INOVIO

# Corporate Presentation

June 2026

# 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; the FDA's acceptance of our BLA for INO-3107 with a PDUFA target action date set for October 30, 2026; and yet-to-be scheduled meeting with the FDA to discuss eligibility for the accelerated approval program; 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, including our expected cash runway into the first quarter of 2027; 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 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 Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, which has been filed with the Securities and Exchange Commission (SEC) and is 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 Overview

- Focused on developing and commercializing DNA medicines to treat and protect people from HPV-related diseases, cancer, and infectious diseases
- Targeting diseases with high unmet need and market opportunity

- Biologics License Application (BLA) for lead program (INO-3107) accepted for review by FDA Dec 2025
  - Potential treatment for Recurrent Respiratory Papillomatosis (RRP) – rare, HPV-related disease
  - Under active review under Accelerated Approval program with a PDUFA target date of October 30, 2026
  - FDA reiterated intent to schedule informal meeting to discuss potential review issue noted in file acceptance letter (eligibility for accelerated approval program)
  - Granted Orphan Drug and Breakthrough Therapy designations in US; Orphan Drug in EU

- Established commercial-scale manufacturing for plasmids; device manufacturing in-house
- Deep clinical pipeline with multiple potential near- and mid-term catalysts
- $37.7 M in cash, cash equivalents & short-term investments as of 3/31/26
  - Excluding net proceeds of $16.0 million from public offering in April 2026

# Advancing a Diversified Clinical Pipeline

| PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | REGISTRATION |
|---|---|---|---|---|
| DMAbs<br>Various Targets | INO-5401<br>BRCA 1/2 Mutation | VGX-3100<br>Anal Dysplasia | | INO-3107 *<br>RRP |
| DPROTs<br>Various targets | INO-4201<br>Ebola Booster | INO-3112<br>Head & Neck Cancer | | |
| DLNPs<br>Various targets | INO-6172<br>HIV | INO-5412<br>+ cadonilimab for Glioblastoma | | |
| | INO-6160<br>HIV | INO-5401<br>+ cemiplimab for Glioblastoma | | |
| | DMAbs<br>COVID-19 | | | |

OUT-LICENSED

| | | | | |
|---|---|---|---|---|
| | | | VGX-3100 **<br>Cervical Dysplasia (HSIL) | |

HPV-RELATED DISEASES  IMMUNO-ONCOLOGY  INFECTIOUS DISEASES  VARIOUS DISEASE TARGETS

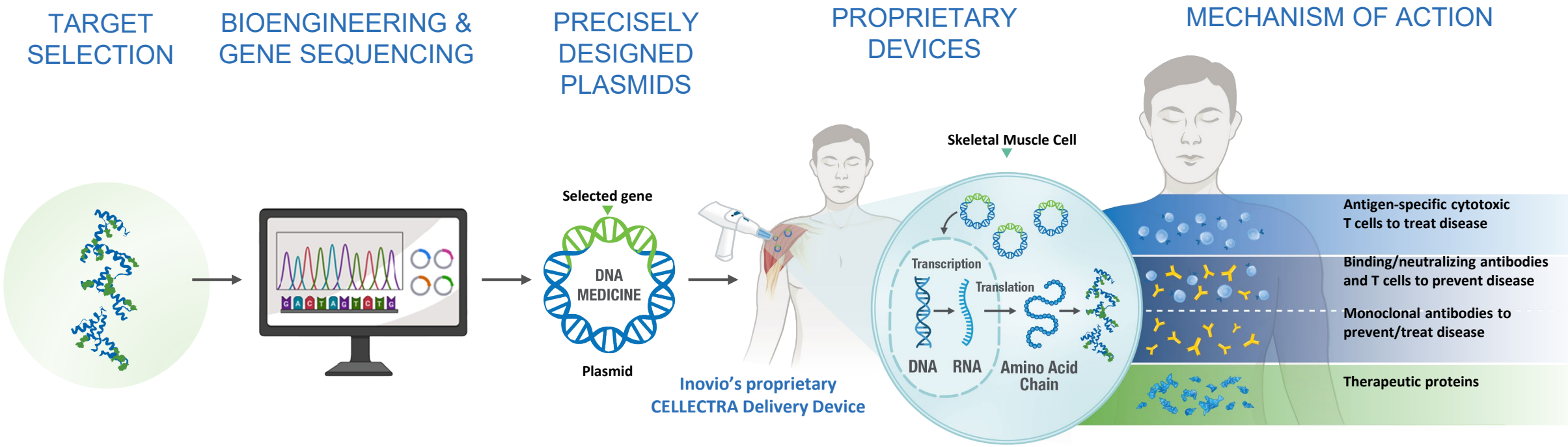
*BLA accepted for review under accelerated approval program in Dec 2025 with a target PDUFA date of Oct 2026 **VGX-3100 to Apollo Bio for China

# DNA Medicine Platform

Harnessing the power of in vivo protein production

INOVIO

# DNA Medicines: Customized *In Vivo*-Generated Proteins




## Inovio's DNA medicines platform enables tailored and sustained in vivo protein expression that can:

- Induce cytotoxic T cells to target specific cancers or viral infections
- Produce monoclonal antibodies for both prevention and treatment of diseases
- Achieve therapeutic levels of protein expression to support disease control in enzyme/protein replacement diseases

# Key Features of our DNA Medicines Platform

## Strengths include versatility & immunogenicity

**Targeted in vivo protein production** to fight disease

**Ability to be re-dosed** and sustain immune responses

**Allows rapid plasmid construct design** and manufacture


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

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

**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

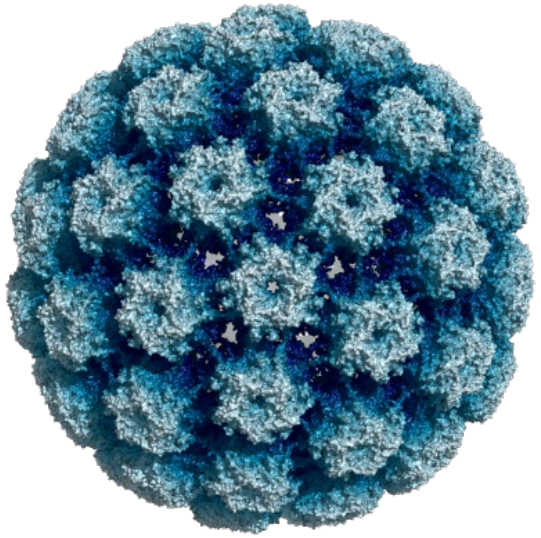
## Track record of success in the clinic:

- 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)

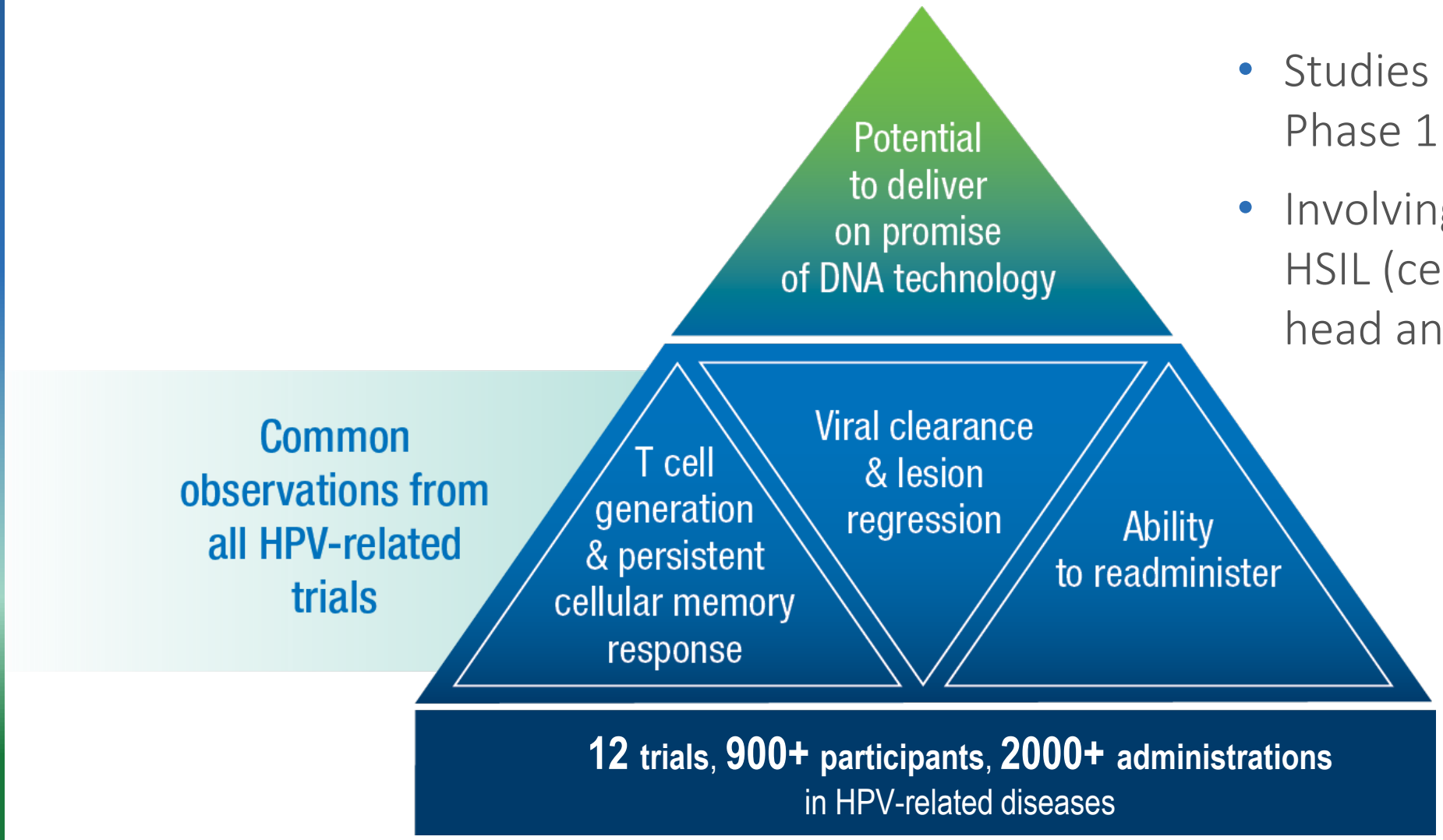
# Focus on HPV-Related Diseases

# 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)

- BLA accepted by FDA for review under Accelerated Approval program
- PDUFA target date of **Oct. 30, 2026**

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

## RRP: rare disease characterized by small, wart-like growths (papillomas) in the respiratory tract

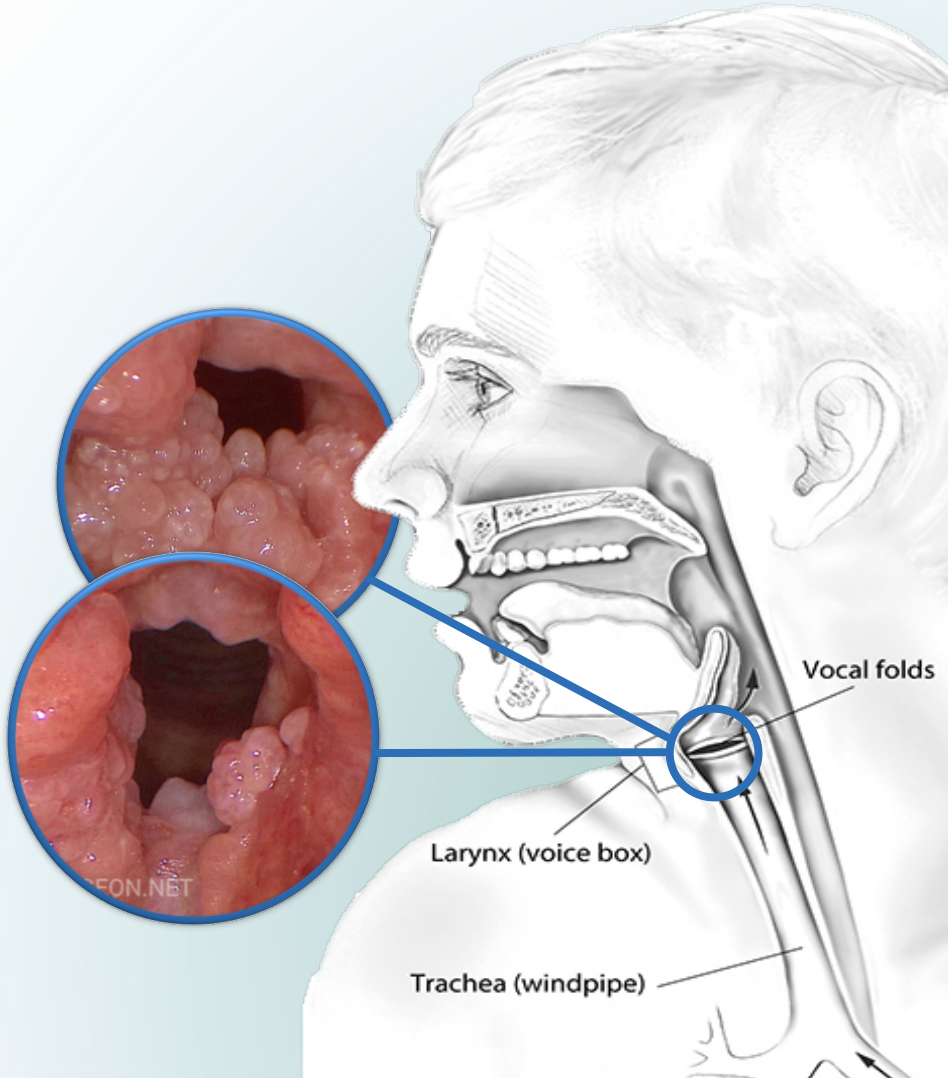
- Insufficient immune response that fails to prevent and clear HPV-6 and -11 infection leads to RRP

## Affects ~14,000 people in U.S., 1.8 per 100,000 new adult cases annually

- Repeated surgery is standard of care
- Every surgery entails significant risk and cost
  - Potential for irreversible damage to vocal cords
  - Impact on quality of life, financial

## INO-3107 addresses primary patient concern: reducing need for surgery

- Designed to generate an antigen-specific T-cell response against HPV-6 and -11, targets underlying cause of RRP



# 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

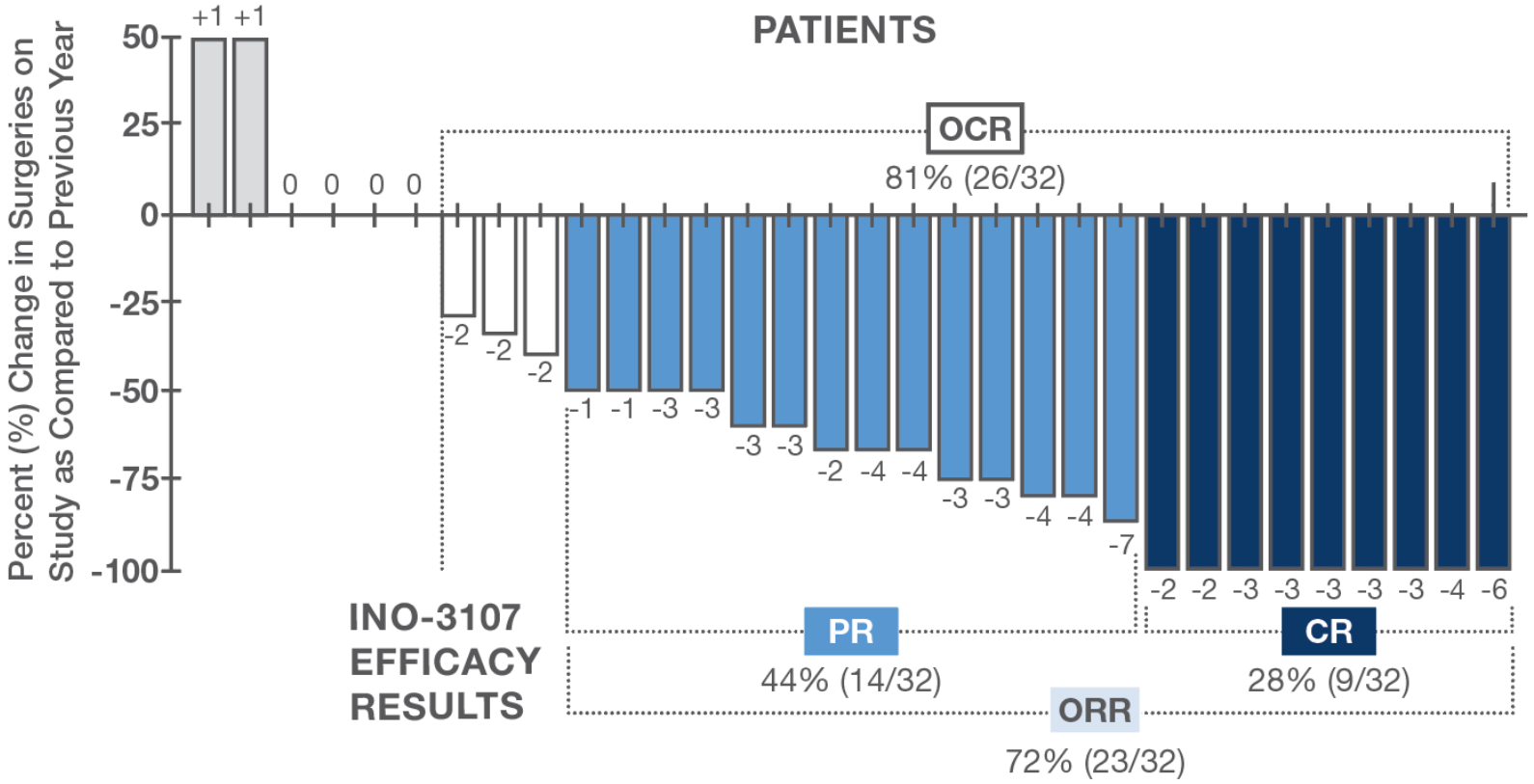
**Patient Population:** Intent-to-treat (ITT): all patients (32)

**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




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

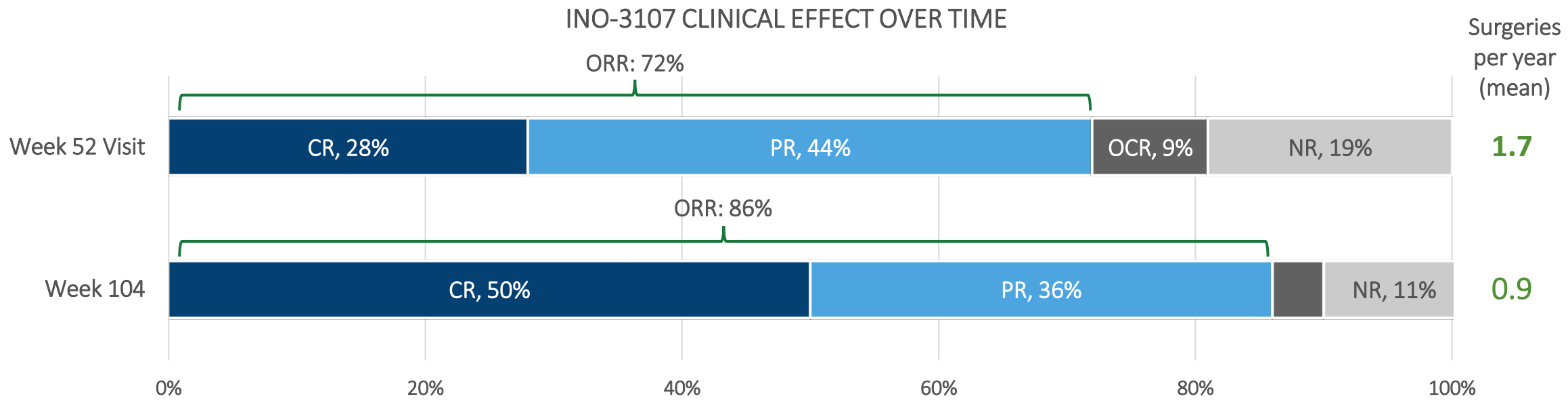
*Median decrease of 3 surgeries (95% Confidence Interval of 2 to 3) when comparing the year before treatment to the year following Day 0 of treatment.

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

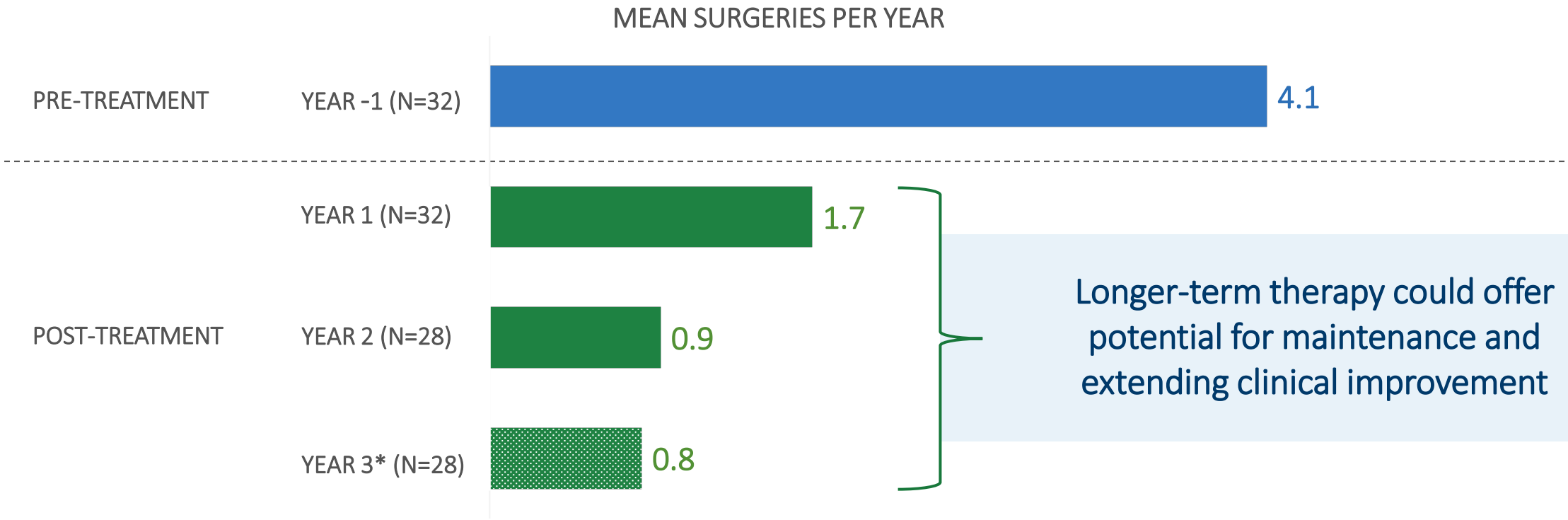
**PR** **Partial Response:** a ≥ 50% reduction and less than 100% in surgeries compared to previous year

**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

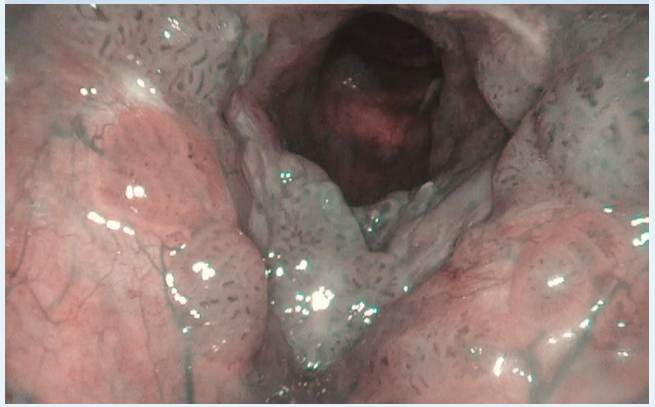
M. R. Amin, P. C. Belafsky, S. R. Best, et al., " DNA Immunotherapy (INO-3107) Results in Long-Term Surgery Reduction in RRP," *The Laryngoscope* (2025): 1–9, https://doi.org/10.1002/lary.32416.

*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



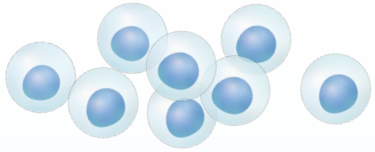
ONE YEAR FOLLOWING INO-3107

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

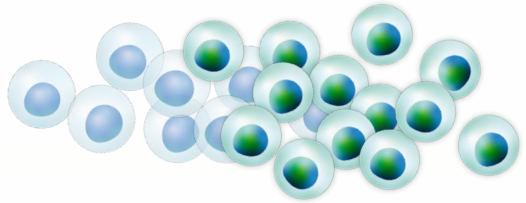
Morrow, M.P., Gillespie, E., Sylvester, A. et al. DNA immunotherapy for recurrent respiratory papillomatosis (RRP): phase 1/2 study assessing efficacy, safety, and immunogenicity of INO-3107. Nat Commun. 2025;16(1):1518.

# 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



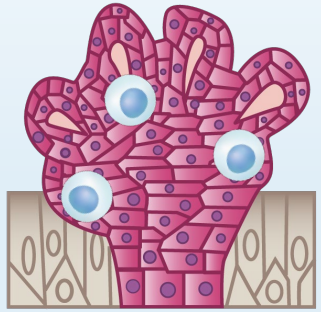
Pre-existing T cells in blood

Treatment with INO-3107 Immunotherapy

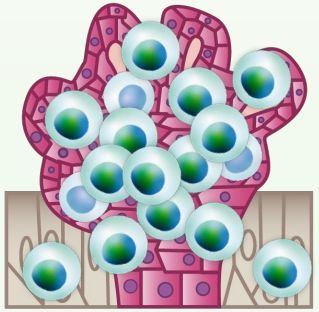
Expansion of pre-existing T cells and Induction of novel T cells in blood

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 year 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 year prior to treatment)

**Baseline: DAY 0** **WEEK 12** ····· **WEEK 64**

**Efficacy Assessment Begins:**

**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. Data from Papzimeos and INO-3107 are derived from different clinical trials at different points in time. No head-to-head trials have been conducted. As a result, cross-trial comparisons cannot be made.

INO-3107

# Accelerated Approval: We Believe INO-3107 Meets FDA Criteria[1]

## Meaningful therapeutic benefit over existing treatments

### EFFICACY

- **50% - 100% reduction in surgeries:**
  - 72% in YR 1
  - 86% in YR 2
- No surgeries (Complete Response):
  - 28% in YR 1
  - 50% in YR 2

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

### SAFETY

- **No required minimal residual disease (MRD) surgery during dosing window**
- PAPZIMEOS™: 72% of complete responders had surgery in dosing window[2]

## Potential to meet remaining critical unmet need

### DIFFERENTIATED MOA

- **Ability to treat patients who are not served by existing therapy**
- No impact from pre-existing neutralizing antibodies to the adenoviral platform or immunosuppressive factors within papilloma microenvironment

1 Guidance for Industry on Expedited Programs for Serious Conditions-Drugs and Biologics - May 2014; Expedited Program for Serious Conditions — Accelerated Approval of Drugs and Biologics Guidance for Industry DRAFT GUIDANCE -December 2024

2 Data from Papzimeos and INO-3107 are derived from different clinical trials at different points in time. No head-to-head trials have been conducted. As a result, cross-trial comparisons cannot be made. The data for Papzimeos is calculated based on data reported in Norberg S. et. al. Lancet Resp Med 2025; 13;318-26.

“The need for therapeutic alternatives to surgery in our RRP community remains immense. Every surgery matters, every patient matters, and every patient deserves a treatment that works for them.”

Kim McClellan
President, RRP Foundation

# 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 Commercial Readiness Plans

## Product Strategy:

- Completed market research to understand unmet medical needs and customer perspective
- Completed targeting, segmentation and product positioning work – supporting positive differentiation
- Developed pricing strategy with price optimization research ongoing
- Incorporating key learnings from competitor launch

## Go to Market Planning:

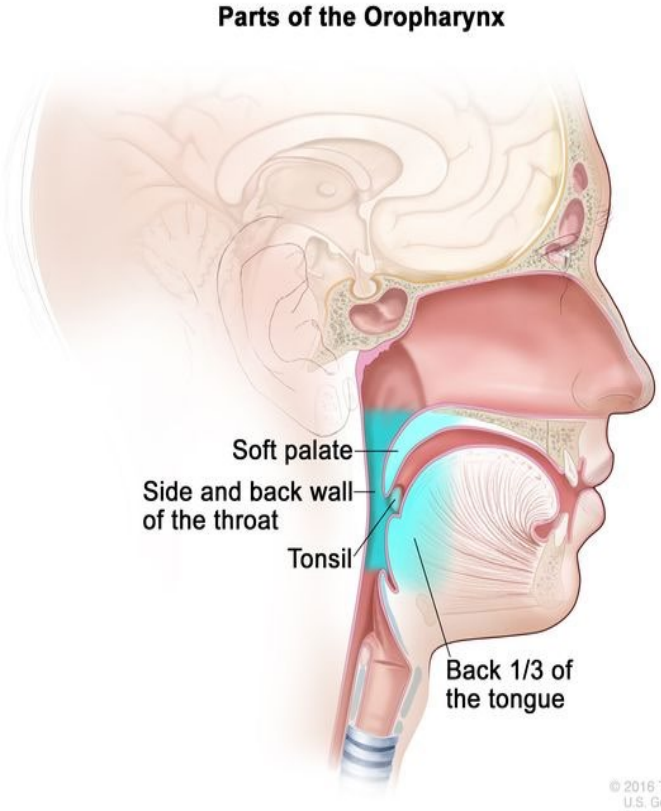
- INOVIO plans to commercialize in US, with support of a Contract Sales Organization
- Selected key commercial partners: third–party logistics provider, specialty distributor, specialty pharmacy, patient services HUB, Agency of Record

# Late-Stage Pipeline Candidates

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

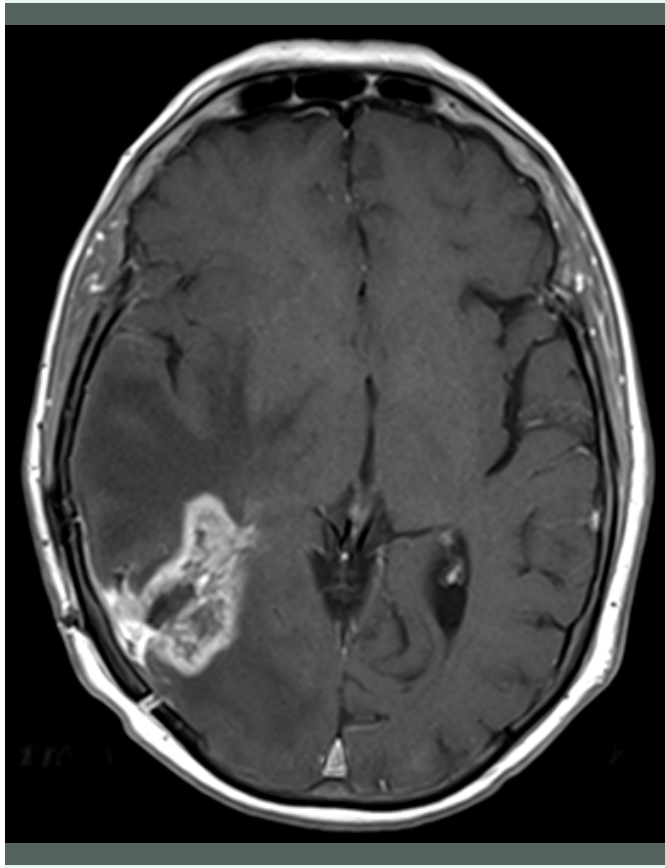
# Opportunity to Impact HPV-Related Locoregionally Advanced Oropharyngeal Squamous Cell Carcinoma (Throat Cancer)

- **Throat cancer: high unmet need in fast-growing indication**
  - Surpassed cervical cancer as most common HPV-related cancer diagnosed in the U.S. (~ 20,000 new cases/yr)
  - Estimated 3k - 4k high-risk new patients per year in US: poor clinical outcomes, <1 year mean survival
- **INO-3112: Strong case for combination therapy based on previously completed trials**
  - 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 checkpoint inhibitor in HPV-16/18 related OPSCC
- **Partnership with Coherus Biosciences**
  - Next steps: Phase 3 trial to evaluate INO-3112 + LOQTORZI, a PD-1 checkpoint inhibitor, FDA approved for treatment of NPC



# Innovative Partnership to Advance Novel Combination Therapy for Glioblastoma (GBM)

- **GBM: most common and aggressive form of brain cancer**
  - ~ 15,000 people diagnosed with GBM each year
  - Poor prognosis: typical life expectancy of 15-18 months, 5-year survival rate <10%
- **INO-5412 + cadonilimab: Potential to further improve patient outcomes**
  - INO-5412 = INO-5401 + T cell immune activator INO-9012
  - Cadonilimab: Akeso's first-in-class PD-1/CTLA-4 bi-specific antibody, could potentially provide additional checkpoint inhibition through CTLA-4 binding
  - Previous data shows potential of INO-5401 + INO-9012 + PD-1 checkpoint inhibitor to improve patient outcomes
- **Partnership with Dana-Farber Cancer Institute & Akeso**
  - Plan to evaluate INO-5412 + cadonilimab in Phase 2 INdividualized Screening trial of Innovative Glioblastoma Therapy (INSIGhT), sponsored by DFCI



*Scan from patient in previous Phase 1/2 trial of INO-5401+INO-9012 + PD1 inhibitor*

Critical unmet need for new, effective GBM treatments

# Support for GBM Research: Completed Phase 1/2 Combination Trial with PD-1 Checkpoint Inhibitor LIBTAYO®

## INO-5401 + INO-9012 in combination with a PD-1 checkpoint inhibitor elicited robust immune responses that potentially correlated with enhanced survival

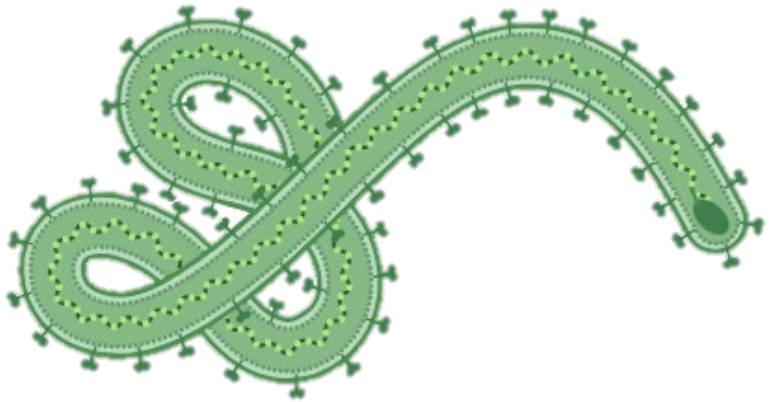
- **LIBTAYO®:** high-affinity, highly potent, human, hinge-stabilized IgG4 mAB to the PD-1 receptor
- INO-5401 + INO-9012 with LIBTAYO and 40 Gy radiation/TMZ were observed to have favorable tolerability and immunogenicity

| | | |
|---|---|---|
| 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) | - |

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

# Leveraging Key Advantages of DNA Medicine to Extend Ebola Protection

- **Existing Ebola vaccines provide protection, but duration unclear**
  - Two vaccines available (ERVEBO® and Zabdeno®)with limited or no boost options
  - With periodic outbreaks, multiple boosters might be needed during lifetime of a person
  - Protecting healthcare providers and others essential to containment efforts
- **INO-4201: Well-suited as (heterologous) booster vaccine**
  - No anti-vector immunity = ability to boost repeatedly
  - Induces antigen-specific immune responses
  - No frozen storage or shipping required
- **Phase 1b trial: INO-4201 boosts binding & neutralizing antibodies against Ebola**
  - Collaboration with University of Geneva, Switzerland (Sponsor), GuardRX, DARPA
  - INO-4201 elicited robust antibody response through Week 24, showing potential to boost vaccine protection
  - Next steps: seeking partnerships to advance research



*Ebola virus*

# Positive Topline Results from ApolloBio's Phase 3 Trial of VGX-3100 in Cervical Dysplasia Patients

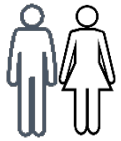
- VGX-3100: INOVIO's investigational DNA immunotherapy licensed to ApolloBio
  - Currently in development by ApolloBio in China as potential treatment for cervical dysplasia
- Trial successfully met predefined primary efficacy endpoint, demonstrated overall favorable safety and tolerability profile
  - Endpoint: composite response rate at Week 36, defined as histopathologic regression of cervical disease to low-grade lesion or normal histology, together with clearance of HPV-16 and/or HPV-18 infection
  - Results highlight potential of INOVIO's DNA medicine platform to treat HPV-related diseases, eliminating/reducing need for surgical interventions
- ApolloBio plans to use results to support future regulatory submission of VGX-3100 in China

ApolloBio

# 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

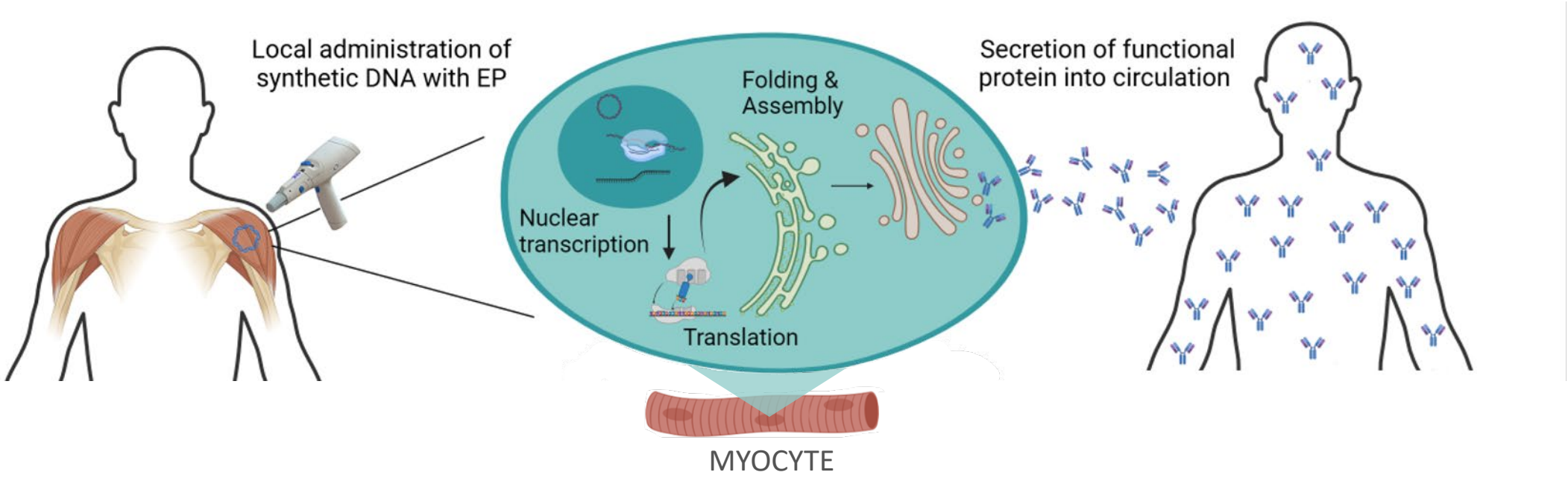
- Trial initiated in September 2018
  - 80-participant, open-label Phase 2 trial
  - 4 doses at week 0, 4, 12, and 24
- Primary endpoint: overall response rate at 48 weeks – defined as regression of anal HSIL to LSIL or normal
- Sponsored by AIDS Malignancy Consortium

# Next-Generation DNA Medicine

- Innovative technology builds on strengths of platform
- Potential to transform treatment paradigm in rare disease

INOVIO

# Next-Gen Technology Enables In Vivo Production of Monoclonal Antibodies

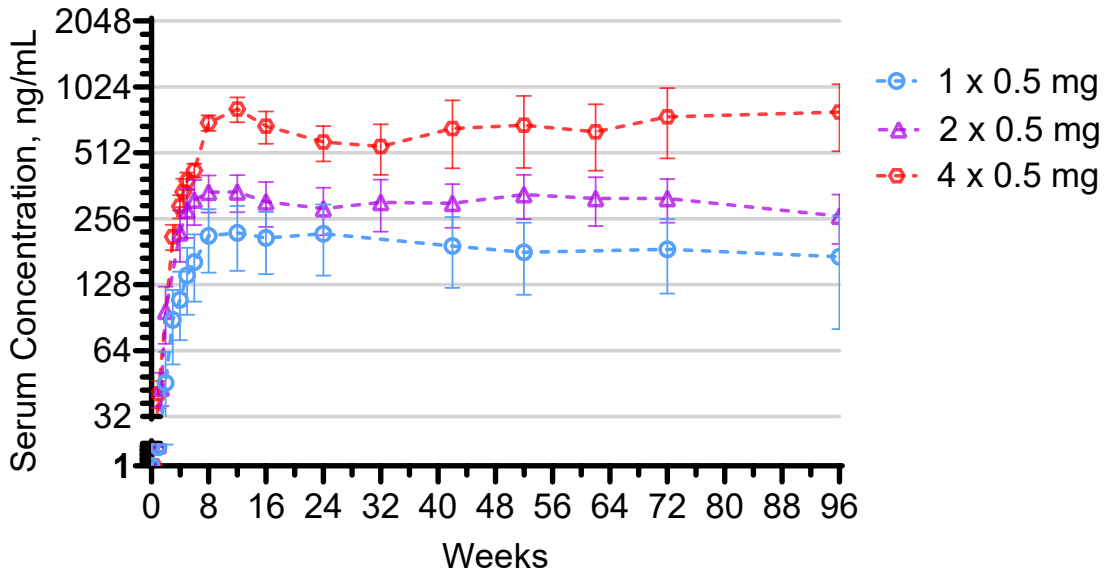



- DNA is administered via CELLECTRA device to enable local expression of the genes coding for the antibodies in the deltoid muscle.
- DMAbs are expressed and assembled in myocytes and secreted into the blood where they can circulate in the body.

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

- **Long-lasting in vivo antibody production:** DMAb levels remained stable for 96 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

DURABLE AND CONSISTENT DMAb EXPRESSION




Quantifiable DMAb expression at all dose levels in all subjects tested

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

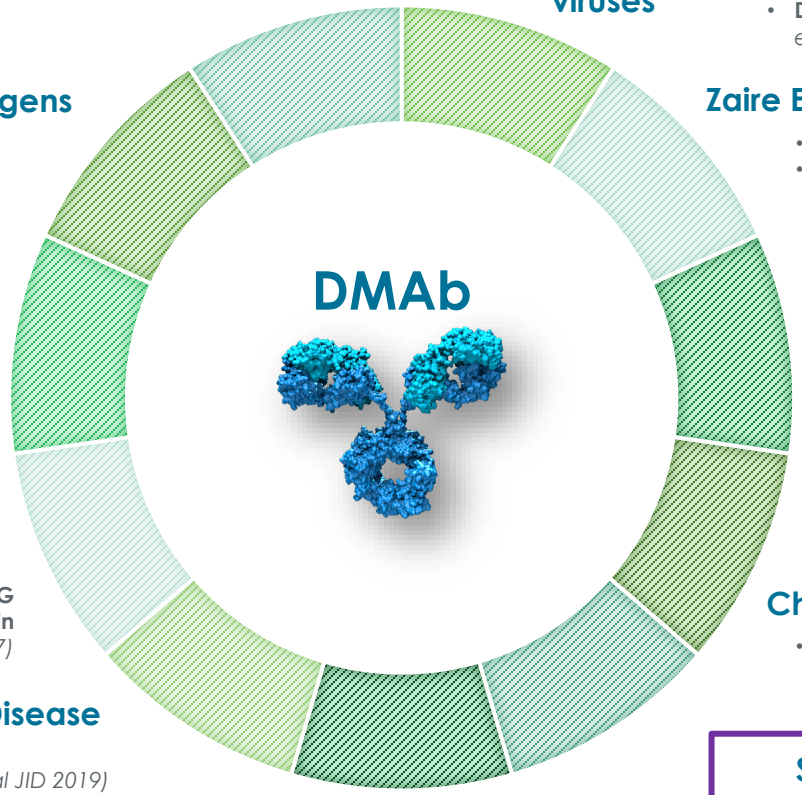
vs

## 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*)

## 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*)

## Zika virus

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

## 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

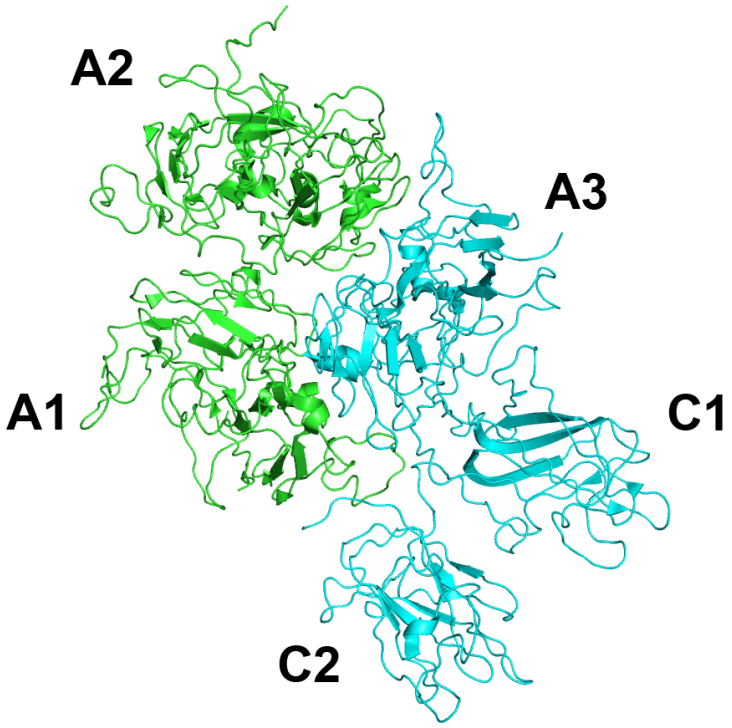
- **Delivery of multiple DMAbs to**
- **a single animal**
- **>10ug/ml in NHPs** (*Wise et al JCI 2020*)
- **DNA encoded post translational modifications** (*Xu, Wise et al EbioMed 2018*)

THE WISTAR INSTITUTE

# Potential as a New Treatment Paradigm in Rare Diseases

- **Builds on DMAb technology**
  - Targets long-term protein expression, with ability to re-dose due to lack of anti-vector immunity
- **Aims to address shortcomings of conventional therapeutic protein/enzyme replacement**
- **Promising preclinical data on DPROTs targeting Hemophilia A presented at World Federation of Hemophilia Global Forum**
  - Expression of FVIII achieved in skeletal muscle cells with activity reaching 50%
  - Confirms complex proteins such as FVIII can be effectively produced, assembled in myocytes and secreted into circulation
  - Treated mice showed significantly reduced bleeding time and blood loss compared to control
- **Seeking partnerships to advance technology in Fabry, Hypophosphatasia (HPP) and other rare disease targets**

FACTOR VIII PROTEIN STRUCTURE



# INOVIO Partnerships

| PRODUCT | INDICATION | PHASE | SPONSOR | FUNDERS/COLLABORATORS |
|---|---|---|---|---|
| VGX-3100 | Cervical Dysplasia (HSIL) – China | 3 | INOVIO | Apollobio |
| VGX-3100 | Anal Dysplasia (HSIL) – HIV+ | 1 | AMC AIDS Malignancy Consortium | NIH National Cancer Institute; AMC AIDS Malignancy Consortium |
| INO-5401 | Glioblastoma | 1/2 | INOVIO | REGENERON |
| INO-5412 | Glioblastoma | 2 | Dana-Farber Cancer Institute | Akesobio; Dana-Farber Cancer Institute |
| INO-5401 | BRCA 1/2 Mutation | 1 | Penn | Penn |
| INO-4800 | COVID-19 (Solidarity) | 3 | World Health Organization | World Health Organization |
| INO-6172 | HIV | 1 | NIH National Cancer Institute | HIV Vaccine Trials Network; The Wistar Institute |
| INO-6160 | HIV | 1 | NIH National Cancer Institute | HIV Vaccine Trials Network; The Wistar Institute |
| DMAbs | COVID-19 | 1 | Penn | DARPA; AstraZeneca; The Wistar Institute |

# Progressing Strategy to Unlock the Promise of DNA Medicine

## NEAR TERM

### Working to Deliver INO-3107 to Patients

- BLA accepted for review under accelerated approval program in Dec 2025
  - Standard review schedule, PDUFA date Oct 30, 2026
  - FDA to schedule meeting to discuss preliminary comments in file acceptance letter regarding accelerated approval eligibility
- Potential to be preferred first-line treatment, if approved, based on:
  - Efficacy
  - Tolerability
  - Simple & patient-centric treatment regimen
- 1st DNA Medicine in U.S. if approved

## MID TERM

### Advancing Diversified Clinical Pipeline

- Additional clinical candidate partnerships, including:*
  - INO-5412: collaboration with Akeso to evaluate combination with cadonilomab in GBM (February 2026)
  - DMAb: 1st proof-of-concept clinical data published in *Nature Medicine* (October 2025)
  - INO-3112: clinical collaboration with Coherus to evaluate combination with LOQTORZI™ in HPV-related throat cancer (January 2024)

*Wholly-owned & in collaboration with 3rd parties

## NEXT GEN

### 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
  - Promising preclinical data presented at World Federation of Hemophilia Global Forum (November 2025)
  - New targets include Fabry Disease, Hypophosphatasia

# Thank you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