INOVIO
POWERING DNA MEDICINES™

# Corporate Presentation

May 2023

NasdaqINO

# 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.

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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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# INOVIO is a DNA Medicines Company

- Ended first quarter 2023 with $223.8M in cash, cash equivalents, and short-term investments
  - Expected to fund company's operations into 1Q25
  - Support strategic developmental plans for early-stage and late-stage pipeline candidates
- Versatile technology platform with strong patent position
- Diversified pipeline of product candidates targeting important diseases with high unmet medical needs
- Experienced management team

# Delivering on our Mission to Bring DNA Medicines to Market

## 2023 Objectives

- **INO-3107 – Recurrent Respiratory Papillomatosis (RRP)**
  - **Completed:** Announced positive Phase 1/2 data
  - **Next milestone:** Initiate Phase 3 (registrational) trial
- **VGX-3100 (REVEAL2) – Cervical High-Grade Squamous Intraepithelial Lesions (HSIL)**
  - **Completed:** Announced Phase 3 data (non-registrational trial)
  - **Next milestone:** Biomarker analysis results in 3rd quarter
- **INO-4201 – Ebola**
  - **Completed:** Announced positive Phase 1b data for INO-4201 as a booster for Ervebo®
  - **Next milestone:** Submit data for publication in peer-reviewed journal and determine next steps with partners
- **INO-3112 – HPV-Related Cancers**
  - **Next milestone:** Provide update for clinical development plan
- **INO-5401 – Glioblastoma (GBM)**
  - **Next milestone:** Provide update for clinical development plan

# Key Features of our DNA Medicines Platform

**Optimized DNA plasmids** delivered through investigational **proprietary smart device**

**Balanced antibody and T cell responses** to a wide range of antigen targets

Demonstrated the ability to drive **CD8⁺ T cell responses** against multiple indications

**Targets multiple antigenic sequences;** combining multiple antigens into single vial


**Well-tolerated** in more than 15,000 administrations (~5k participants)

**No anti-vector response;** ability to readminister and boost

**No frozen storage or shipping required**

Allows **rapid plasmid construct design** and manufacture



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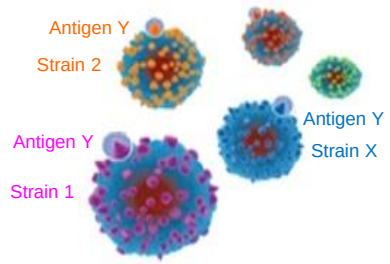
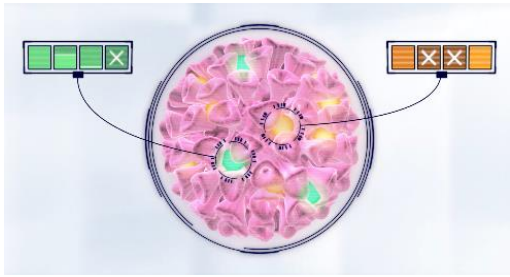
# DNA Medicines Technology – Powering Antigen Specific Immune Responses

1. Identify diverse strains/variants of a target pathogen or cancer




2. Assess gene sequence of selected antigen(s) from chosen strains/variants of the pathogen or cancer



3. Create optimal Consensus Sequence for the selected antigen

| | |
|---|---|
| Sequence 1 | EMEKIVLLFAIV…SL |
| Sequence 2 | AMESIVLLFAIV…SL |
| Sequence X Consensus | AMEKIVILLFAIV…SK |
| | AMEKIVILLFAIV…SL |

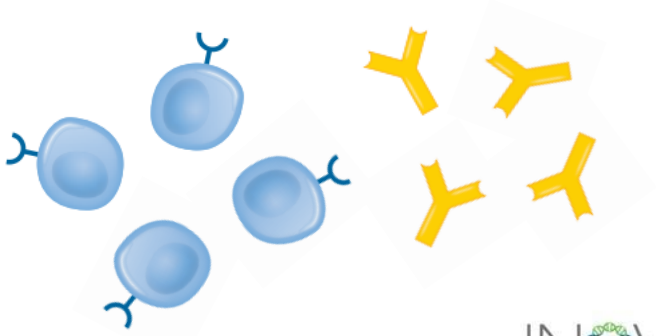
4. Insert optimized sequence for each selected antigen to construct precisely designed plasmid


5. Manufacture DNA medicine and deliver into muscle (IM) or skin (ID) using proprietary smart device

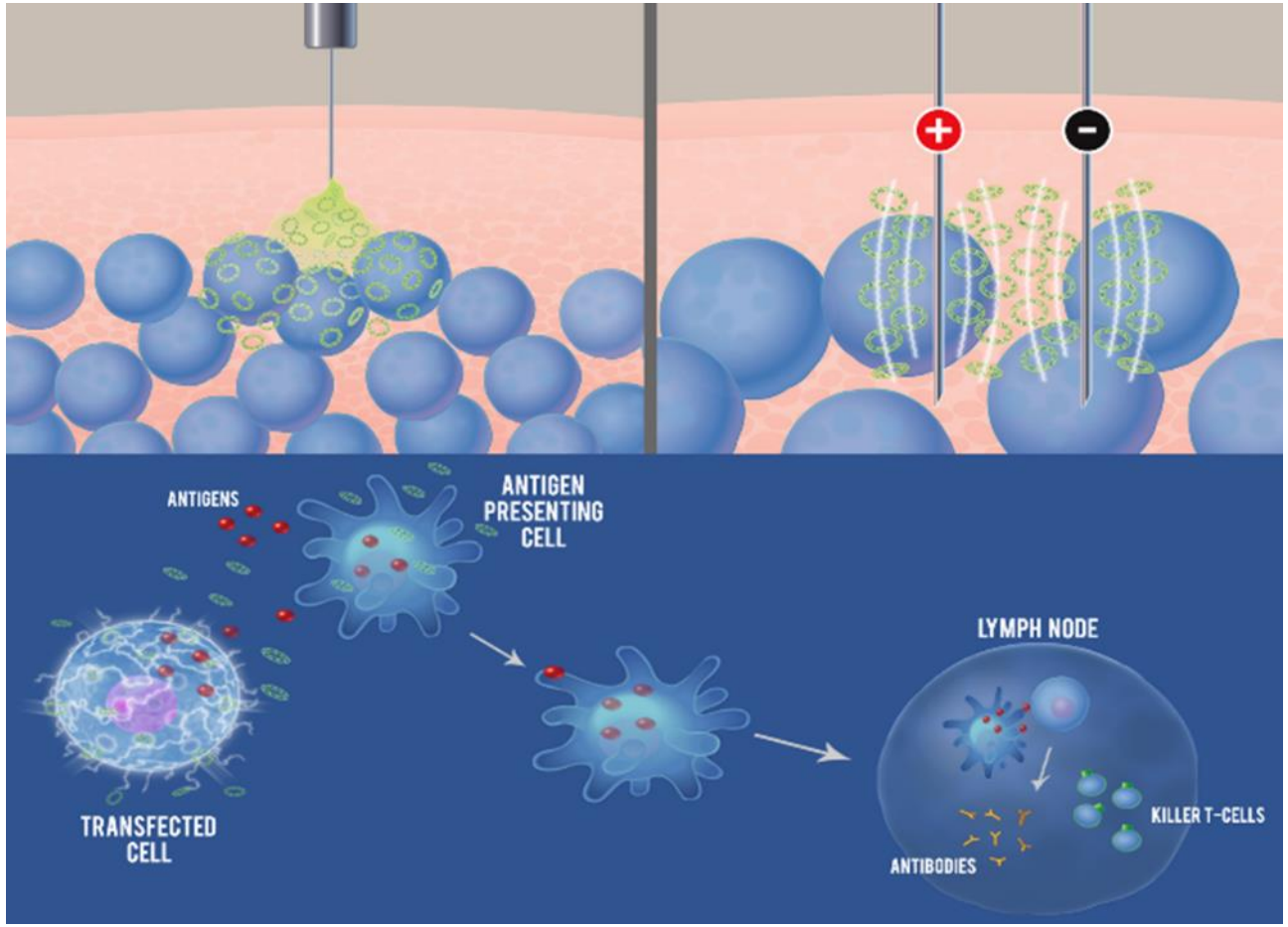
Intramuscular (IM) Device
for Pre-Cancers & Cancers

Intradermal (ID) Device
for Vaccines

6. Protective antibody and killer T cells ($CD8^+$) produced by immune system



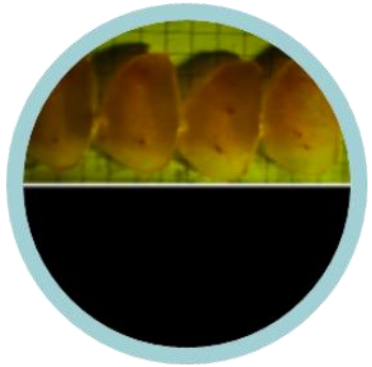
# Delivery with CELLECTRA® Results in Improved Immune Responses




**No CELLECTRA®**

Rabbit Muscle +GFP

GFP



**With CELLECTRA®**

Rabbit Muscle +GFP

GFP

Sardesai NY, et al. *Curr Opin Immunol.* 2011;23(3):421–429.
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"GFP" – Green Fluorescent Protein



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# INOVIO DNA Medicines Pipeline

| | PRODUCT | INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | PARTNER/COLLABORATOR/ FUNDER |
|---|---|---|---|---|---|---|---|
| HPV-TARGETED | VGX-3100 | Cervical Dysplasia (HSIL) | | | | | |
| | | Anal Dysplasia (HSIL) (HIV-) | | | | | |
| | | Vulvar Dysplasia (HSIL) | | | | | |
| | | Cervical Dysplasia (HSIL) - China | | | | | Apollobio |
| | | Anal Dysplasia (HSIL) (HIV+) | | | | | AMC AIDS Malignancy Consortium |
| | INO-3107 | Recurrent Respiratory Papillomatosis (RRP) | | | | | |
| IMMUNO-ONCOLOGY | INO-5401 | Glioblastoma (GBM) | | | | | REGENERON |
| INFECTIOUS DISEASES | INO-4800 | COVID-19 (Solidarity) | | | | | World Health Organization |
| | INO-4201 | Ebola (Booster) | | | | | DARPA, Université de Genève, GuardRX |
| | | HIV | | | | | NIH National Institute of Allergy and Infectious Diseases, HIV Vaccine, The Wistar Institute |
| dMAb™ | | COVID-19 | | | | | AstraZeneca, DARPA, The Wistar Institute |
| | INO-A002 | Zika | | | | | Bill & Melinda Gates foundation |

INTERNALLY FUNDED

EXTERNALLY FUNDED

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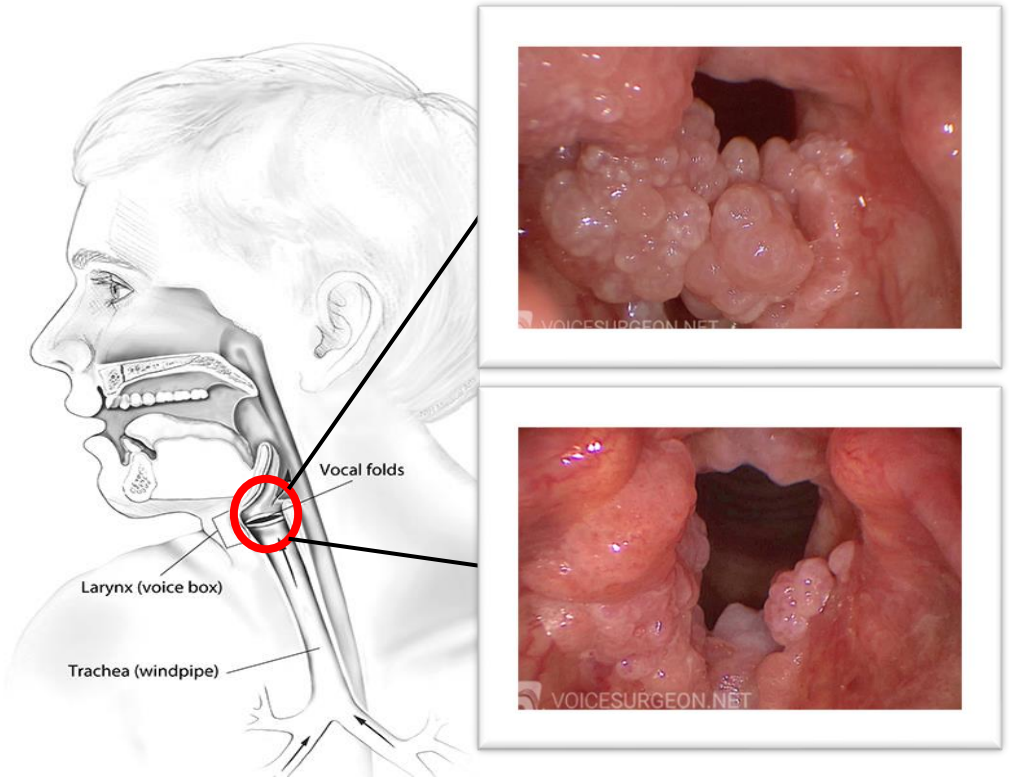
# What is Recurrent Respiratory Papillomatosis (RRP)?

- RRP is a rare disease caused by HPV-6/11, impacting both children and adults
- Symptoms result from benign tumors – papillomas – in throat and on voice box
  - Can obstruct airway and cause difficulty speaking
  - Can lead to chronic cough, infections, pneumonia, hoarseness and failure to thrive
  - Rare risk of progression to lung disease and cancer
- Surgery is current standard of care
  - Patients can require hundreds of surgeries during their lifetime
  - In severe cases with aggressive tumor growth, tracheostomies may be needed to help with breathing
- The most widely cited U.S. epidemiology data comes from a Task Force led by Craig Derkay. At that time, there were around 14K active cases and around 1.8 per 100,000 new cases in adults each year

# Potential Benefits of Therapeutic DNA Medicine in Treating HPV-6 and HPV-11-Related RRP




- INO-3107 represents a potential first-in-class non-surgical therapeutic option for HPV-6 and HPV-11-related RRP
- Potential benefits could include:
  - Reduced number of surgical interventions needed to control regrowth of papillomas
  - Clearance of underlying HPV infection
  - Increased quality of life by eliminating and/or controlling symptoms
  - Reduced risk associated with repeat surgical interventions
- INO-3107 granted Orphan Drug Designation by FDA in July 2020

Image Source: National Institute on Deafness and Other Communication Disorders; Available at www.nidcd.nih.gov/health/recurrent-respiratory-papillomatosis; accessed July 27, 2022;

Photographs courtesy Aaron Friedman MD, University of Cincinnati College of Medicine (https://voicesurgeon.net/voice-disorders/recurrent-respiratory-papillomatosis-rrp/). Used with permission.



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# INO-3107: Phase 1/2 Trial Design for RRP

Phase 1/2 open-label,
multi-center clinical trial

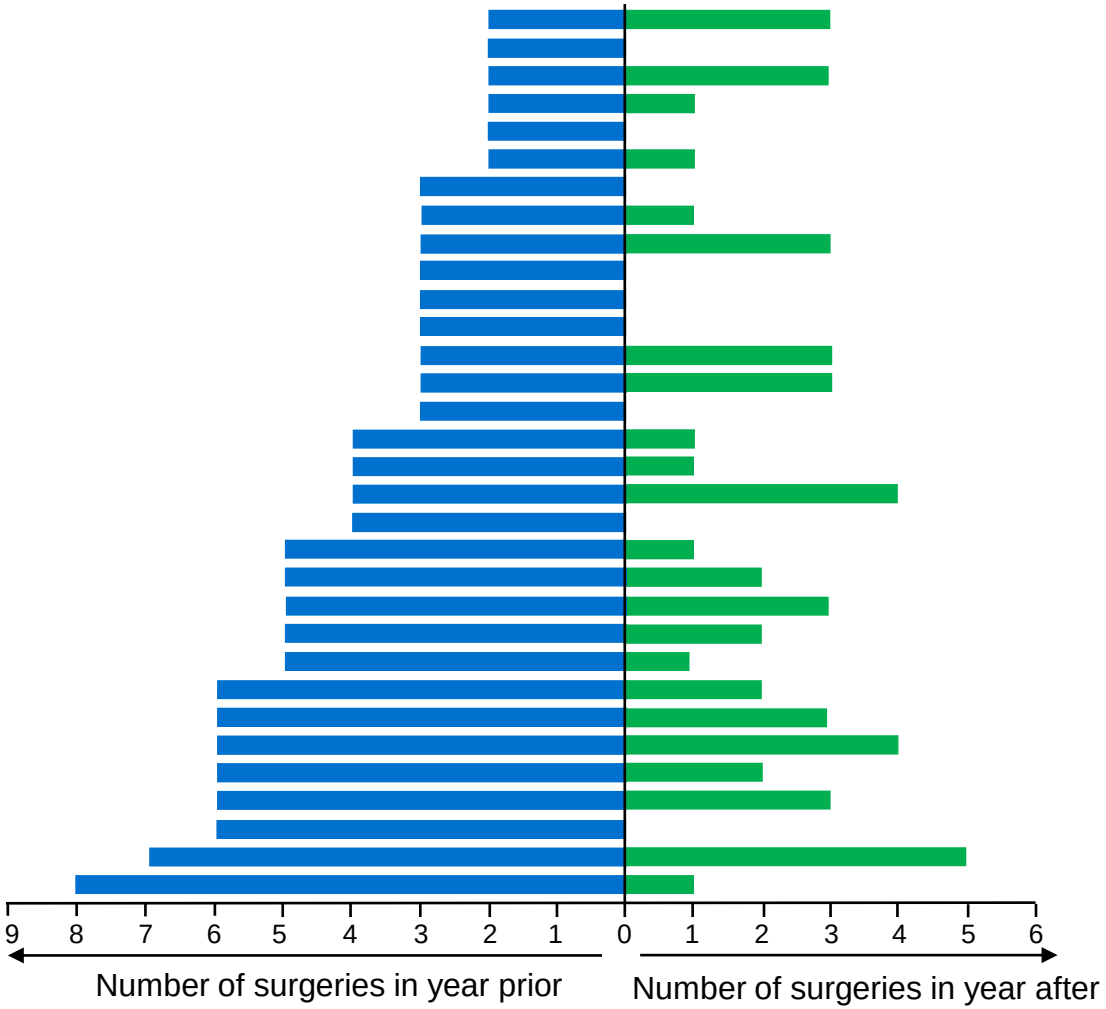
n=32

32 patients enrolled;
two cohorts

4 doses of INO-3107
on Day 0, Weeks 3, 6, 9

- **INO-3107:** composed of plasmids encoding for HPV-6, HPV-11, and human interleukin-12
- **Enrollment criteria:** Patients who have required at least two surgical interventions per year for the past year for the removal of HPV-6/11-related papilloma(s)
- **Efficacy endpoint:** Change in number of surgical interventions in year prior to Day 0 when compared with year following Day 0
- **Surgeries:** counted from Day 0, **even during dosing**

# INO-3107 Phase 1/2 Trial: Decrease in Number of Surgeries




- Overall, **26 patients (81.3%) had a decrease in surgical interventions** in the year after INO-3107 administration versus the prior year
- 9 patients (28.1%) required **no surgical intervention**
- Median change in the number of surgeries from the year prior to baseline to the year following was -3 (95% CI: -3 to -2)



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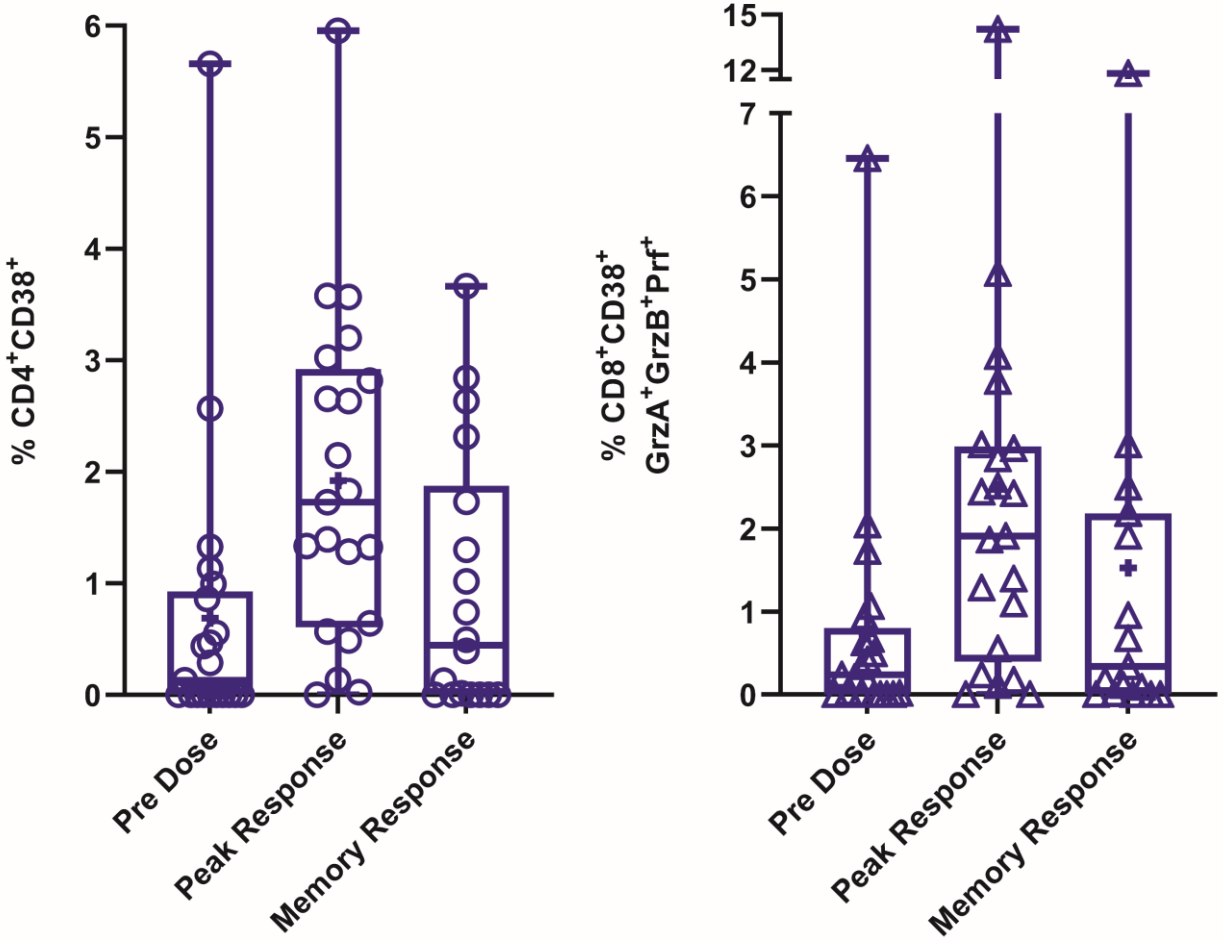
# INO-3107: Cellular Response

- Treatment induced activated CD4 T cells and activated CD8 T cells with lytic potential
  - Percentages similar for HPV-6 and HPV-11
- T-cell responses were observed at Week 52 indicating a persistent cellular memory response
- Additional analyses are ongoing to determine a possible relationship between CD4 and CD8 phenotypes and clinical outcomes




GrzA, granzyme A; GrzB, granzyme B; HPV, human papillomavirus; Prf, perforin.



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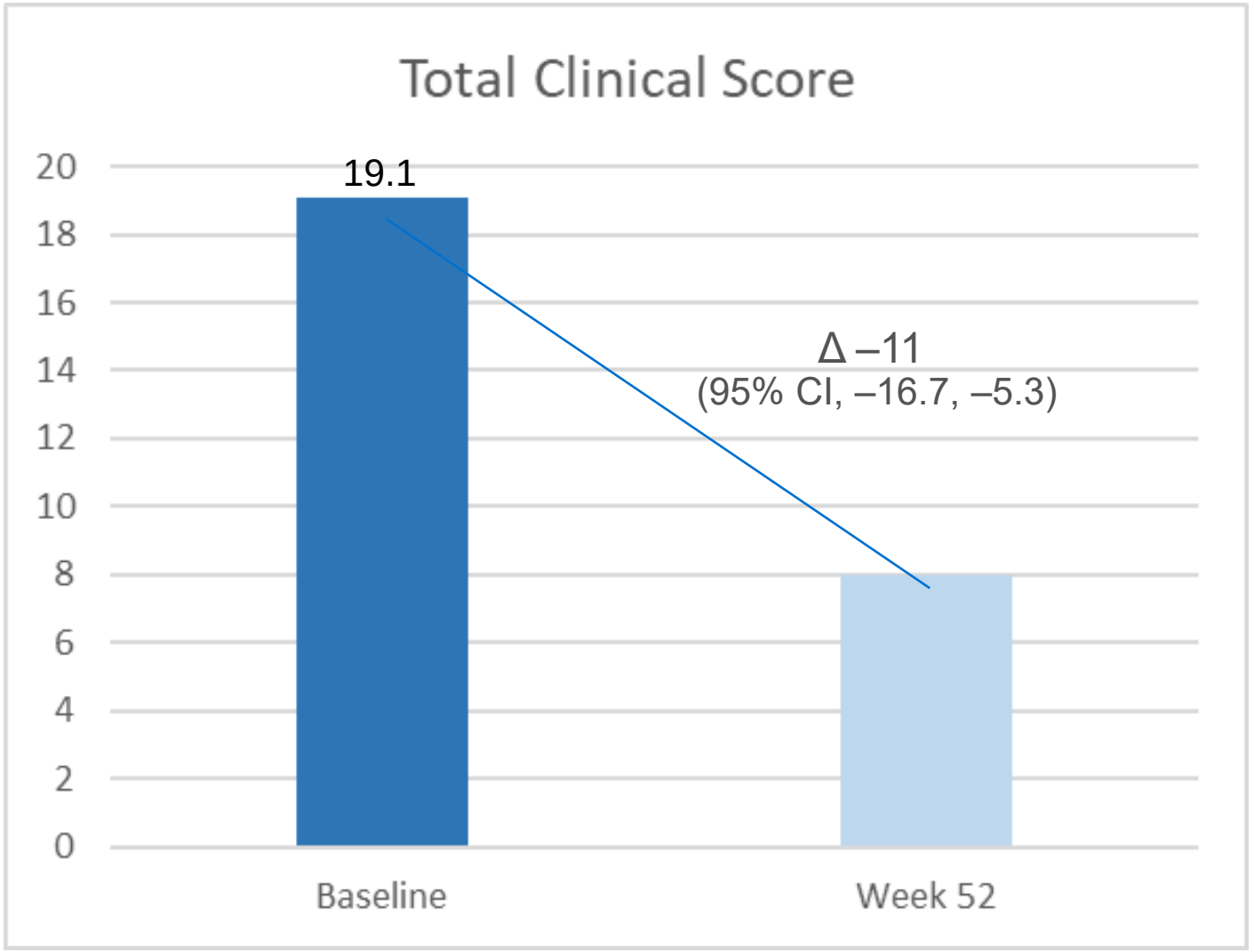
# INO-3107 Phase 1/2 Trial: Overall Safety Profile

| | Standard needle (n = 21) | Side port needle (n = 11) | Total (N = 32) |
|---|---|---|---|
| **Any pre-treatment AE** | 4 (19.0) | 1 (9.1) | 5 (15.6) |
| **Any TEAE** | 15 (71.4) | 5 (45.5) | 20 (62.5) |
| **Any treatment-related TEAE** | 9 (42.9) | 4 (36.4) | 14 (43.8) |
| **Any treatment-emergent SAE** | 1 (4.8) | 0 (0) | 1 (3.1) |
| **Any treatment-related treatment-emergent SAE** | 0 (0) | 0 (0) | 0 (0) |
| **Any TEAE by severity** | | | |
| Any Grade 1 | 11 (52.4) | 4 (36.4) | 15 (46.9) |
| Any Grade 2 | 6 (28.6) | 3 (27.3) | 9 (28.1) |
| Any Grade 3 | 3 (14.3) | 1 (9.1) | 4 (12.5) |
| Any Grade ≥4 | 0 (0) | 0 (0) | 0 (0) |
| **Any TEAE leading to treatment discontinuation** | 0 (0) | 0 (0) | 0 (0) |
| **Any TEAE leading to death** | 0 (0) | 0 (0) | 0 (0) |

# INO-3107 Phase 1/2 Trial: Improvement in RRP Staging Assessment Score




Improvement in total clinical score at Week 52 for all 32 patients in trial

(11 points lower than at baseline; 95% confidence interval -16.7, -5.3)

CI, confidence interval.



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# INO-3107: Results of Phase 1/2 Trial for RRP

## Trial Results from First Cohort

*21 total participants*

- Demonstrated statistical significance based on clinical endpoint of reduction in overall number of surgical interventions compared with previous year
- 16 of 21 (76%) participants saw a reduction in the number of surgical interventions compared to previous year, of which 5 participants required no surgical intervention during the trial
- Median decrease of 3 surgical interventions (95% CI 1, 3)
- Cellular response observed:
  - INO-3107 induced cellular responses against both HPV 6 and HPV 11, inducing both CD4 and CD8 T cells
  - T-cell activity against HPV 6 and HPV 11 was present at study end (43 weeks after treatment completion), indicating persistent cellular memory response
- INO-3107 was observed to be well-tolerated

## Trial Results from Second Cohort

*11 total participants*

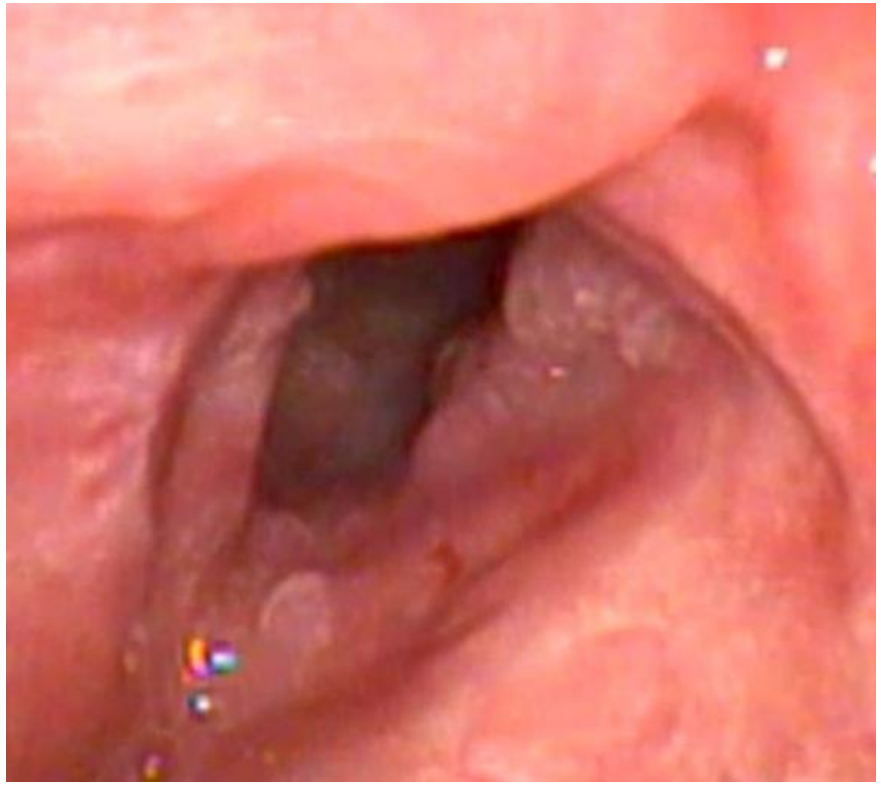
*Administered using exploratory side port needle*

- Demonstrated statistical significance based on clinical endpoint of reduction in overall number of surgical interventions compared with previous year
  - Median decrease of 3 surgical interventions (95% CI 1, 4)
- 10 of 11 (91%) participants saw reduction in surgical interventions compared to previous year
  - 4 patients required no surgical intervention during the trial
  - In the year prior to treatment, surgical interventions ranged between 2 and 8; median was 5
- Induced cellular responses and observed to be well-tolerated
- Results consistent with first cohort

# 81% (26/32) of patients saw a reduction in the number of surgical interventions compared to previous year

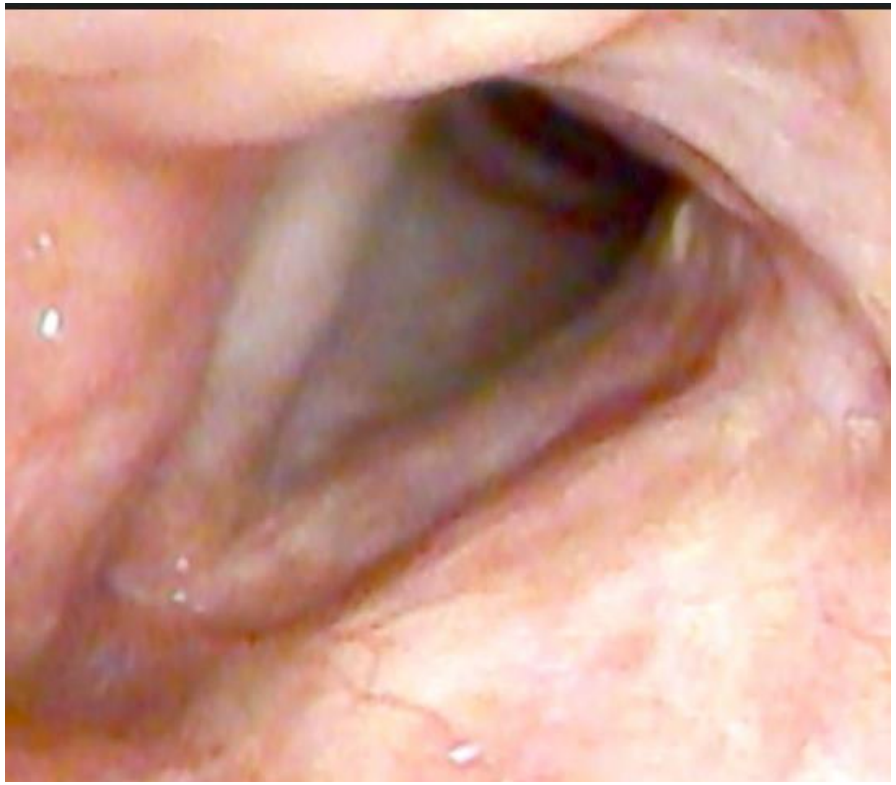
## Prior to INO-3107

Required frequent surgeries in the prior year



## One Year Following INO-3107

Required no surgeries after the dosing window



*Vocal cord images*

*RRP is a highly individualized disease and results of treatment with INO-3107 may vary*



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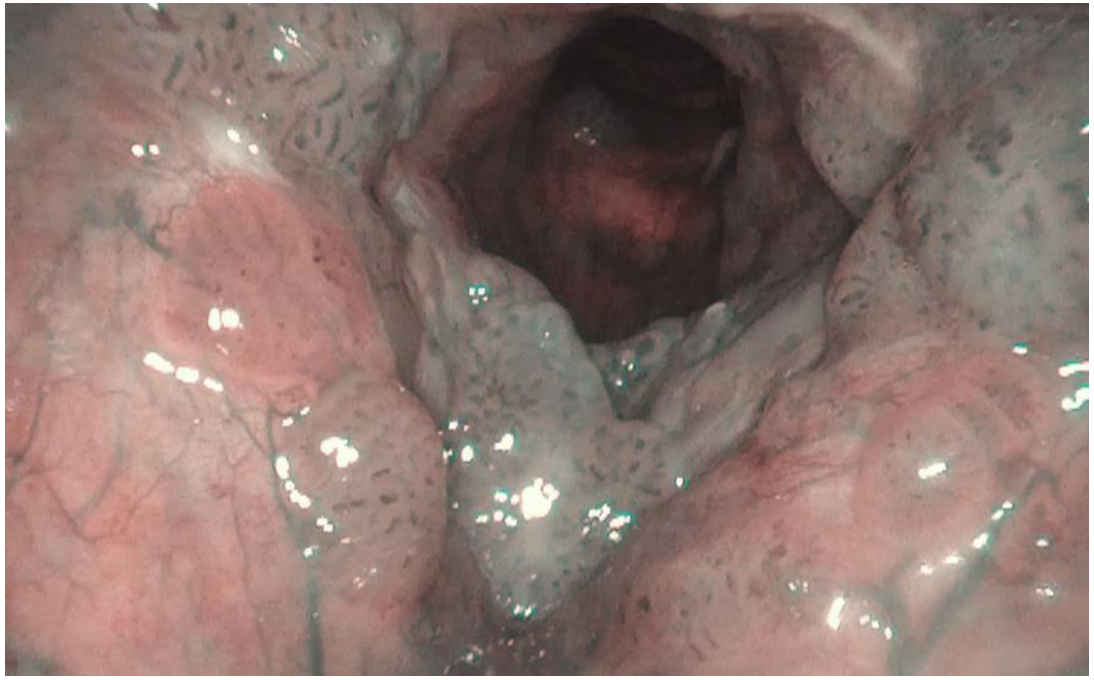
# INO-3107 Trial Participant – Vocal Cord Images

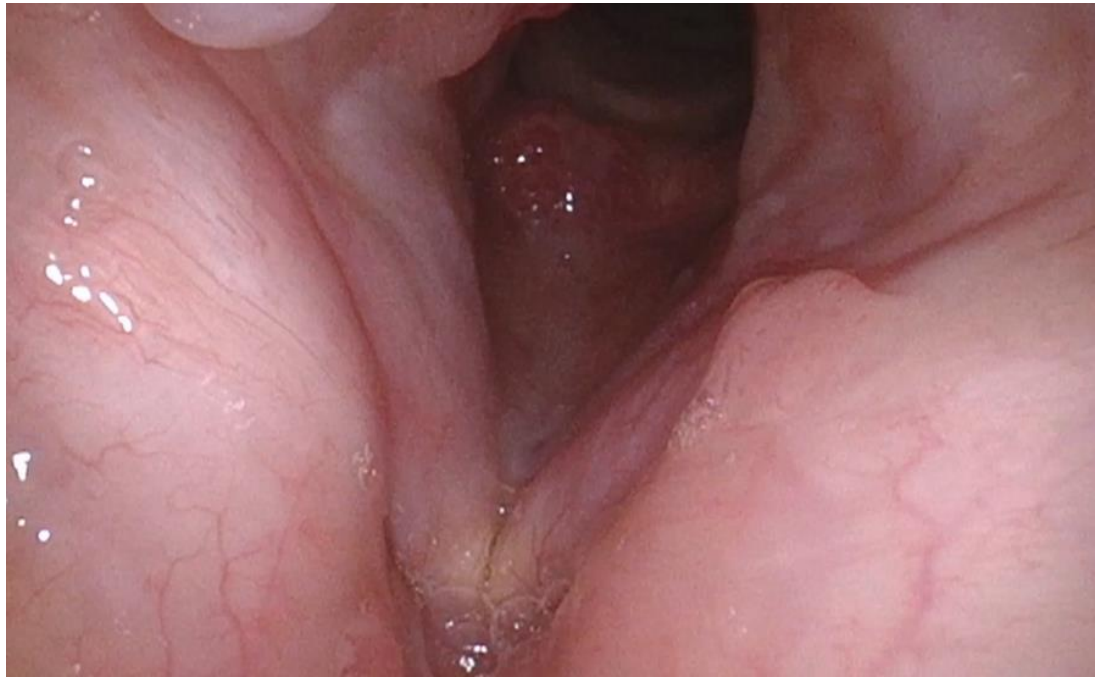
## Prior to INO-3107

Required frequent surgeries in the prior year

## One Year Following INO-3107

Required no surgeries after Day 0





*Vocal cord images*

*RRP is a highly individualized disease and results of treatment with INO-3107 may vary*



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# INO-3107 Development Updates and Next Steps

- Productive interactions with the FDA, framework for Phase 3 program in place
  - Preparing to conduct a randomized placebo-controlled trial
  - Addressing additional questions
  - Engaged a CRO; actively identifying global sites
- Dr. Ted Mau presented Phase 1/2 expanded dataset at ABEA program at COSM

- EU orphan drug designation – positive opinion from COMP, final decision in May
- Plan to meet with EU national authorities to discuss clinical development plans before the year end
- U.S. and EU proposal pediatric development approach

# Trial Design for VGX-3100 REVEAL Program

Two Phase 3 randomized (2:1), double-blinded, placebo controlled

n=201 REVEAL1

n=203 REVEAL2

3 dose regimen at Months 0, 1, 3

- **VGX-3100:** targets HPV-16/18 infected cervical cells; E6/E7 oncogenes
- Designed to treat **cervical high-grade squamous intraepithelial lesions (HSIL)**
- **Primary endpoint:** Regression of HSIL (CIN2/3) and clearance of HPV-16/18 in the cervix

# REVEAL2 Trial Amendment

- REVEAL1 evaluated VGX-3100 in all-participants population as primary
- REVEAL2 amended to evaluate VGX-3100 in investigational biomarker-selected population as primary, based on data analysis from REVEAL1
- As a result, FDA indicated that additional one or two trials required for BLA submission

# Topline Results for REVEAL1 and REVEAL2

**Primary endpoint:**
Regression of HSIL (CIN2/3) and clearance of HPV-16/18 in the cervix

**REVEAL1:** All-participants population

**Statistical significance not achieved in intention-to-treat (ITT) population**

- 22.5% (31/138) – VGX-3100
- 11.1% (7/63) – Placebo

**Statistical significance achieved in modified intention-to-treat (mITT) population**

- 23.7% (31/131) – VGX-3100
- 11.3% (7/62) – Placebo

**REVEAL2:** Investigational biomarker-selected population

**Statistical significance not achieved in the ITT biomarker-selected population**

- 28.6% (6/21) – VGX-3100
- 0% (0/4) – Placebo

# Detailed Results from REVEAL1 and REVEAL2

| | REVEAL1 | REVEAL2 |
|---|---|---|
| Number of Participants | 201 | 203 |
| **All-Participants Results** | Did not achieve statistical significance | Achieved statistical significance |
| VGX-3100<br>Placebo | 22.5% (31/138)<br>11.1% (7/63) | 27.6% (37/134)<br>8.7% (6/69) |
| **Biomarker-selected Results** | Achieved statistical significance | Did not achieve statistical significance |
| VGX-3100<br>Placebo | 66.0% (31/47)<br>15.0% (3/20) | 28.6% (6/21)<br>0.0% (0/4) |

# Integrated Results from REVEAL1 + REVEAL2

- **Statistical significance met in both populations** when efficacy results are integrated
  - **No treatment-related SAEs;** most AEs were considered to be mild to moderate

| Biomarker-Selected (92 participants) | All Participants (404 participants) |
|---|---|
| • *68 VGX-3100; 24 Placebo*<br><br>*Regression of HSIL and Clearance of HPV*<br>***54.4% vs. 12.5%***<br>*p<0.001* | • *272 VGX-3100; 132 Placebo*<br><br>*Regression of HSIL and Clearance of HPV*<br>***25% vs. 9.8%***<br>*p<0.001* |

# Next Steps and Implications of REVEAL1 and 2

- INOVIO will continue to evaluate the results to determine the path forward for VGX-3100 in cervical HSIL; REVEAL2 biomarker analysis to be completed in Q3
- Plan to use the combined data set in future regulatory interactions for VGX-3100
- Plan to submit the data for publication in a peer-reviewed journal later this year
- Given the importance of viral clearance in removing the underlying cause of the HPV-related diseases, the data from REVEAL2 may have positive implications for our other HPV-related programs
- INOVIO's partner, ApolloBio, is currently conducting a Phase 3 trial for VGX-3100 in China

# About HPV-Related Anal HSIL

- HPV-16 and HPV-18 infection can also cause high-grade squamous intraepithelial lesions (HSIL) in the anus
  - HSIL are precancerous lesions; if left untreated may progress to anal cancer
  - Spontaneous regression of anal HSIL is observed in approximately 20% of patients
- Anal HSIL treatment reduces risk of progression to anal cancer (as shown in ANCHOR* study's recent results)
  - Treatment usually is surgical, consisting of ablation, most commonly radiofrequency ablation (RFA), resections or laser therapy
  - Ablation does not clear the underlying HPV infection, resulting in an unmet medical need
  - Recurrence rates are high, up to 49% one year after treatment
  - Thus, repeated surgeries/treatments are necessary
- Anal HSIL occurs in both men and women
  - In the US alone, HPV-16/18 anal HSIL estimated prevalent cases range from 210K to 1.1 million
  - It is estimated that Europe has a similar prevalence of HPV-16/18 anal HSIL
  - Majority of anal HSIL cases are undiagnosed
- New treatment guidelines will increase emphasis in diagnosis and treatment



* = *Treatment of Anal High-Grade Squamous Intraepithelial Lesions to Prevent Anal Cancer (ANCHOR Study) – Palefsky, JM et al., June 2022* - https://www.nejm.org/doi/full/10.1056/NEJMoa2201048

# VGX-3100 Phase 2 Trial in HPV-Related Anal HSIL

**TRIALS: VGX-3100**

- Target HPV 16/18 subtypes; E6/E7 oncogenes
- Treat high-grade squamous intraepithelial lesions (HSIL)
- HIV-negative HPV-positive anal HSIL

**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%

- Open-label trial of VGX-3100 + EP with CELLECTRA in 24 HIV-negative participants with HPV-16 and/or -18-positive anal HSIL
- Primary endpoint of histological regression and virological clearance, with key secondary endpoints of regression alone and clearance of virus alone, at Week 36
  - Fifty percent (11/22 evaluable) of participants showed no evidence of HPV-16/18-positive HSIL at Week 36
  - Forty-six percent (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



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# AMC-sponsored Phase 2 Trial of VGX-3100 for Anal HSIL in HIV-positive Individuals

- VGX-3100 targets HPV-16 and -18 E6 and E7 Protein
- Anal High-Grade Squamous Intraepithelial Lesions (HSIL) in HIV-Positive Individuals
- 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

# VGX-3100 Anal HSIL Next Steps

- INOVIO is currently advancing Anal HSIL indication, while analyzing recent REVEAL2 data
- Given current standard of care, adjuvant therapy for Anal HSIL could be well received
  - ANCHOR trial (NEJM 2022; randomized ~4000 patient study)
    - Results showed that in HIV+ Anal HSIL patients, ablation is superior to watchful waiting in preventing progression to cancer
    - Prior to the ANCHOR study, Colorectal surgeons were unclear if ablation had an appreciable impact on anal cancer progression.
    - *Results implies treatment of HSIL should be the standard of care*
- Engaged with regulatory agencies regarding next steps towards registration
  - Considering Phase 3 trial designs in combination with ablation (adjuvant setting)
  - Obtained KOL feedback in EU and previously in US

*Globally, despite vaccination rates, anal cancer is on the rise particularly in HIV-negative women, VGX-3100 may provide the potential for clinical benefit in preventing recurrence and thus in progression to anal cancer*

# Infectious Diseases Vaccine Candidates

## INO-4201 for Ebola

- Phase 1b clinical trial – 46 participants
- Evaluated INO-4201 as a booster in participants previously vaccinated with Ervebo®
- Collaborators: GuardRX, Geneva University Hospitals, DARPA
- INO-4201 was **well-tolerated and boosted humoral responses** in 100% (36 of 36) of treated participants.

## Candidates for HIV

- INO-6172 – Phase 1 clinical trial – 45 participants
- INO-6160 – Phase 1 clinical trial – 20 participants
- Sponsor: National Institute of Allergy and Infectious Disease
- Collaborator: HIV Vaccine Trials Network, Wistar Institute

## INO-4800 for COVID-19

- WHO-sponsored Solidarity Trial Vaccines
- International, multi-center Phase 3 trial
- INO-4800 selected by the WHO's independent vaccine prioritization advisory group

# INO-5401 + INO-9012 and Libtayo® for Newly Diagnosed GBM

- INO-5401 is a DNA medicine composed of plasmids that encode for three 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 monoclonal antibody to the PD-1 receptor
- In a Phase 1/2 trial, INO-5401 and INO-9012 are combined with Libtayo®, in order to create an antigen-specific, activated T cell population

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

- **INO-5401+INO-9012 with Libtayo® and 40 Gy radiation/TMZ were observed to have favorable tolerability and immunogenicity**

NR: not reached.
Gilbert et al. J Clin Oncol 2013; Gilbert et al. N Eng J Med 2014. Comparison is limited due to differences in trial population.
Data was presented at 2022 ASCO Annual Meeting.

# DNA Encoded Monoclonal Antibody (dMAb™)

- INOVIO is developing a novel DNA-encoded monoclonal antibody (dMAb) technology
- The dMAb technology facilitates direct *in vivo* transfection to target tissue to produce and secrete mAbs into the blood at biologically relevant levels
- dMAbs may be a potentially transformative approach for the prevention and treatment of infectious diseases and cancer
- **Wistar Institute-led Phase 1 clinical trial in collaboration with AstraZeneca, the University of Pennsylvania, Indiana University, and INOVIO to develop anti-SARS-CoV-2-specific dMAbs is ongoing**