



# Powering a New Decade of DNA Medicines

September 2021



# 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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# Powering DNA Medicines

15 DNA medicine clinical programs in development  
(HPV-associated diseases, cancer, and infectious diseases; including COVID-19)

Precisely designed plasmids delivered  
through **proprietary smart device**

**Extensive patent portfolio**  
protecting technology platform

Designed to **treat and prevent cancers  
& infectious diseases**

**Strong and experienced**  
management team

**Well-tolerated and robust immune responses**  
in more than 3,000 patients

**No anti-vector response**

**No frozen storage issues**  
(room temp storage >1 yr.)

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

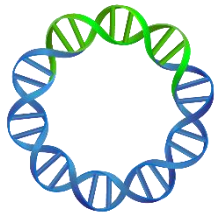




# DNA Medicines Platform Built on INOVIO's Proprietary Technology

## OPTIMIZED PLASMID DESIGN AND DELIVERY TECHNOLOGY

### PRECISELY DESIGNED PLASMIDS (SynCon®)



### PROPRIETARY SMART DEVICES (CELLECTRA®)

**Intramuscular  
Device** for  
Pre-Cancers &  
Cancers



**Intradermal  
Device** for  
Vaccines



*IN VIVO*



# INOVIO's Technology Advantages

## Clinical Efficacy

- Demonstrated clinical efficacy in Phase 3 study for VGX-3100
- Lead candidate VGX-3100 in Phase 3 for precancerous cervical dysplasia

## Tolerability

- Favorable safety profile tested in over 3,000 patients and over 7,000 administrations
- Carries no potential toxicity from viral vectors

## Versatility and Boosting

- Targets virtually any antigenic sequence; combining multi-antigens into single vial
- Initiated first-in-human study of optimized dMAb™ plasmid
- **No anti-vector response** – allows for additional boosting

## Rapid and Scalable Manufacturing

- “Off-the-shelf” product; **no cold chain required** (room temp storage >1 yr.)
- Rapid development from concept to human in <3 months (COVID-19 vaccine)
- Relatively inexpensive to manufacture; produce large quantities

# INOVIO DNA Medicines Pipeline

	PRODUCT	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER/COLLABORATOR/FUNDER
COVID-19	INO-4800	COVID-19 (INNOVATE)					    
	INO-4802	Pan-COVID-19					
	INO-4700	MERS					CEPI
	INO-4500	Lassa Fever					CEPI
	INO-4201	Ebola					DARPA
	PENNVAX-GP	HIV					NIH  
INFECTION DISEASES	VGX-3100	Precancerous Cervical Dysplasia (HSIL)					 (China; INOVIO maintains global rights)
		Precancerous Vulvar Dysplasia (HSIL)					
		Precancerous Anal Dysplasia (HSIL)					
	INO-3107	Recurrent Respiratory Papillomatosis (RRP)					AstraZeneca 
	MEDI0457	Head & Neck Cancer					
		Cervical, Anal, Penile, Vulvar Cancers					
IMMUNO-ONCOLOGY	INO-5401	Glioblastoma Multiforme (GBM)					REGENERON
		Breast Cancer (BRCA1/2)					 Penn
	INO-5151	Prostate Cancer					 
dMAb™		COVID-19					AstraZeneca  DARPA 
	INO-A002	Zika					Bill & Melinda Gates foundation

INTERNALLY FUNDED



EXTERNALLY FUNDED



# Infectious Disease Update & Overview of COVID-19 Vaccine Programs



# Infectious Disease Program Progress

- INOVIO continues to make advancements in the Infectious Disease space
- Advanced COVID-19 vaccine candidate INO-4800 into a global Phase 3 trial
- Lassa Fever, Middle East Respiratory Syndrome (MERS), and Ebola booster programs progressed to Phase 1/2 trials
- Our experiences with infectious diseases, including coronaviruses, have supported faster development of INO-4800 as well as our second-generation, pan-COVID vaccine candidate, INO-4802

## Collaborations & Partnerships for ID Programs





# COVID-19 Vaccine Program Progress

## INO-4800 – COVID-19 Vaccine Candidate



- **Ability to generate balanced immune response** coupled with a **favorable transport, thermostability, and tolerability profile**
- Leveraging prior coronavirus experience in MERS

### Addressing New Variants of Concerns

- INO-4800 provided **broad, cross-reactive immune responses in humans against VOC\***
- **INO-4800 vaccination maintained a similar level of T cell responses against the delta variant** and showed a similar level of reduced neutralizing antibody activity against the delta variant by mRNA vaccines (Moderna & Pfizer)

## Clinical Data and Plan



- **Phase 2 showed favorable safety and tolerability profile** in 400 subjects
- Binding, neutralizing antibody levels and T cell immunity responses were statistically significant and greater in the 2.0 mg dose group versus the 1.0 mg dose group

### Global Phase 3 Trial (INNOVATE)

- **Evaluating efficacy and safety of INO-4800 in a two-dose regimen (2.0 mg) across several countries – focus on Latin America, Asia and Africa**
- Primary endpoint of the Phase 3 segment will be virologically confirmed COVID-19
- Regulatory approval to conduct Phase 3 received in Brazil and Philippines; other countries anticipated to follow

## Manufacturing & Scale up



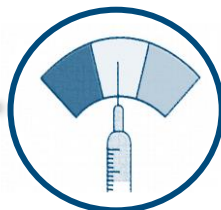
- Strong thermostability profile, **room temperature for >1 year**, anticipated **5-year shelf life at 2-8°C**
- Scaling up plasmid and device through consortium of CMOs and partnerships globally
- **Thermo Fisher**, a member of INOVIO's global manufacturing consortium, **opened a new cGMP plasmid DNA manufacturing facility** in Carlsbad, California in July 2021 with **INOVIO as its first client**

# INO-4800 Clinical Pathway & Global Presence



## INNOVATE Global Phase 3 Trial

- INOVIO with Advaccine jointly conducting a global Phase 3 trial for INO-4800
- Healthy men and non-pregnant women 18 years and older (2.0 mg dose)
- **Focus on countries currently underserved by vaccines**, primarily in Latin America, Asia and Africa
- **Recently received regulatory approval to proceed from Brazil and Philippines**, with other countries anticipated to follow



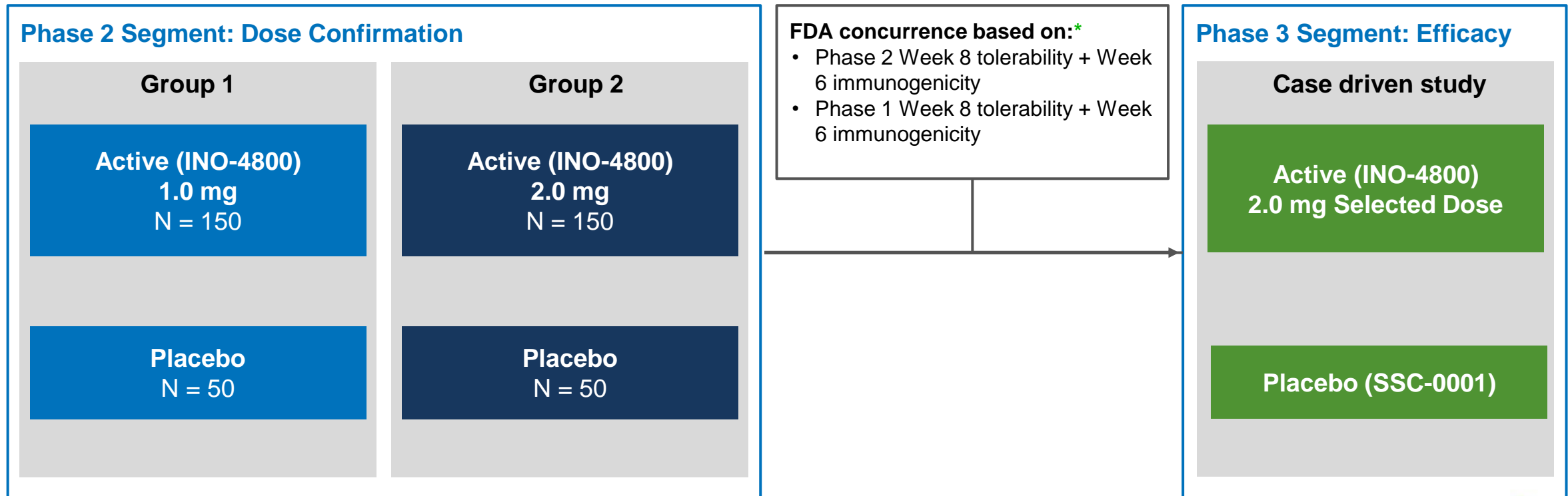
## Heterologous Prime-Boost Trials

- **Received regulatory allowance in China** to conduct two clinical trials investigating **heterologous boosting with INO-4800**
  - Heterologous prime-boost sequential immunizations using INO-4800 and CoronaVac®
  - Completed cross prime-boost pre-clinical animal tests; prime-boost strategy stimulated high-level of humoral and cellular response

# Phase 2/3 Clinical Trial – INNOVATE (INOVIO INO-4800 VAccine Trial for Efficacy)

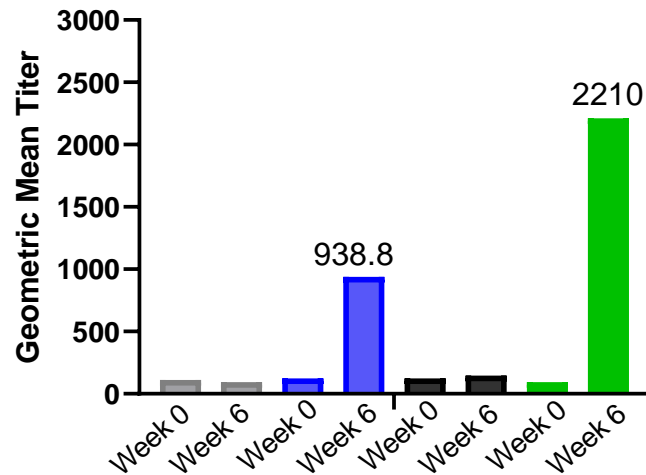
## ***Evaluating efficacy in subjects 18+ years of age with optimal dose for each age group***

- Phase 2 segment: to evaluate tolerability and immunogenicity in order to select dose(s) for efficacy evaluation in Phase 3
- Phase 3 segment: to evaluate efficacy using the 2.0 mg dose in a case-driven fashion

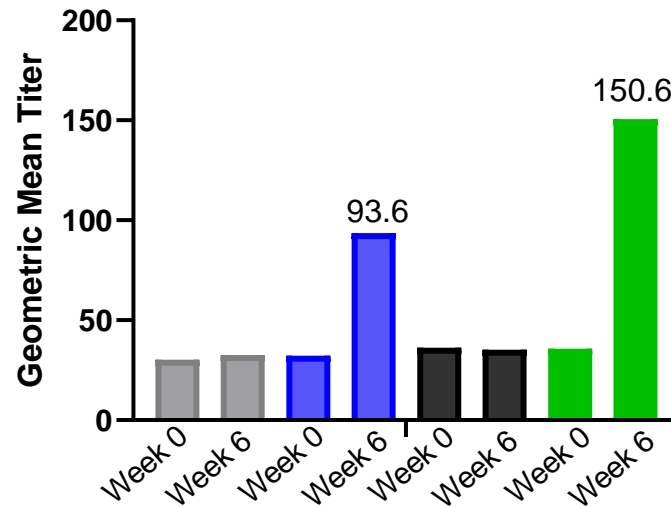


# INO-4800 Generated Balanced Immune Responses across All Age Groups in Phase 2

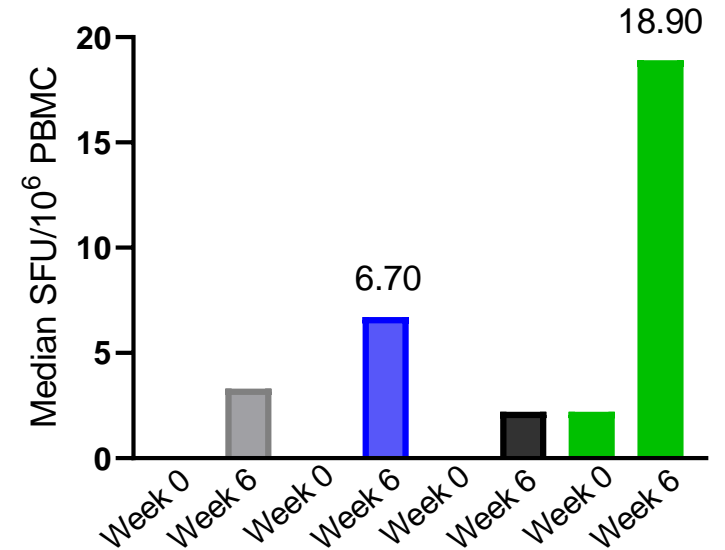
## Binding Ab



## Neutralizing Ab



## T Cell Responses

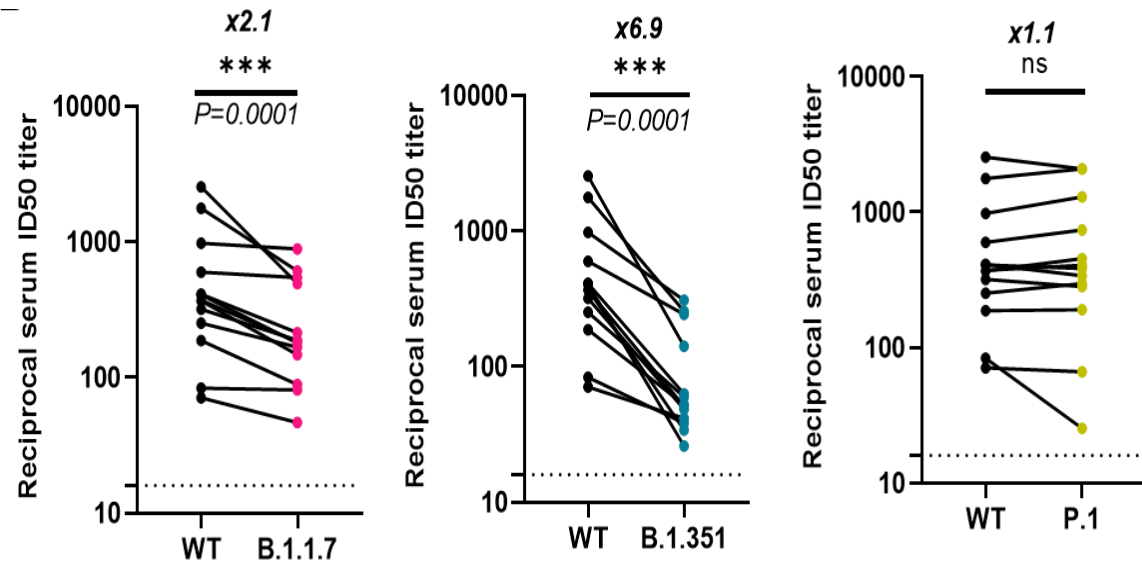


- 1 Injection Placebo
- 1mg INO-4800
- 2 Injections Placebo
- 2mg INO-4800

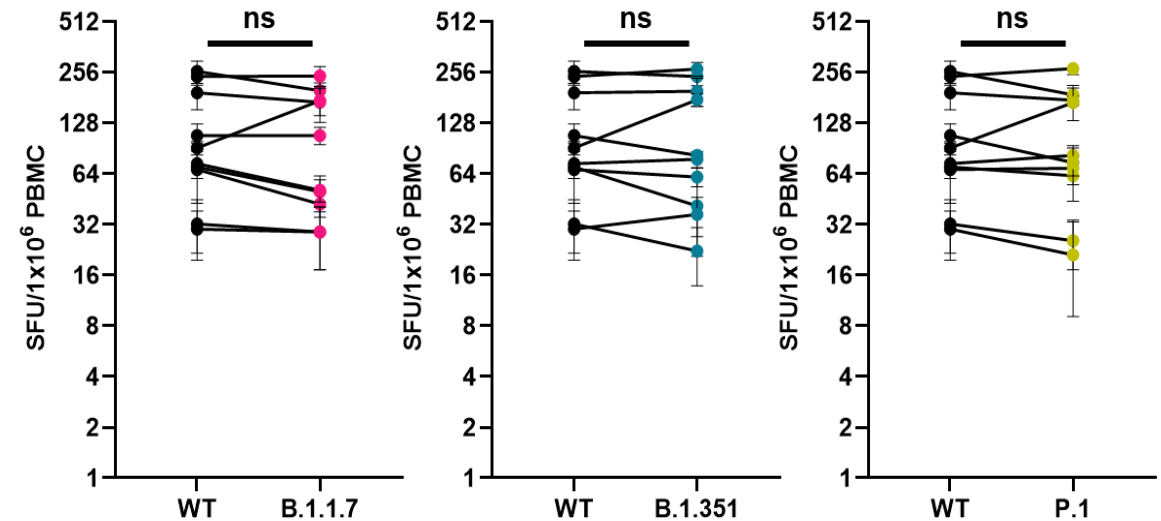


# Addressing Variants of Concern (VOC): INO-4800 DNA Vaccine Induces Neutralizing Antibodies and T cell Activity Against Global SARS-CoV-2 VoC

**Humoral antibody cross-reactivity responses against SARS-CoV-2 variants.** a) Sera from Phase 1 INO-4800 vaccinees were neutralization to WT, B.1.1.7, B.1.351, and P.1 variants.



**INO-4800 Cellular immune response against SARS-CoV-2 variants.** PBMCs from 10 Phase 1 subjects were collected 8 weeks after receiving the second dose of INO-4800.



# INO-4802: Second-generation, Pan-COVID Vaccine Candidate

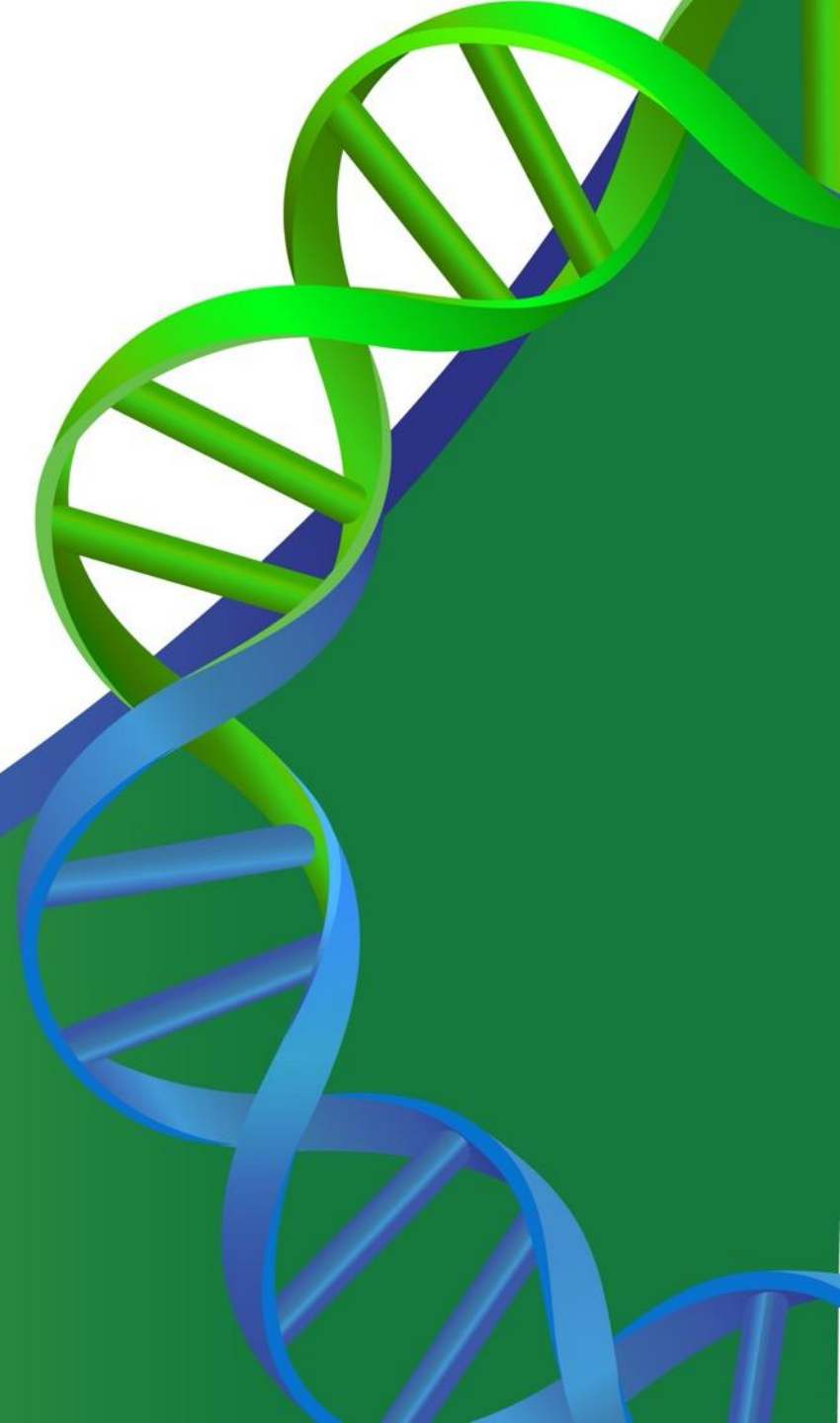
## IMPACT (INOVIO INO-4802 Multi-variant Pan-COVID-19 Vaccine Trial)

- In parallel with INO-4800, INOVIO is developing a second generation, pan-COVID vaccine candidate, INO-4802
- Strategy against current **and** future variants of concern
- Can potentially provide boosting capabilities in addition to an initial vaccination regimen with INO-4800 and/or other first-generation vaccines, including **both** adenovirus and mRNA-based platforms

## Key Findings for INO-4802 include:

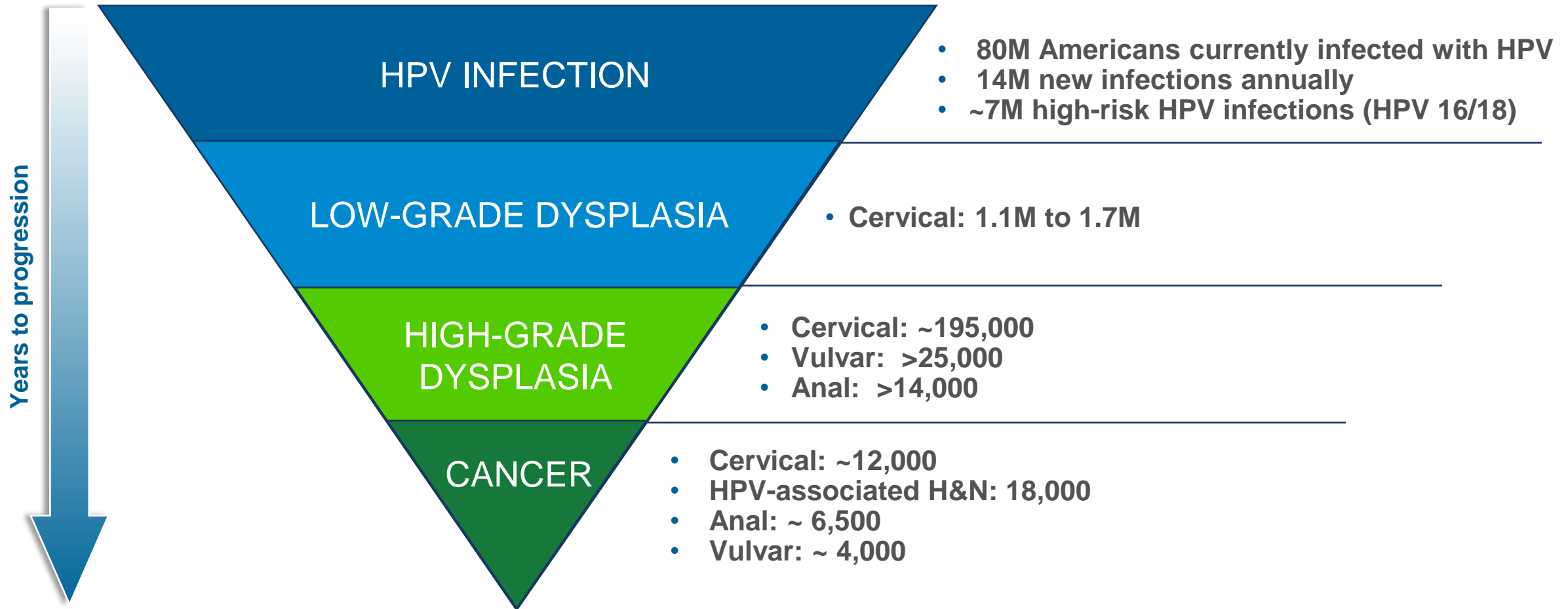
- Cross-reactive immune responses demonstrated against current **and** emerging viral variants\*
- Induced potent neutralizing antibodies, T cell responses, and protection in a pre-clinical model against the original wildtype strain as well as against the alpha, beta, gamma, and delta variants
- Findings build on our deep roots in infectious diseases and commitment to global public health

# HPV Programs



# HPV-Associated Diseases Market Overview

## HPV-associated conditions per year in US:



**Sources:** US CDC (2018) HPV and Cancer, available at: <https://www.cdc.gov/cancer/hpv/statistics/cases.htm> (accessed July 22, 2019); Saraiya M, Unger ER, Thompson TD, Lynch CF, Hernandez BY, Lyu CW, Steinau M, Watson M, Wilkinson EJ, Hopenhayn C, Copeland G, Cozen W, Peters ES, Huang Y, Saber MS, Altekruze S, Goodman MT; HPV Typing of Cancers Workgroup. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. J Natl Cancer Inst. 2015 Apr 29;107(6):djv086; Inovio Pharmaceuticals, internal estimates from published data (2015-16, 2017-18); US CDC, personal communication (2015); NCI SEER Cancer Stat Facts: Cervix Uteri, Vulvar, and Anal Cancers – <https://seer.cancer.gov/statfacts> (accessed 2017-18); \*Measured as: Genital Warts – Initial Visits to Physicians' Offices, United States, 1966-2014. Fig. 47; Schiffman M, Solomon D. Findings to date from the ASCUS-LSIL Triage Study (ALTS). Arch Pathol Lab Med. 2003 Aug;127(8):946-9; US CDC. Genital HPV Infection – Fact Sheet.



# Complications of Current Standard of Care: Loop Electrosurgical Excision Procedure (LEEP)

## Pain<sup>1,2</sup>

- Local anesthetic injections
- Excision
- Post-procedural cramping



## Surgical Complications<sup>1,3</sup>

- Disfigurement
- Swelling, drainage, bleeding, numbness, redness, burning
- Opening of suture, itching, scarred skin
- Cervical stenosis



## Loss of Reproductive Health

Increased risk of:

- Preterm delivery<sup>6,7</sup>
- Premature rupture of membranes<sup>6,7</sup>
- 2nd trimester miscarriage<sup>8</sup>
- Terminations<sup>8</sup>



<sup>1</sup>Harper DM, et al. *J Family Practice*. 1994;39:249–256.

<sup>2</sup>Ferenczy A, et al. *Obstet Gynecol*. 1996;87:332–337.

<sup>3</sup>Mitchell MF, et al. *Obstet Gynecol*. 1998;92:737–744.

<sup>4</sup>Wright TC, et al. *Obstet Gynecol*. 1992;79:173–178.

<sup>5</sup>IARC. *Colposcopy and Treatment of CIN: A Beginner's Manual*. 2003.

<sup>6</sup>Kyrgiou M, et al. *Lancet*. 2006;367:489–498.

<sup>7</sup>Kyrgiou M, et al. *BMJ*. 2016;354:i3633.

<sup>8</sup>Kyrgiou M, et al. *Cochrane Database Syst Rev*. 2015;CD008478.

# VGX-3100 Phase 3 Program: HPV-Associated Cervical HSIL/ Precancerous Dysplasia

## TRIAL: **VGX-3100**

- Targets HPV 16/18 subtypes; E6/E7 oncogenes
- Designed to treat high-grade squamous intraepithelial lesions (HSIL)



**Phase 3 consists of 2 studies in parallel:**

**REVEAL 1 (primary) n=201 – Enrollment Closed**  
Study follow-up through week 88 (as in Phase 2b)  
Topline efficacy data reported 1Q21

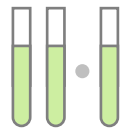
**REVEAL 2 (confirmatory) n=198 – Now Enrolling**  
Study follow-up through week 40

**FIRST** treatment  
for HPV infection of  
the cervix

**FIRST** non-invasive  
treatment for cervical  
pre-cancer

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

**2:1** Randomized (2:1), double-blind, placebo-controlled



Dosing: month 0, 1, 3  
(as in P2b)

**6 mo.**

Primary endpoint measured 6 months after completion of dosing (as in Phase 2b)

# REVEAL 1: VGX-3100 Phase 3 Pivotal Trial for Cervical HSIL Meets Primary & Secondary Efficacy Objectives for All Evaluable Subjects

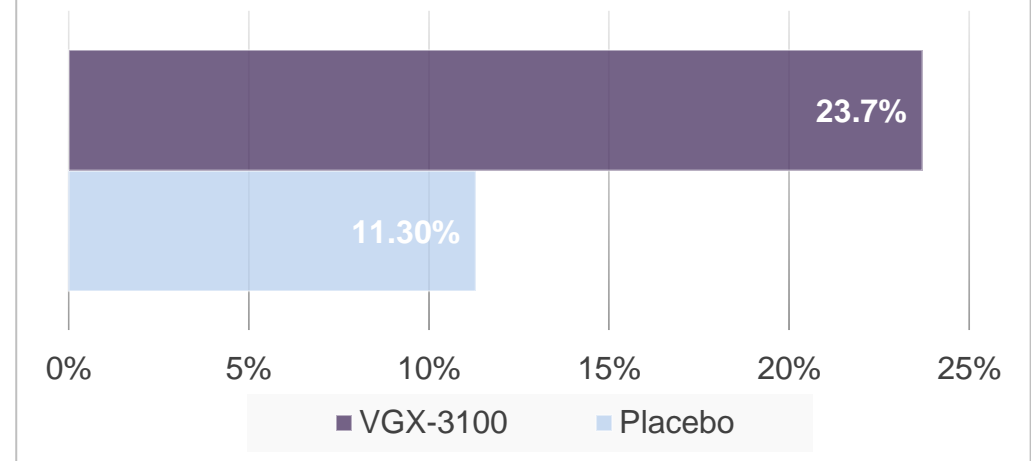
**First DNA medicine to achieve efficacy endpoints in a Phase 3 trial**

**No treatment-related serious adverse events;** most adverse events were mild to moderate and self-resolving

**Partnership with QIAGEN** to develop **pre-treatment predictive biomarker** to help identify those likely to respond to VGX-3100

- **Achieved statistical significance for primary objective:** regression of cervical HSIL combined with virologic clearance of HPV-16/18, 6 months after administration
  - 23.7% (31/131) in treatment group vs. 11.3% (7/62) in placebo group
  - $p=0.022$ ; 12.4 difference in percentage, 95%CI: 0.4,22.5
  - mITT includes all subjects w/ endpoint data (N=193) \*
- **All secondary efficacy objectives achieved**
- REVEAL 2 is currently ongoing

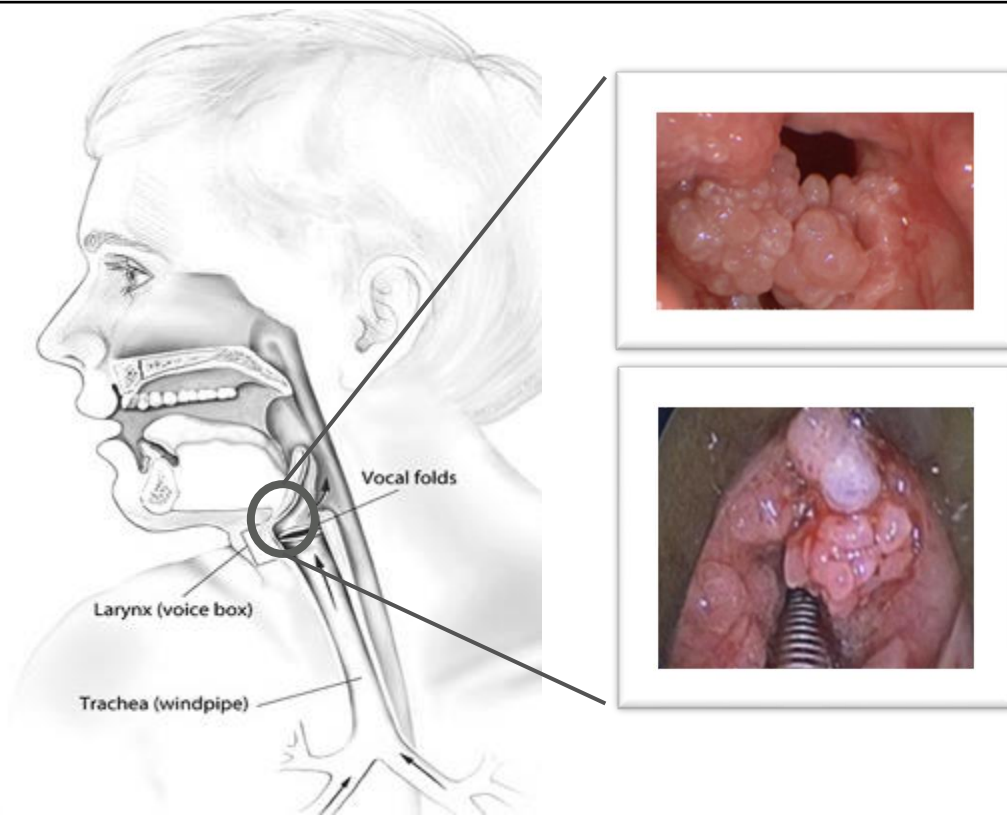
## Regression of Cervical HSIL with Virologic Clearance



\* mITT, ITT and a third per-protocol (PP) were pre-specified in trial protocol. PP analysis will be performed upon trial completion.

# Recurrent Respiratory Papillomatosis (RRP) Caused by HPV 6 and 11

## Areas affected by Recurrent Respiratory Papillomatosis (RRP)



- HPV-associated disease; **caused by HPV 6 and 11**
- Rare, orphan disease with **~15,000 total active cases** within the U.S., where **virtually all of those require surgical procedures**
  - **~6,000 new cases per yr. in the U.S.**
- Growths can lead to life-threatening airway obstructions
- **SoC is lifelong surgery (repeated/multiple times per yr)**
  - Currently, disease is incurable and can only be treated by surgery to remove tumors, which temporarily restores the airway
- RRP may occur in adults as well as in children who are thought to have contracted the virus during childbirth



# Immuno-Oncology Programs (INO-5401 for Newly Diagnosed GBM)



# INO-5401 for Newly Diagnosed GBM in Phase 1/2 Study in Collaboration with Regeneron

TRIAL: **INO-5401** (encoding tumor-associated antigens: hTERT, WT1, PSMA)



Phase 1b/2 open label study for **newly diagnosed glioblastoma (GBM)**



Combination with Regeneron's PD-1 checkpoint inhibitor cemiplimab (Libtayo®)

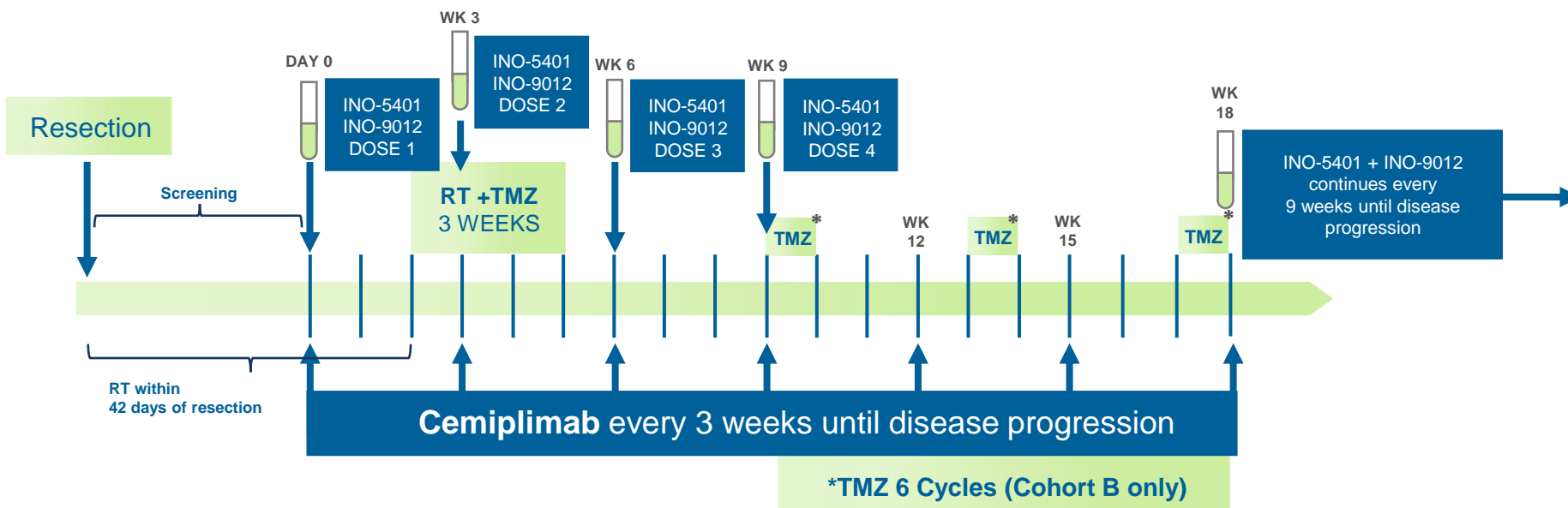
**Primary Endpoints:**  
Safety, tolerability  
**Secondary Endpoints:**  
Immunological impact, **PFS and OS**

 **x32**

**Cohort A:**  
MGMT Promoter  
Unmethylated:  
32 patients

 **x20**

**Cohort B:**  
MGMT Promoter  
Methylated:  
20 patients

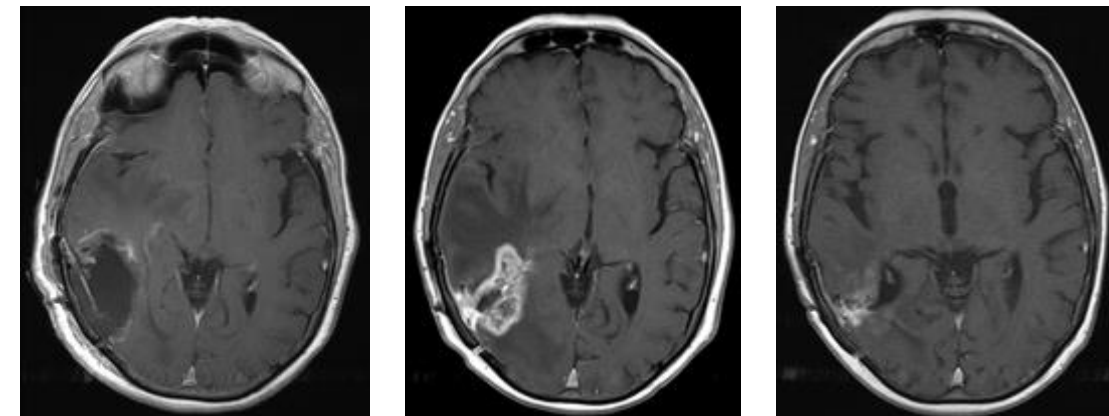
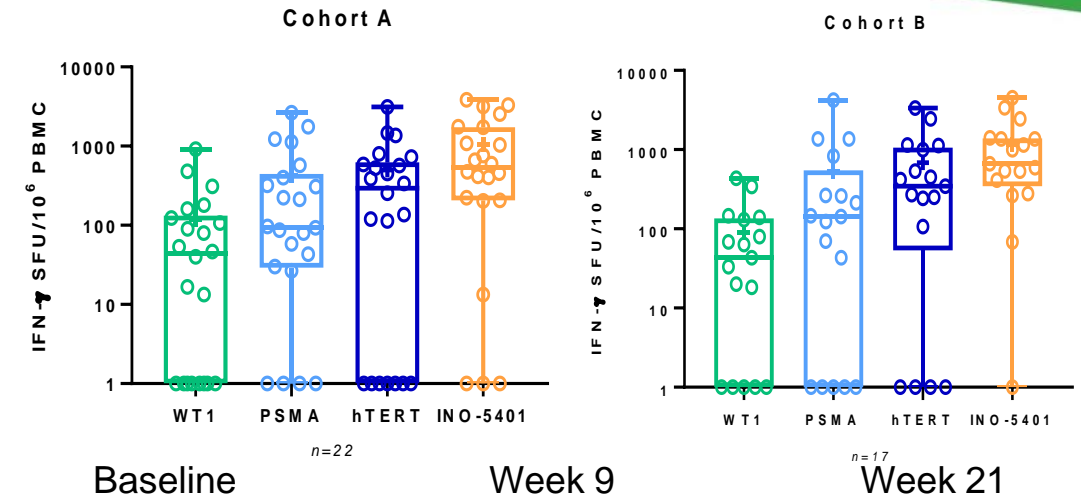


# INO-5401 Results: Interim review in newly diagnosed GBM patients

## OS18 data, demonstrated immunogenicity and tolerability in a majority of patients

- **Overall survival at 18 months (OS18)** presented at SNO 2020 Annual Meeting:
  - Promoter Methylated OS18 of 70% (14/20)
  - MGMT Promoter Unmethylated OS18 of 50% (16/32)
- **Median overall survival in the unmethylated GBM patients was 17.9 months, which compares favorably to historical controls**
  - Median OS for methylated patients has not yet been reached and the study is ongoing
- This study shows that INO-5401+INO-9012 with cemiplimab and radiation/TMZ have an acceptable tolerability profile, are immunogenic, and may improve survival in newly diagnosed GBM
- *24-month OS data expected later this year, including correlative immunology and tissue data, as well as total study drug exposure and concomitant medication use*

### Immunology Output to Date



Several patients have experienced pseudo-progression, with progression by RANO criteria and radiographic evidence of progression on MRI, without evidence of tumor on repeat biopsy

# Overall Survival at 18 Months

Median OS; unmethylated (Cohort A)	17.9 mo. (14.5 - NR)	Historical 14.6-16 mo.**
Median OS; methylated (Cohort B)	NR (18.4 – NR)	Historical 23.2-25 mo.**

Overall Survival at 12 Months	n Alive/N Total	OS12% (95% CI)
MGMT Unmethylated (Cohort A)	27/32	84.4 (67.2-94.7)
MGMT Methylated (Cohort B)	17/20	85.0 (62.1-96.8)
Combined	44/52	84.6 (71.9-93.1)

Overall Survival at 18 Months	n Alive/N Total	OS18% (95% CI)
MGMT Unmethylated (Cohort A)	16/32	<b>50</b> (31.9 - 68.1)
MGMT Methylated (Cohort B)	14/20*	<b>70</b> (45.7 – 88.1)
Combined	30/52	<b>57.7</b> (14.5 – 71.3)

NR: not reached

\*Two patients in Cohort B withdrew consent for additional follow-up at Week 3 and were considered deceased

\*\*Gilbert et al. J Clin Oncol 2013; Gilbert et al. N Eng J Med 2014. Comparison is limited due to differences in study population



# Management & Financials



# Experienced Executive Team and Board of Directors



**J. Joseph Kim, Ph.D.**  
**President & CEO**

- Decades of biotech/ pharma management
- Merck: hepatitis A and B vaccines manufacturing; HIV vaccine (Ad5) R&D



**Peter Kies**  
**CFO**

- Ernst & Young
- Experience with growth companies



**Jacqueline Shea, Ph.D.**  
**COO**

- Former CEO/COO of Aeras
- Held management positions at Emergent BioSolutions and Microscience Ltd.



**Laurent Humeau, Ph.D.**  
**CSO**

- Extensive R&D leadership exp. in vaccine, cell and gene therapy developments at Intrexon and VIRxSYS

## Board of Directors

**Simon X. Benito**

Chairman of the Board, Former SVP, Merck Vaccine Division

**Roger Dansey, M.D.**

Former Head of Late-Stage Oncology at Merck & Co.

**J. Joseph Kim, Ph.D.**

President & CEO, INOVIO Pharmaceuticals

**Ann. C. Miller, M.D.**

Former Head of Sanofi Oncology Global Marketing

**Jay Shepard**

Former President & CEO, Aravive

**David B. Weiner, Ph.D.**

Executive VP, Director, Vaccine Center, The Wistar Institute

**Wendy L. Yarno, Ph.D.,**

Former Executive VP and Chief Marketing Officer, Merck

**Lota S. Zoth**

Former CFO, MedImmune

# Well-Balanced Pipeline of Milestones Supported by Strong Balance Sheet

NASDAQ:INO

**\$443.7M**

Cash and short-term investments

As of June 30, 2021

**210.1M**

Common stock shares outstanding

As of June 30, 2021

## INO-4800

- ✓ May 2021: Successful dose selection from Phase 2 segment of INNOVATE
- ✓ August 2021: Received first regulatory approval to begin Phase 3 segment of global INNOVATE efficacy trial

- 1H22: Report interim efficacy data from Phase 3 INNOVATE trial

## VGX-3100

- ✓ 1H21: REVEAL 1 Phase 3 top-line efficacy & tolerability data
- 4Q21: Report complete REVEAL 1 data (ITT, mITT, per protocol)
- 4Q21: Report on pre-treatment biomarker with QIAGEN

## INO-5401

- ✓ 4Q20: OS18 data from Phase 1/2 GBM clinical trial (INO-5401 plus Libtayo®)
- 4Q21: Present 24-month overall survival and immunology data

## Platform Development

- ✓ 3Q21: Initiate Phase 2 MERS study with INO-4700 funded by CEPI
- 4Q21: Fully enroll Phase 1B field study for Lassa with INO-4500 funded by CEPI



# INOVIO

POWERING DNA MEDICINES™