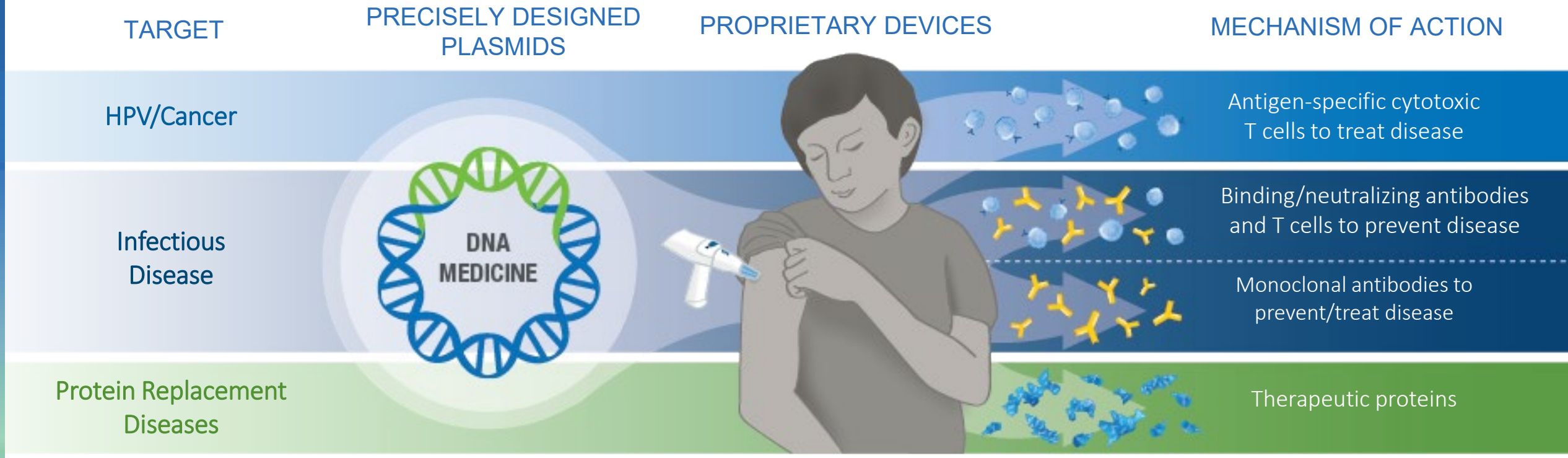
INOVIO's DNA Medicines Platform



In Vivo Protein Production:

Teaching the body to make its own disease-fighting tools

Key Features of our DNA Medicines Platform

Strengths include versatility & immunogenicity

Induces antigen/protein-specific immune responses offering **therapeutic and prophylactic protection**

Well tolerated in nearly 19,000 administrations (~6k clinical trial participants)

Ability to be re-dosed and sustain immune responses

Ability to drive antibody and CD8+ T cell responses against multiple indications

Allows rapid plasmid construct design and manufacture

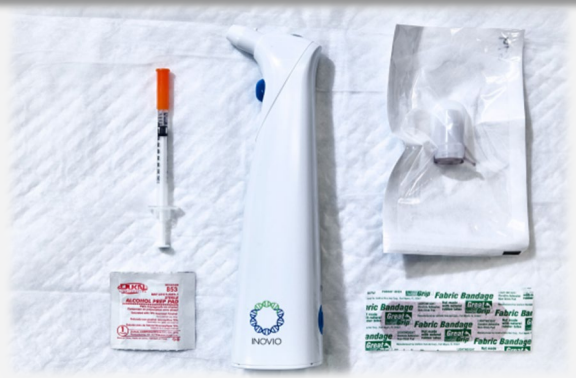
No frozen storage or shipping required

CELLECTRA® Delivery Device Enhances Uptake of DNA Medicine

CELLECTRA 5PSP

- Intramuscular (IM) injection
- Delivers DNA plasmid contained in cartridge
- Utilized in INOVIO's therapeutic programs

CELLECTRA 3PSP



- Intradermal (ID) injection
- Primarily used for prophylactic programs with potential to broaden use in pediatrics and other indications

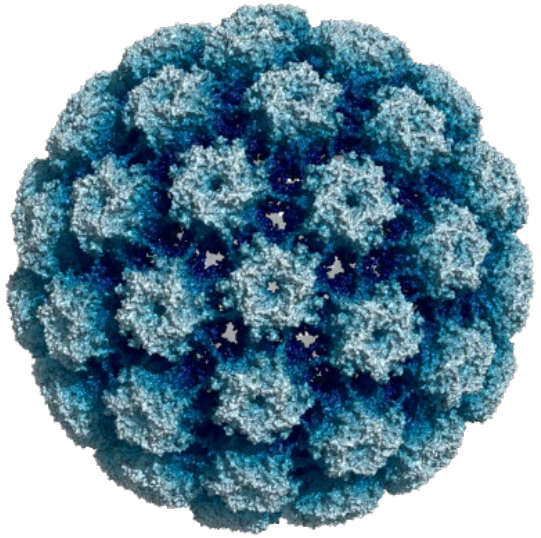
Track record of success in the clinic:

- Nearly 6,000 subjects & 19,000 doses given by both investigational/ commercial-ready CELLECTRA devices
- 2 generations: CELLECTRA 2000, followed by CELLECTRA 5PSP & 3PSP developed to support commercial launch
- 2000 & 5PSP are CE Marked in the EU
- Clinical trials conducted in 36 countries across 6 continents (N.S. America, Europe, Africa, Asia, Australia)

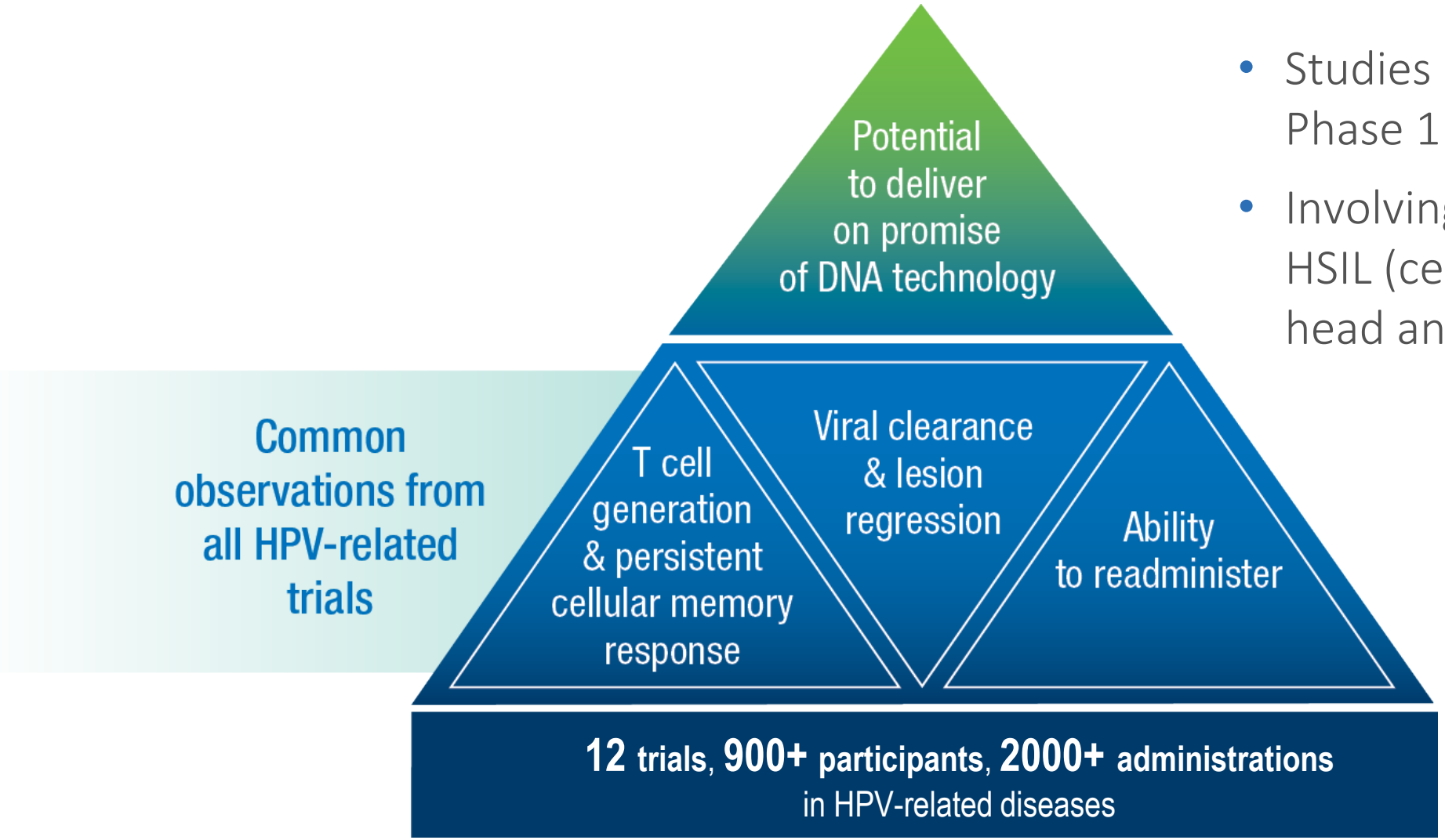
Focus on HPV-Related Diseases

Human Papillomavirus: A Global Concern

- HPV is a group of viruses with approximately 200 types
- Nearly everyone will become infected with some HPV type in their lifetime
  - The good news: ~90% of all infections clear naturally and don't result in disease
  - The bad news: persistent infection can lead to cancer and other debilitating, life-threatening diseases affecting quality of life
- HPV types fall into 2 groups:
  - Low-risk HPV (e.g., HPV-6 and HPV-11) often lead to benign growths (warts or papillomas) that can develop into conditions such as RRP
  - High-risk HPV (e.g., HPV-16 and HPV-18) often lead to cell changes and lesions (precancerous dysplasia) that can become malignant, such as cervical HSIL, which can lead to cervical cancer
- Preventative HPV vaccines have reduced the prevalence of HPV infections, but have not eliminated them – nor can they clear or treat established infections
- Some HPV related diseases such as HPV related OPSCC are rapidly increasing in high income countries



INOVIO's Development Experience Across HPV Spectrum



- Studies ranging from Phase 1 to Phase 3
- Involving patients with RRP, HSIL (cervical, anal & vulvar), head and neck cancers

Lead Candidate:
INO-3107 for Recurrent Respiratory Papillomatosis (RRP)

Potentially transformational therapy
under accelerated approval pathway

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Recurrent Respiratory Papillomatosis (RRP)

Rare disease characterized by small, wart-like growths (papillomas) in the respiratory tract

- Can form anywhere but primarily affect larynx & vocal cord
- Can cause difficulty speaking or complete voice loss, difficulty swallowing, shortness of breath and choking episodes
- Pulmonary spread is ~8% to lungs with higher risk of malignancy
- Papillomas grow back since underlying infection remains

Insufficient immune response that fails to prevent and clear HPV-6 and HPV-11 infections leads to RRP

- Patients and their physicians want a therapeutic alternative that addresses underlying cause of RRP/eliminates need for surgery

Repeated surgery is the standard of care

- Some patients require hundreds of surgeries over a lifetime
- Risk - potential for irreversible damage to vocal cords, bleeding, infection
- Cost - impact to quality of life, financial (to the patient and the healthcare system)

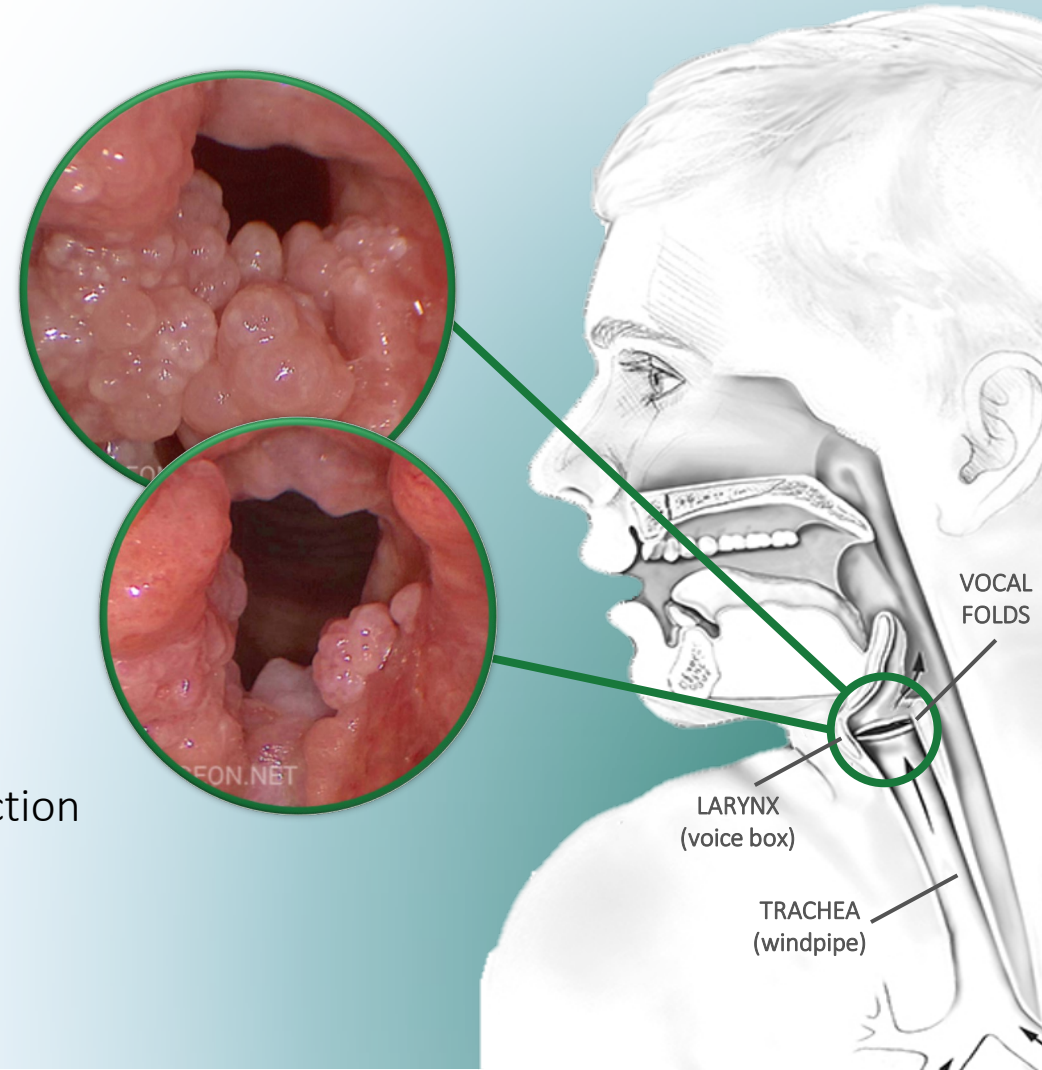


Image Source: National Institute on Deafness and Other Communication Disorders; accessed July 27, 2022;
Photographs courtesy Aaron Friedman MD, University of Cincinnati College of Medicine

Why every surgery matters to RRP patients:

> “The cumulative risk for injury increases with every surgery, but ultimately it only takes 1 surgical misadventure to permanently damage the larynx.”

Factors Associated with Iatrogenic Laryngeal Injury in RRP
Otolaryngology, 2024 Apr;170(4):1091-1098. doi: 10.1002/ohn.629. Epub 2023 Dec 20

Phase 1/2 Multi-Center Clinical Trial at 8 Clinical Sites

RRP-001 PHASE 1/2 OPEN-LABEL STUDY | **RRP-002 DURABILITY EXTENSION / FOLLOW-UP**

Baseline: DAY 0 ····· **52 WEEKS** ····· **104 WEEKS** ····· **156 WEEKS**

Patients Enrolled

N=32

4 Doses of INO-3107

Day 0. Weeks 3, 6, 9

Completed Study

N=32

Consented to Follow Up

N=28

N=4 Lost to Follow Up

Median Follow Up

Completed Follow Up

Enrollment criteria: Patients who required at least two surgical interventions in the past year for the removal of HPV-6/11-related papilloma(s)

Study Design

- Surgeries: Up to 14 days before Day 0, patients had RRP tissue surgically removed and any surgery performed after Day 0 during the dosing window was counted against the efficacy endpoint

Secondary endpoint: efficacy - Change in number of surgical interventions pre- vs. post-treatment

- Primary Endpoint: Safety of INO-3107
- Limited symptom assessment

Patient Population: Intent-to-treat (ITT): all patients (32)

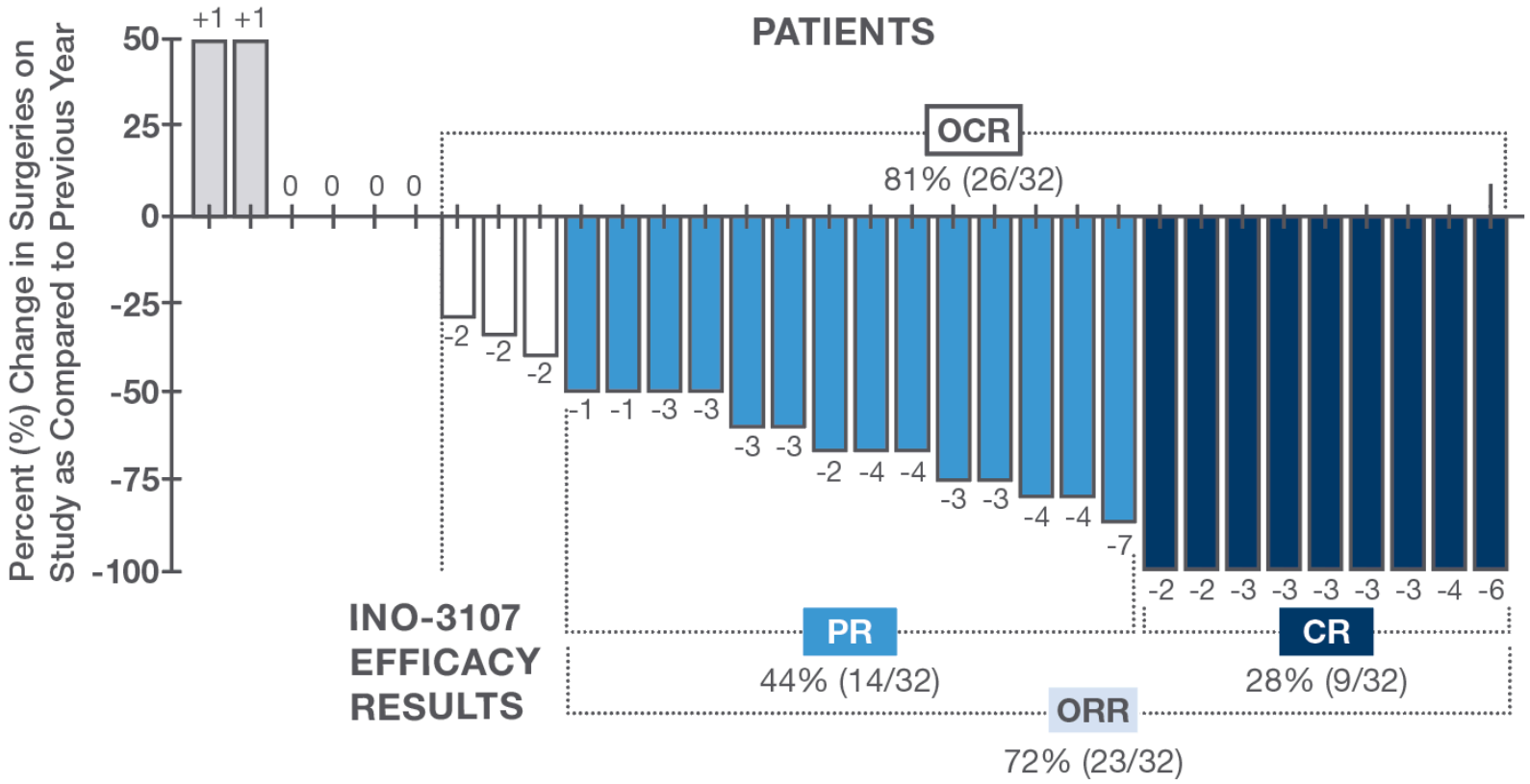
Extension Study: Retrospective assessment of treatment effect up to 3-years after initial dose of INO-3107

- Four patients were lost to follow-up (n=28)
  - Two refused consent, two not able to be contacted
- Median follow up ~1025 days, or 2.8 years

Statistically Significant Reduction in Surgeries*

Vast Majority of Patients Saw a Reduction in Surgery

Data published in Nature Communications February 12, 2025[1]



PARAMETERS

CR **Complete Response:** no surgeries during a 52-week treatment phase

PR **Partial Response:** a ≥ 50% reduction and less than 100% in surgeries compared to previous year

ORR **Overall Response Rate = CR+PR:** Patients with complete or partial response to treatment

OCR **Overall Clinical Response:** reduction of ≥ 1 surgery compared to previous year

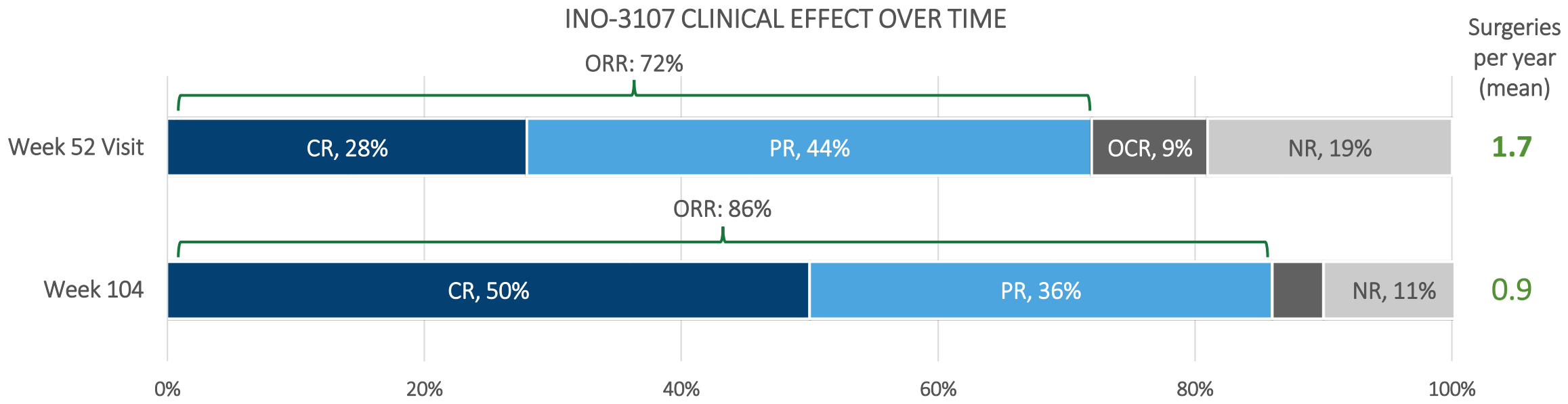
*Median decrease of 3 surgeries (95% Confidence Interval of 2 to 3) when comparing the year before treatment to the year following Day 0 of treatment.

1 Morrow, M.P., Gillespie, E., Sylvester, A. *et al.* DNA immunotherapy for recurrent respiratory papillomatosis (RRP): phase 1/2 study assessing efficacy, safety, and immunogenicity of INO-3107. *Nat Commun* **16**, 1518 (2025). https://doi.org/10.1038/s41467-025-56729-6

Reduction in Surgeries Continued to Improve After Year 1

ORR was 72% at Week 52, improving to 86% by Week 104 for second twelve-month period

The pre-treatment mean for surgeries in the year prior to start of INO-3107 was 4.1 (range 2-8) *vs. 1.7 in Year 1 and 0.9 in Year 2*



PARAMETERS

CR **Complete Response:** no surgeries during a 52-week treatment phase

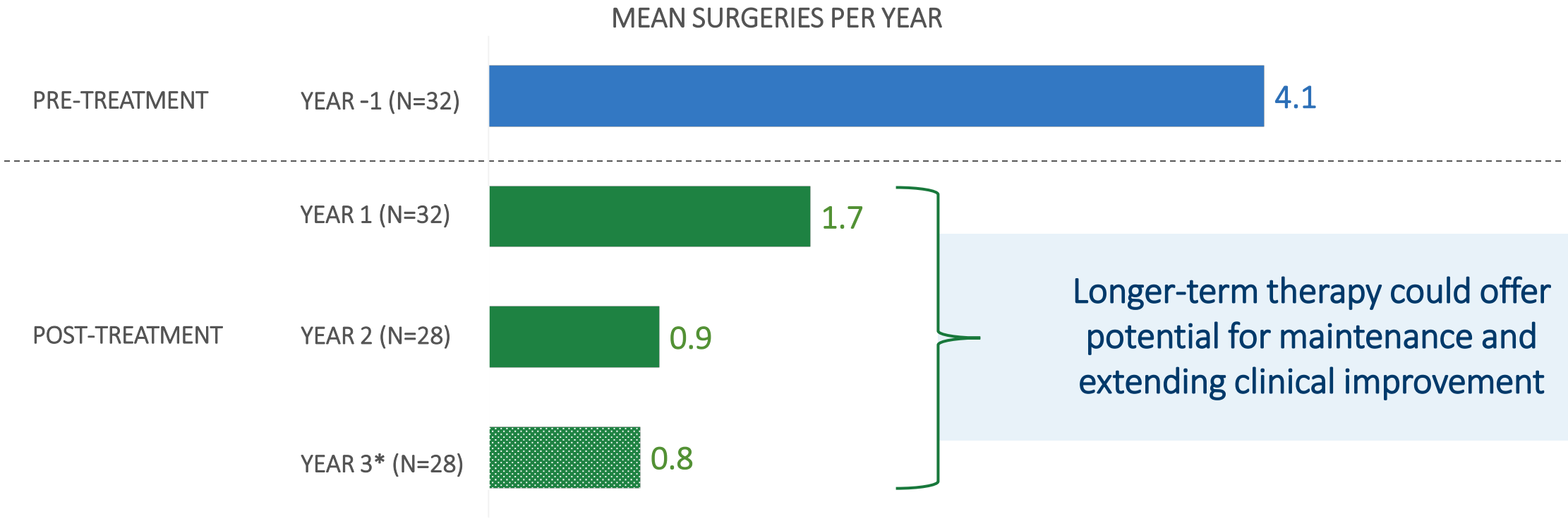
PR **Partial Response:** a ≥ 50% reduction and less than 100% in surgeries compared to previous year

OCR **Overall Clinical Response:** reduction of ≥ 1 surgery compared to previous year

NR **Non-Responders:** No reduction in surgeries vs. baseline

M. R. Amin, P. C. Belafsky, S. R. Best, et al., " DNA Immunotherapy (INO-3107) Results in Long-Term Surgery Reduction in RRP," *The Laryngoscope* (2025): 1–9, https://doi.org/10.1002/lary.32416.

Over 75% Fewer Surgeries 2 Years After Initial Treatment Regimen*



Longer-term therapy could offer potential for maintenance and extending clinical improvement

*Median follow up Year 3: 0.8 years

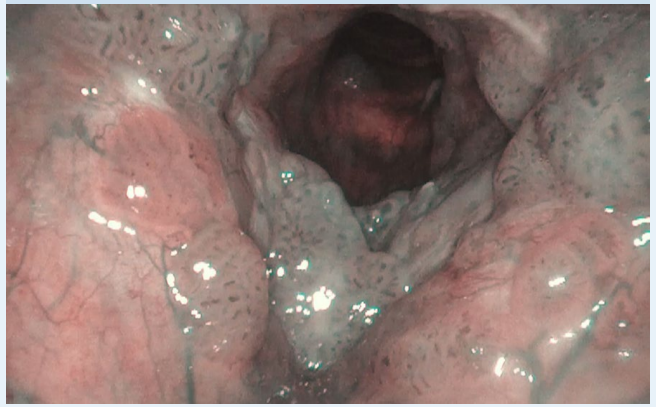
M. R. Amin, P. C. Belafsky, S. R. Best, et al., " DNA Immunotherapy (INO-3107) Results in Long-Term Surgery Reduction in RRP," *The Laryngoscope* (2025): 1–9, https://doi.org/10.1002/lary.32416.

*Compared to baseline

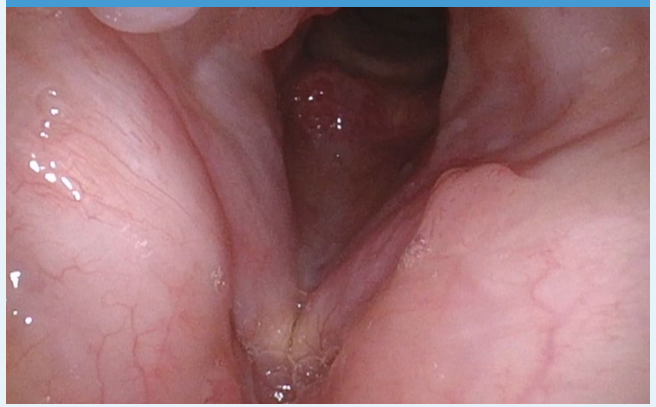
Immunology Data Correlates with Clinical Response

- Right kind of immune responses generated to fight HPV in all 32 patients (antigen specific cytotoxic T cell response)
- T cells observed to infiltrate the papilloma/airway tissue
- Created an anti-viral immune response in papilloma/ airway tissue that was observed to reduce or eliminate the need for surgery
- Papilloma microenvironment did not appear to restrict clinical benefit
- Immune responses in clinical responders were different than in non-responders

PRIOR TO INO-3107



ONE YEAR FOLLOWING INO-3107

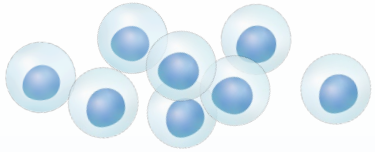


Images courtesy of A Friedman. RRP is a highly individualized disease and results of treatment with INO-3107 may vary

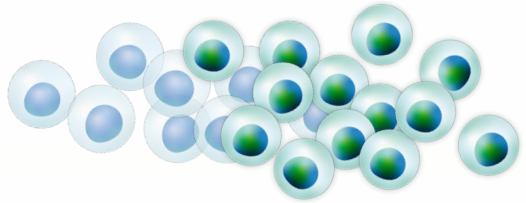
Morrow, M.P., Gillespie, E., Sylvester, A. et al. DNA immunotherapy for recurrent respiratory papillomatosis (RRP): phase 1/2 study assessing efficacy, safety, and immunogenicity of INO-3107. Nat Commun. 2025;16(1):1518.

Proposed Mechanism of Action

- Induce HPV antigen-specific T cell responses in periphery
- Track to/infiltrate papilloma/airway tissue
- Eradicate HPV infected cells to control/eliminate disease



CIRCULATION



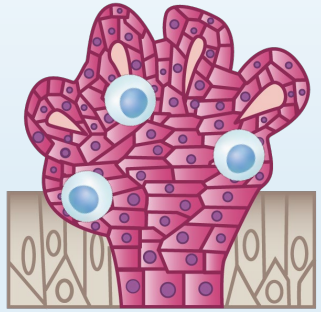
Pre-existing T cells in blood

Treatment with INO-3107 Immunotherapy

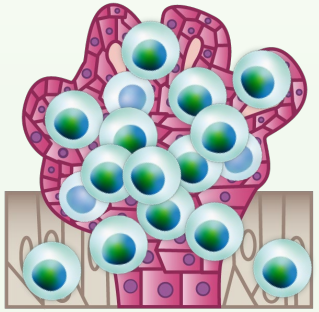
Expansion of pre-existing T cells and Induction of novel T cells in blood

Low T cell trafficking

Mass trafficking by INO-3107 induced T Cells



PAPILLOMAS



- Poorly infiltrated papillomas
- Low Inflammatory signatures
- Low cytokine and chemokine production
- Uncontrolled and/or progressive disease

- Increased Inflammatory signatures
- Increased cytokine and chemokine production
- Elimination of HPV-infected cells = Controlled disease, reduction/elimination of surgical interventions

Surgery Should Be a Last Resort, Not a First-line Treatment

INO-3107: RRP-001 PHASE 1/2 OPEN-LABEL STUDY AT 8 SITES
PATIENTS WITH 2+ SURGERIES IN YR PRIOR TO TREATMENT

Baseline: DAY 0 ····· **WEEK 52**

Patients Enrolled
N=32

4 Doses of INO-3107

Day 0. Weeks 3, 6, 9

Completed Study
N=32

- **Initial Surgery:** up to 14 days before first dose
- **Efficacy:** All surgeries performed after Day 0 counted against the efficacy endpoint through week 52

PAPZIMEOS: PHASE 1/2 OPEN-LABEL STUDY AT 1 SITE*
PATIENTS WITH 3+ SURGERIES IN YR PRIOR TO TREATMENT

Baseline: DAY 0

Efficacy Assessment Begins: Week 12 ····· **WEEK 64**

Patients Enrolled
N=35*

4 Doses of PAPZIMEOS

Day 0. Weeks 2, 6, 12

Completed Study
N=35

- **Initial surgery:** prior to first dose of PAPZIMEOS, a surgical debulking of visible papilloma performed to establish minimal residual disease (MRD)
- **Prior to third and fourth doses:** **remove visible papilloma**, if present, to maintain MRD during treatment with PAPZIMEOS
- **Efficacy:** Surgeries conducted between Day 0 and Week 12 **not included against efficacy endpoint**

*Source: package insert

Market Research Continues to Support Preferred Product Profile

EFFICACY

Improving response over time

- Overall Response Rate (50% to 100% reduction in surgeries): 72% in year 1; 86% in year 2*
- Complete response (no surgeries): 28% in year 1; 50% in year 2*

The complete response rate of 50% is good... but a 50-100% reduction in surgeries in ~8 out if 10 patients, that's the most compelling. The vast majority see significant benefit from treatment."

– Laryngologist, manages ~50 RRP patients

*YR 1 = first 12-month treatment period,
YR 2 = second 12-month treatment period

TOLERABILITY

Well tolerated

- 41% (13/32) reported treatment-related AEs grade 2 or lower
- Most common AEs: transient injection site pain (31%) and fatigue (9%)
- No discontinuations

The tolerability profile looks good – 31% with pain, fatigue 9%. This suggests patients can go back to work... this is important, especially when patients receive multiple doses over a relatively short timeframe."

– Laryngologist, manages ~15 RRP patients

SIMPLICITY

Patient-centric treatment

- Office-based administration that leaves doctor in control
- CELLECTRA device easy to use by HCPs
- No requirement for scoping/surgeries during dosing window

Sending my patients on a referral is not always the best thing. You're defeating yourself by handing off care. I prefer to treat patients in my clinic, so I can maintain control."

– Laryngologist, manages ~30 RRP patients

Advancing Launch Preparations

Key Market Research and Planning:

- Continued critical research with payers
- Developed initial pricing strategy with price optimization research ongoing
- Completed targeting, segmentation and product positioning work - supporting positive differentiation

Operational:

- Finalizing contracts with our specialty distributor, specialty pharmacy, HUB (patient services) and Agency of Record partners
- Finalizing GTM model and advancing build-out of commercial organization

300-400

laryngologists treat the majority of RRP patients

Late-Stage Pipeline Candidates

Designed to address high unmet needs,
multiple near- and mid-term catalysts

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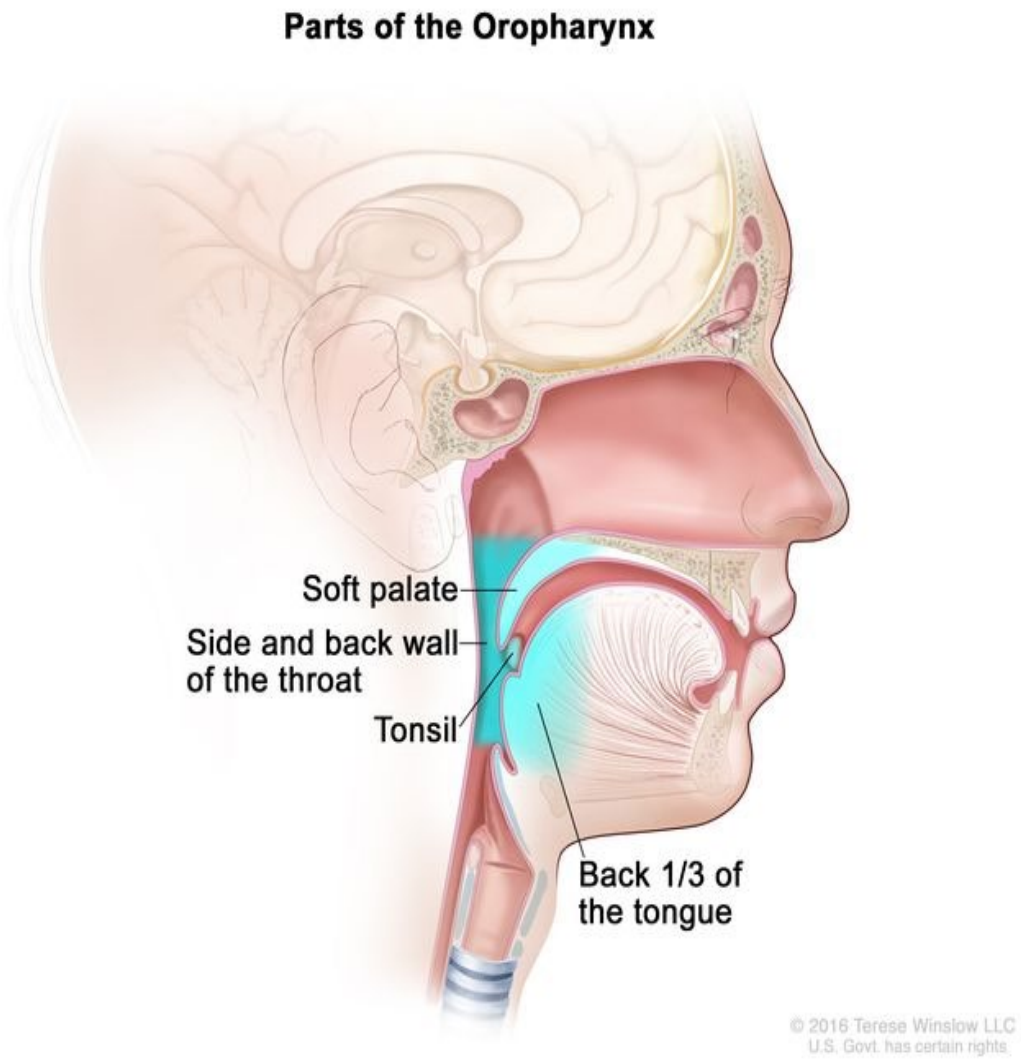
Clinical Collaboration & Supply Agreement with Coherus Biosciences

INO-3112: DNA medicine candidate targeting HPV-16/18, combined with interleukin-12 (immune activator)

LOQTORZI: Proven anti-PD-1 monoclonal antibody

Advancing plans for Phase 3 trial to evaluate combination therapy as treatment for locoregionally advanced, high-risk, HPV-16/18+ oropharyngeal squamous cell carcinoma (OPSCC/throat cancer)

What is Oropharyngeal Squamous Cell Carcinoma?



- Type of head and neck cancer commonly known as throat cancer
- Occurs in the base of the tongue, tonsils and/or soft palate
- Usually related to high-risk subtypes of HPV; some cases are carcinogen-driven
- HPV+ throat cancer rapidly increasing in incidence among patients in high-income countries
  - Surpassed cervical cancer as most common HPV-related cancer diagnosed in the U.S. (~ 20,000 new cases/yr)
- HPV estimated to cause 70%-80% of all oropharyngeal cancers diagnosed in the U.S

https://www.cancer.gov/types/head-and-neck/patient/adult/oropharyngeal-treatment-pdq

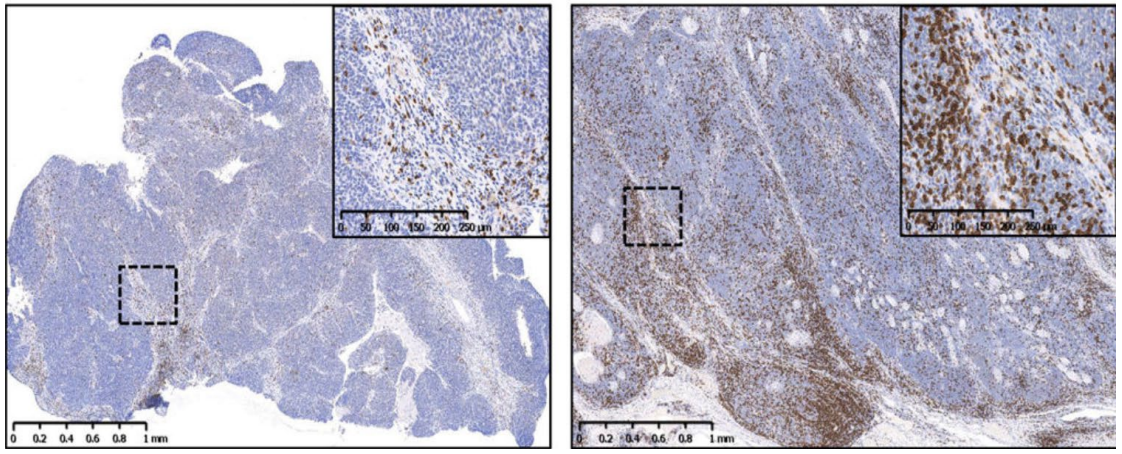
Opportunity to Impact HPV-Related Locoregionally Advanced OPSCC (Throat Cancer)

- Most throat cancer patients diagnosed with locoregionally advanced (LA) disease
- Current treatment: curative intent through use of multi-modal therapy, including surgery & chemoradiotherapy (CRT)
- Outcomes
  - 3-year probability of progression-free survival (PFS) is good (70-75%)
  - Patients who progress: clinical outcomes poor, even with addition of immune-checkpoint blockade therapy
  - Survival of patients who progress is under a year on average
  - Estimated 3k - 4k high-risk new patients per year in US
- Proposed Phase 3 trial: target high-risk patients with HPV-related LA throat cancer
  - To be conducted in North America and Europe
  - Aligned with FDA on trial design; received initial feedback from European regulators

Strong Case for Combination Therapy Based on Previously Completed Trials

Monotherapy: Phase 1/2a in pre-surgery or post CRT patient

PUBLISHED IN CLINICAL CANCER RESEARCH, 2019



CD8 STAINING PRIOR TO DOSING

CD8 STAINING AFTER TO DOSING

Combination Therapy: Phase 1b/2a in recurrent/metastatic patients

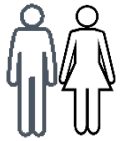
- Combined with AstraZeneca's PD-L checkpoint inhibitor, durvalumab
- ORR: 27.6% (4 CR, 4 PR) in 29 evaluable patients
  - Median OS was 29.2 months (confidence interval: 15.2-not calculable)
  - Peripheral HPV-specific T cells increased after treatment
- Updated results and published in *Clinical Cancer Research, 2023*

Existing trial data highlights strong rationale and potential benefit of combining INO-3112 to generate T cells targeting the HPV E6 & E7 oncogenes with a PD-1 inhibitor in HPV-16/18 related OPSCC

Completed Phase 2 Trial in HIV-Negative Participants

Precancerous Anal Dysplasia:

Phase 2 open-label trial



N=24

3 or 4 dose regimen at Months 0, 1, 3 and Week 36 (optional)

Final findings (6 months after start of treatment)

Clearance of HPV-16/18+ lesions: 50% of patients

The Spontaneous Rate is estimated to be less than 27%

- VGX-3100: composed of plasmids encoding for HPV-16 and HPV-18 subtypes; E6 and E7 oncogenes
- Open-label trial of VGX-3100 in 24 HIV-negative participants with HPV-16 and/or -18-positive anal HSIL
- 50% (11/22 evaluable) of participants showed no evidence of HPV-16/18-positive HSIL at Week 36
- 46% (10/22) of participants showed no evidence of HPV-16/18 virus at Week 36
- Adverse events were predominantly mild or moderate, and were in general associated with injection site reactions

Ongoing Phase 2 Trial in HIV-Positive Participants

- Trial initiated in September 2018
- 80-participant, open-label Phase 2 trial
- 4 doses at week 0, 4, 12, and 24
- Primary endpoint: overall response rate at 48 weeks – defined as regression of anal HSIL to LSIL or normal
- Sponsored by AIDS Malignancy Consortium

AMC
AIDS Malignancy Consortium

INO-5401 + INO-9012 for Newly Diagnosed Glioblastoma (GBM)

Completed Phase 1/2 Combination Trial with LIBTAYO®

- INO-5401 + INO-9012 with LIBTAYO and 40 Gy radiation/TMZ were observed to have favorable tolerability and immunogenicity
  - INO-5401 is a DNA medicine composed of plasmids that encode for 3 tumor-associated antigens: human telomerase (hTERT), Wilms tumor-1 (WT-1), and prostate-specific membrane antigen (PSMA)
  - INO-9012 is a DNA plasmid that encodes for human IL-12
  - LIBTAYO is a high-affinity, highly potent, human, hinge-stabilized IgG4 mAB to the PD-1 receptor

- Trial results:

Median OS; unmethylated (A)	17.9 mo. (14.5 – 19.8)	*Historical 14.6-16 mo.*
Median OS; methylated (B)	32.5 (18.4 – NR)	*Historical 23.2-25 mo.*
Median OS; combined (A+B)	19.5 (16.9 – 23.3)	-

NR: not reached.

Next steps:

Finalize protocol for controlled Phase 2; complete manufacture of drug for clinical supply

Gilbert et al. J Clin Oncol 2013; Gilbert et al. N Eng J Med 2014; Comparison to historical results do not represent head-to head comparisons and are limited due to differences in trial population and other factors; Data was presented at 2022 ASCO Annual Meeting; Libtayo® is owned, developed, and marketed globally by Regeneron

Boosts Binding & Neutralizing Antibodies Against Ebola

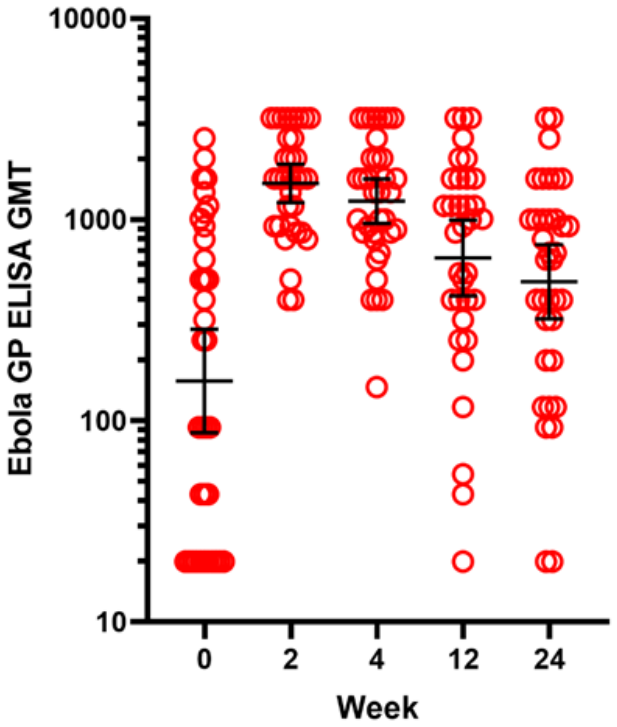
Recent progress:

- Re-submitted Ph 2 trial design to FDA
- Preparing to submit Phase 1b trial data to peer-reviewed journal with collaborators
- New FANG assay data: indicates INO-4201 elicits antibody response comparable to Ervebo® primary series vaccination

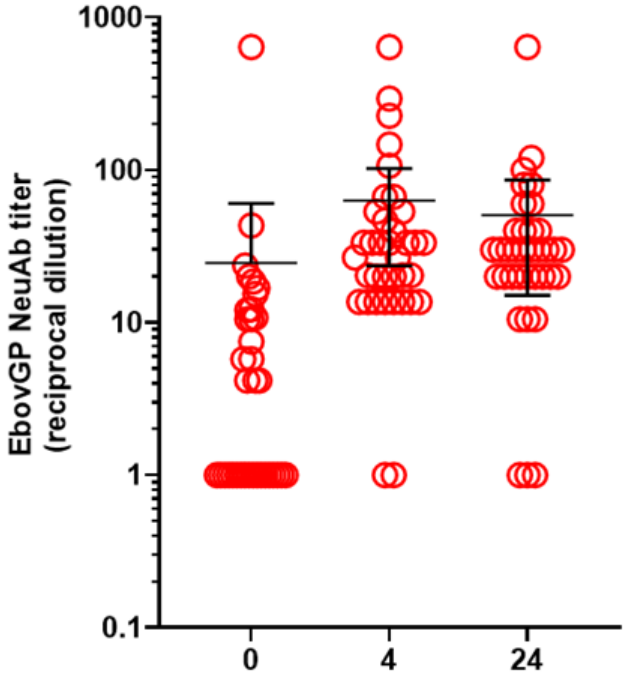
Phase 1b trial data as booster for Ervebo

- Safety & immunological data presented at ECCMID 2023
- Robust immune response, potential to extend vaccine protection

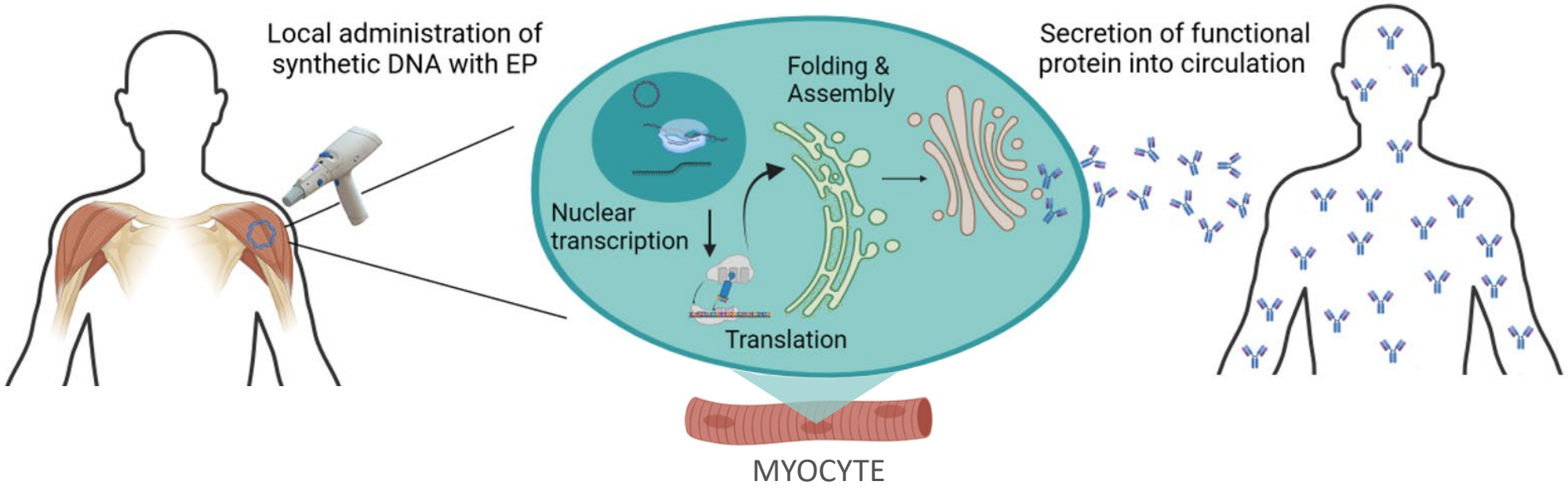
BINDING ANTIBODIES



NEUTRALIZING ANTIBODIES



The Next Generation of DNA Medicine

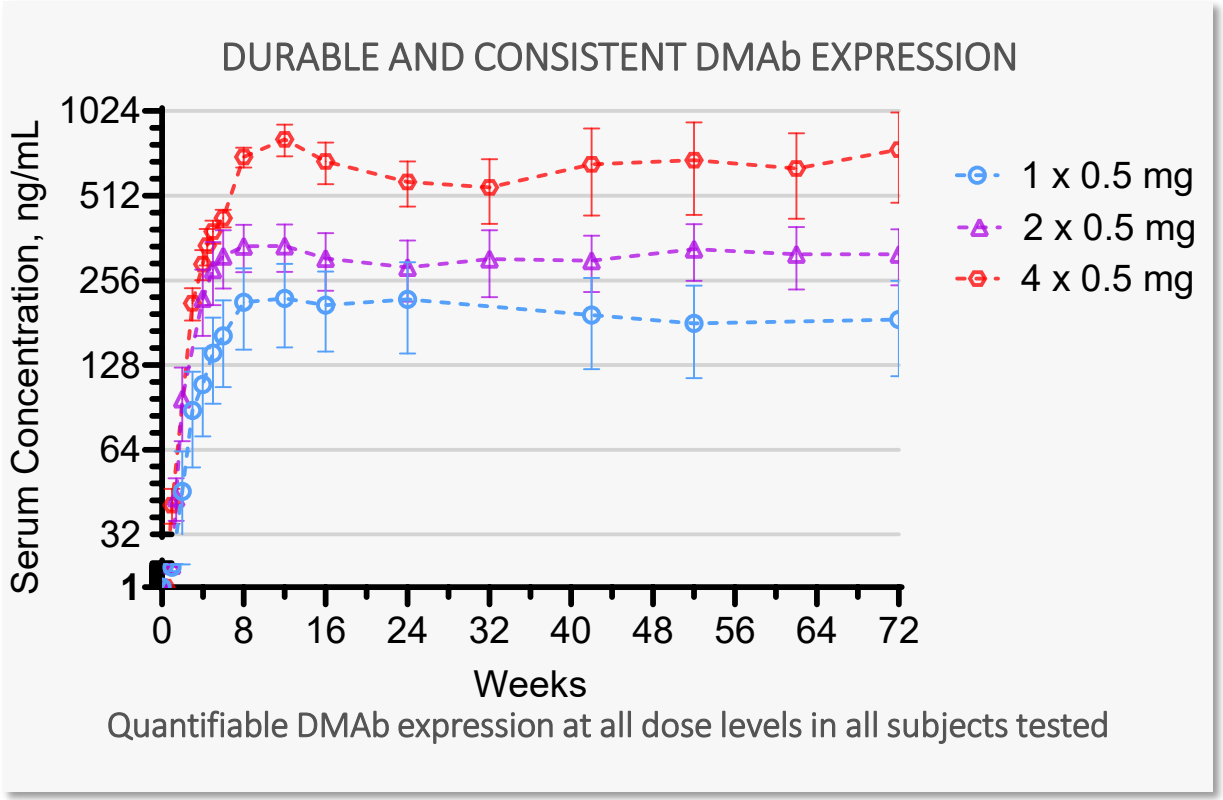


DMAb technology enables in vivo production of monoclonal antibodies (mAbs)

- DNA is administered via CELLECTRA device to enable local expression of the genes coding for the antibodies in the deltoid muscle.
- DMAbs are expressed and assembled in myocytes and secreted into the blood where they can circulate in the body.

Ongoing Phase 1 Trial: Data Published in *Nature Medicine*

- Long-lasting in vivo antibody production: DMAb levels remained stable for 72 weeks in all participants reaching that timepoint
- No anti-drug antibodies (ADA): no immune rejection of the DMAbs detected across ~1,000 blood samples
- Effective target binding: expressed DMAbs successfully bound to SARS-CoV-2 Spike protein receptor-binding domain, confirming functional activity through week 72
- Re-dosing at days 28 & 31 achieved DMAb levels over 1 µg/ml: Redosing appeared to be more effective at increasing DMAb concentrations compared with escalating single doses
- Well-tolerated: most common side effects were mild, temporary injection site reactions; no SAEs related to study drug



David Weiner, Pablo Tebas et al. Phase 1, dose-escalation trial of the safety and pharmacokinetics of SARS-CoV-2 DNA-encoded monoclonal antibodies (DMAb) in healthy adults. *Nature Medicine.* https://www.nature.com/articles/s41591-025-03969-0

Potential to Address Challenges of Conventional mAbs

Challenges with mAbs[1]

- Stability: susceptible to a variety of chemically- and temperature-induced structural changes
- Limited prophylactic use due to biologic half-life and complexities if mAb is not administered SC
- Even with half-life extension, repeated administration is required
- Production of recombinant mAbs in bioreactors is time intensive and costly
- Limited use in low resource settings

vs

INOVIO's DMAb technology

- Rapid manufacturing, low cost of production, and temperature-stable storage and distribution
- DNA is a non-live, non-integrating, non-replicating platform, with ability to be redosed
- Have exhibited prolonged expression in preclinical models with maintenance of serum levels >15µg/ml for over a year[2]
- Shortened development time compared to classic mAbs and re-administration due to lack of serological interference

Source: (1). Development issues: antibody stability, developability, immunogenicity, and comparability. In Woodhead Publishing Series in Biomedicine, Therapeutic Antibody Engineering, Woodhead Publishing, 2012, Pages 377-595, ISBN 9781907568374, https://doi.org/10.1533/9781908818096.377. (2). Duperret EK, Trautz A, Stoltz R, Patel A, Wise MC, Perales-Puchalt A, Smith T, Broderick KE, Masteller E, Kim JJ, Humeau L, Muthumani K, Weiner DB. Synthetic DNA-Encoded Monoclonal Antibody Delivery of Anti-CTLA-4 Antibodies Induces Tumor Shrinkage In Vivo. Cancer Res. 2018 Nov 15;78(22):6363-6370. doi: 10.1158/0008-5472.CAN-18-1429. Epub 2018 Oct 4. PMID: 30287678; PMCID: PMC6239932.

Potential Shown in Multiple Disease Models

PCSK-9

- **Delivery of anti PCSK-9 in mice lowers LDL cholesterol** (*Khoshnejad et al Mol Ther 2018*)

Influenza A & B viruses

- **Broadly neutralizing pan-influenza A & B approach**
- **Delivery of multiple antibodies** (*Elliott et al NJV 2017*)
- **Demonstrated disease protection in pig model** (*McNee et al. JI 2020*)

Cancer Antigens

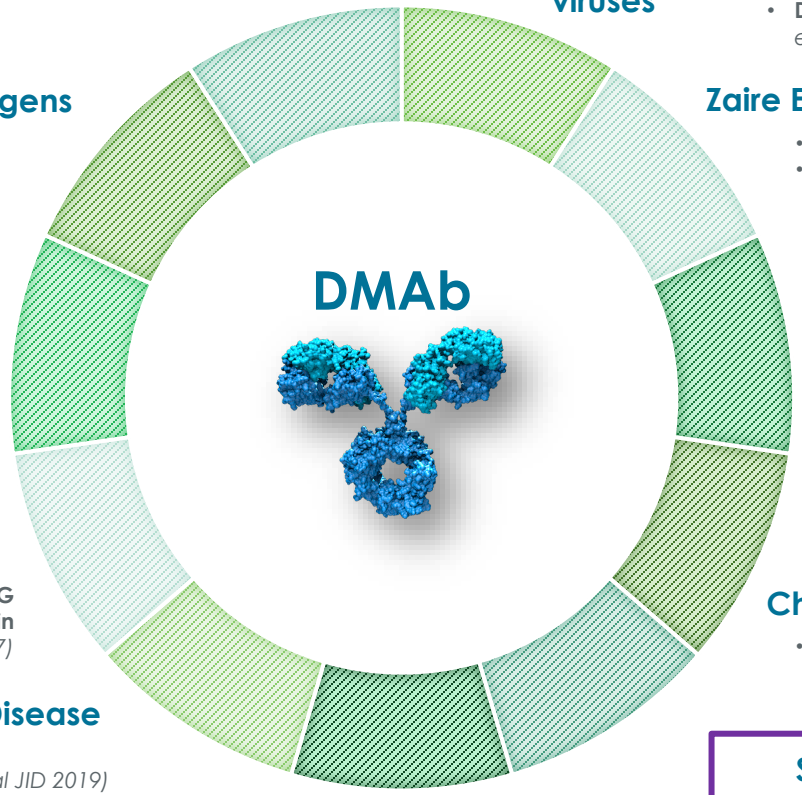
- **Demonstrated HER2/CD3 dBTEs can reduce tumor burden in mice** (Perales-Puchalt et al. JCI Insight. 2019)
- **Delivery of anti PSMA in mice impacted tumor challenge** (*Muthumani et al Cancer Immuno 2017*)

Zaire Ebolavirus

- **DMAb modifications and mouse model development**
- **Pre-exposure protection against highly lethal challenge in mice** (*Patel et al Cell Reports 2018*)

Checkpoint Inhibitors

- **Delivery of CPI in mice impacted and protected against tumor challenge** (Perales-Puchalt et al. *Oncotarget. 2019, Duperret et al. Cancer Res 2018*)



Dengue virus (DENV)

- **Protection against ADE** (*Flingai et al. Sci Rep 2015*)

Zika virus

- **scFV approach**
- **Protection from disease in NHPs** (*Esquivel et al. Mol Ther. 2019*)

Multi-drug resistant Pseudomonas aeruginosa

- **Multiple forms of DMAbs: monospecific, bispecific IgG**
- **Lowering pathogen burden and complementation in antibiotic resistant model** (*Patel et al Nat Comm. 2017*)

Chikungunya virus (CHIKV)

- **Rapid protection & complementarity with a vaccine** (*Muthumani et al., JID 2016*)

Lyme Disease

- **DMAb modifications** (*Yang et al JID 2019*)

SARS-CoV-2 – In P1 clinical trial

- **Highly potent DMAbs expressed in vivo** (candidates under clinical evaluation)

HIV

- **Delivery of multiple DMAbs to**
- **a single animal**
- **>10ug/ml in NHPs** (*Wise et al JCI 2020*)
- **DNA encoded post translational modifications** (*Xu, Wise et al EbioMed 2018*)

THE WISTAR INSTITUTE

Partnered Programs

PRODUCT	INDICATION	PHASE	SPONSOR	FUNDER/COLLABORATOR
VGX-3100	Cervical Dysplasia (HSIL) - China	3	INOVIO	ApolloBio
VGX-3100	Anal Dysplasia (HSIL) - HIV +	2	AMC AIDS Malignancy Consortium	NIH National Cancer Institute; AMC AIDS Malignancy Consortium
INO-5401	Glioblastoma	1/2	INOVIO	REGENERON
INO-5401	BRCA1/2 Mutation	1	Penn	Penn
INO-4800	COVID-19 (Solidarity)	3	World Health Organization	World Health Organization
INO-6172	HIV	1	NIH National Institute of Allergy and Infectious Diseases	HIV Vaccine Trials Network; The Wistar Institute
INO-6160	HIV	1	NIH National Institute of Allergy and Infectious Diseases	HIV Vaccine Trials Network; The Wistar Institute
DMAbs	COVID-19	1	Penn	DARPA; AstraZeneca; The Wistar Institute

Anticipated Upcoming Key Catalysts

INO-3107

- BLA file acceptance expected by EOY, potential PDUFA date in mid-2026
- Finalize confirmatory trial design and enroll first patient prior to approval of INO-3107
- Submit continued treatment trial design for sBLA to FDA after BLA approval
- Continue to present/ publish data

Commercialization

- Be ready to launch quickly and efficiently if approved
- Continue to build on market research
- Finalize planning for go-to-market strategy
- Complete plans for commercial organization

Pipeline

Next Gen Candidates

- Complete Phase 1 DMAb trial
- Identify partnership opportunities for DPROT/DMAb research

INO-3112 for OPSCC

- Finalize protocol for Phase 3
- Complete manufacture of drug supply for trial

INO-5401 for GBM

- Finalize protocol for Phase 2
- Complete manufacture of drug supply for trial

Thank you

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