



# Powering a New Decade of DNA Medicines

January 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.

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 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-K for the year ended December 31, 2019 and Form 10-Q for the quarter ended September 30, 2020, which have been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at [www.sec.gov](http://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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# Powering DNA Medicines

**15 DNA medicine clinical programs currently 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.)**

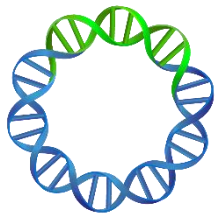
**Targets multiple antigenic sequences;  
combining multiple antigens into single vial**



# 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 2b study
- Lead candidate VGX-3100 in Phase 3 for precancerous cervical dysplasia

## Tolerability

- Favorable safety profile tested in over 3,000 patients and over 6,000 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 frozen storage issues** (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
INFECTIOUS DISEASES	INO-4800	COVID-19 (Coronavirus)					
	INO-4700	MERS					
	INO-4500	Lassa Fever					
	INO-4201	Ebola					
	PENNVAX-GP	HIV					
HPV-TARGETED	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)					
	MEDI0457	Head & Neck Cancer					
		Cervical, Anal, Penile, Vulvar Cancers					
IMMUNO-ONCOLOGY	INO-5401	Glioblastoma Multiforme (GBM)					
	INO-5151	Prostate Cancer					
mAb™		COVID-19 (Coronavirus)					
	INO-A002	Zika					

INTERNALLY FUNDED



EXTERNALLY FUNDED



# Infectious Disease Programs & COVID-19 Vaccine Program

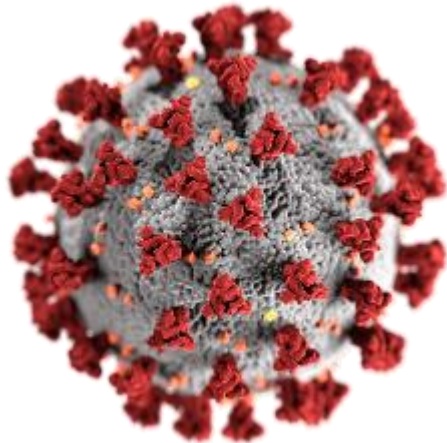


# INO-4800 Clinical and Manufacturing Plan/Strategy



## COVID- 19 vaccine

INOVIO is developing a two-dose **INO-4800 regimen** for protection against **COVID-19 disease**



## Clinical data and plan

- **Phase 1 dosing regimen complete**
  - Showed favorable safety and tolerability profile
- **Elicited a broad immune response across multiple assays, preliminary clinical responses**
- **Demonstrated binding, neutralizing antibodies & cellular responses at week 6**

### Phase 2 ongoing in U.S.

- Fully funded by U.S. DoD

### Phase 3 planned

- Fully funded by U.S. DoD
- Multi-site, blinded, case-driven, immunogenicity and efficacy trial in U.S.
- **Ongoing Phase 2 clinical trials in China and South Korea**



## Manufacturing & scale up

- Scaling up plasmid and device through consortium of CMOs and partnerships globally
- Excellent stability profile, room temperature for >1 year, anticipated 5- year shelf life at 2-8°C





# INO-4800 Key Differentiators

## Tolerable and Easy to Administer:

- INO-4800 has a strong tolerability profile
- Administered intradermally and has caused only very limited side effects (mild injection site reactions)

## Immunogenic:

- 100% of Phase 1 participants demonstrated overall immunological response rates
- Balance of neutralizing antibodies and favorable T-cell responses (CD8 and CD4)

## Temperature Stable and Transportable:

- Vaccine is projected stable at room temperature for more than a year, at 37°C for more than a month
- Five-year projected shelf life at normal refrigeration temperature and does not need to be frozen during transport or storage

## Repeat Administration:

- INO-4800 can be re-administered if immunity wanes
- Potential for seasonal boosting usage with no concerns of generating an anti-vector response, based on observations to date

# INO-4800 Ph 1 Trial Data: Regimen was well-tolerated and generated both B and T cell immune response

A

## Tolerability

- 1.0mg and 2.0mg doses of INO-4800 in a 2-dose regimen is well tolerated in initial cohort of younger (18-50) subjects evaluated in the U.S.

B

## Immunogenicity

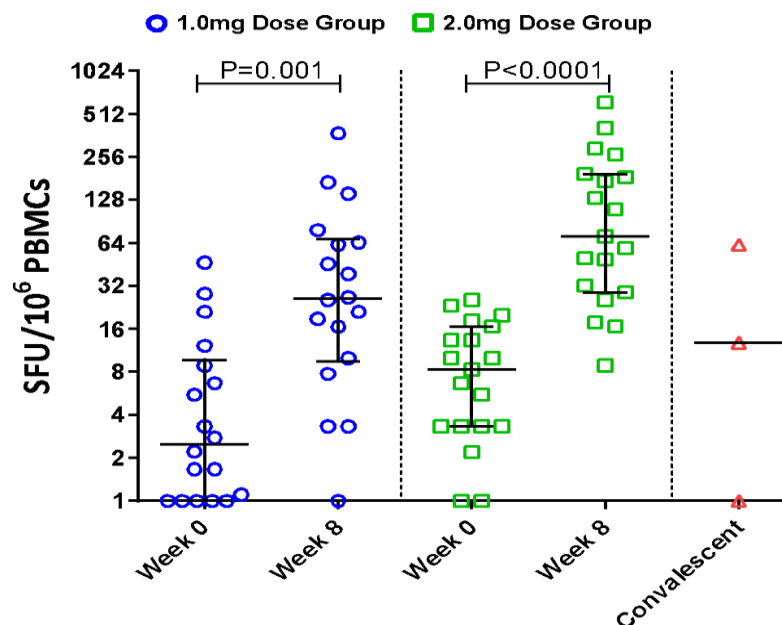
- INO-4800 induced a balanced immune response comprising both B cell (neutralizing and binding antibodies) and T cell (Th1 effector and memory cell) responses

**Data from cohort of Phase 1 peer-reviewed and published in EClinical Medicine;  
Phase 1 expansion study is ongoing:**

- Tolerability and immunogenicity of 1.0mg and 2.0mg doses in expanded age groups of older subjects (51-64) and elderly (65 years and older)
- Tolerability and immunogenicity of 0.5mg dose in a 2-dose regimen (Days 0, 28) at age groups of 18-50, 51-64 and 65+ years

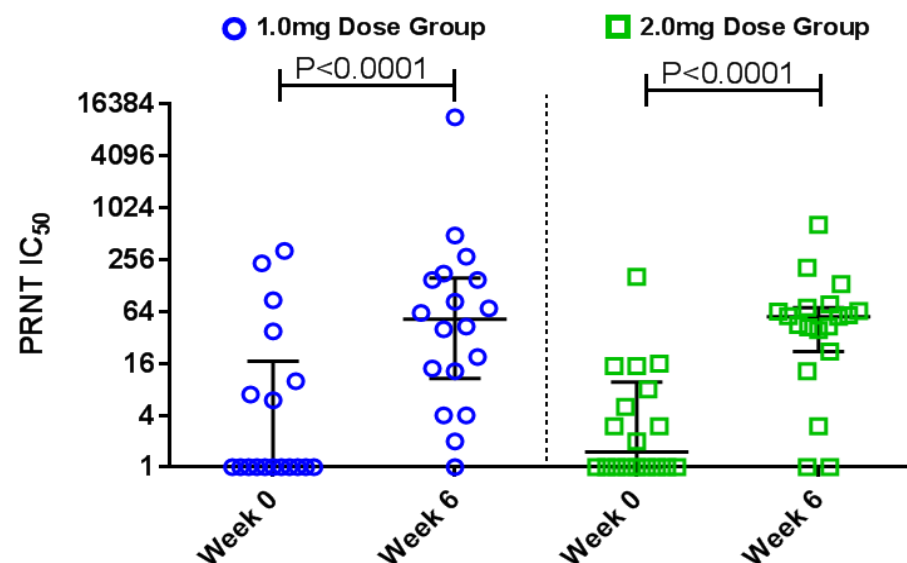
# U.S. Phase 1: Week 8 Immunogenicity on 40 Subjects in 18-50 year age group

Induction of Antigen Specific T Cells by ELISpot\*  
1.0mg vs 2.0mg



- Strong CD4 and CD8 T cell responses generated to multiple regions of the spike protein
- 74% of the subjects had T cell responses at the 1.0 mg dose group and 100% of the subjects in the 2.0 mg dose group demonstrated cellular responses

LIVE SARS-CoV-2 Neutralization\*  
1.0mg vs 2.0mg

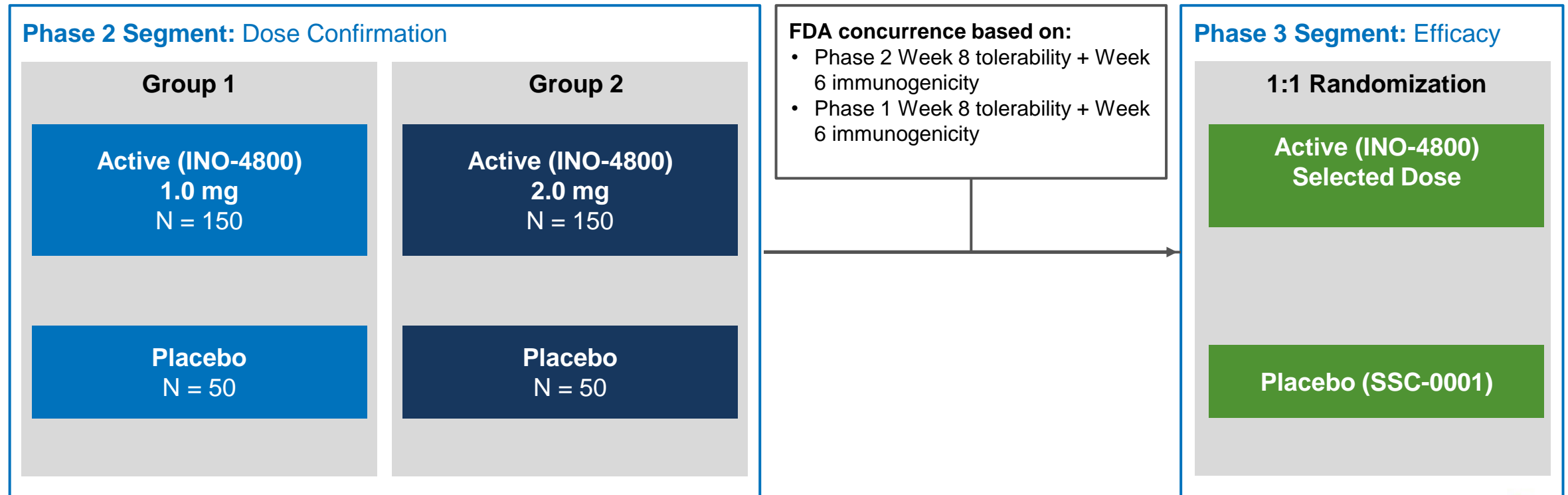


- The 1.0 mg and 2.0 mg dose group both demonstrated seroconversion in 95% of the subjects
- 78% demonstrating neutralizing antibodies in the 1.0 mg dose group and 84% demonstrating neutralizing antibodies in the 2.0 mg dose group

# 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 selected dose(s) from Phase 2 segment in a case-driven fashion



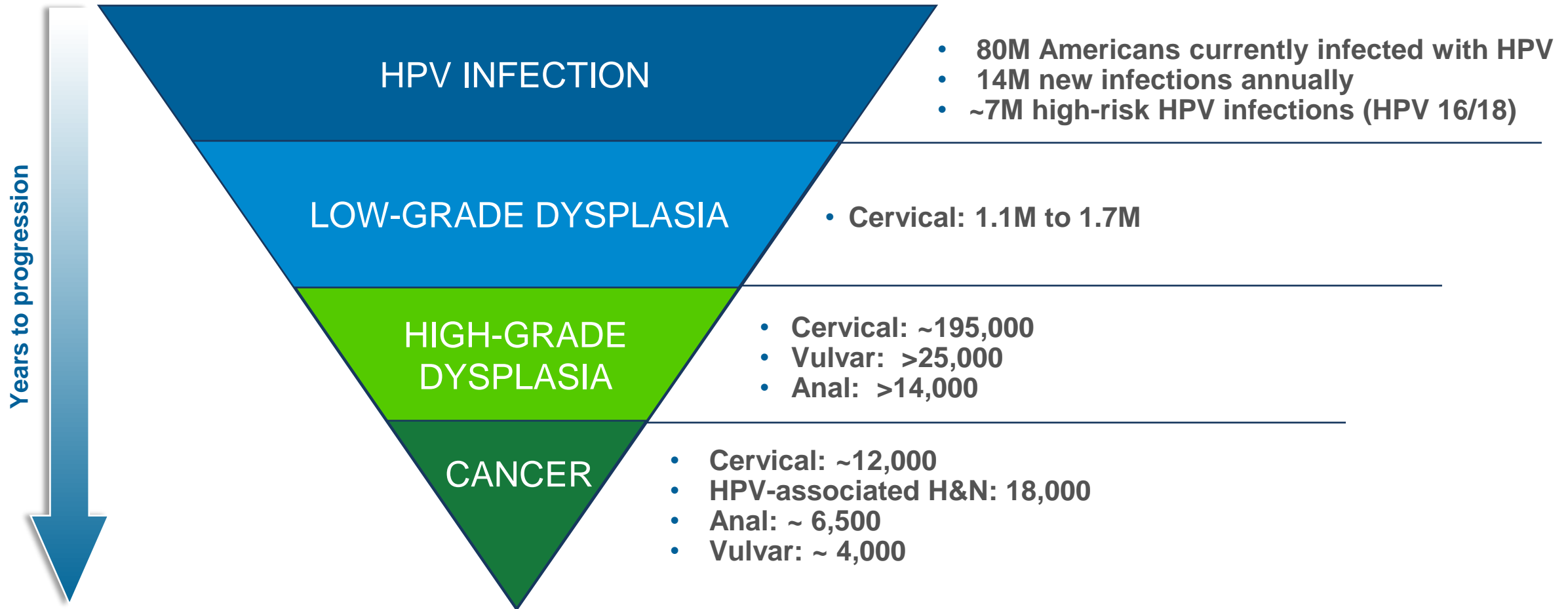


# HPV-Related Programs



# HPV-Associated Diseases Market Overview

## HPV-associated conditions per year in US:

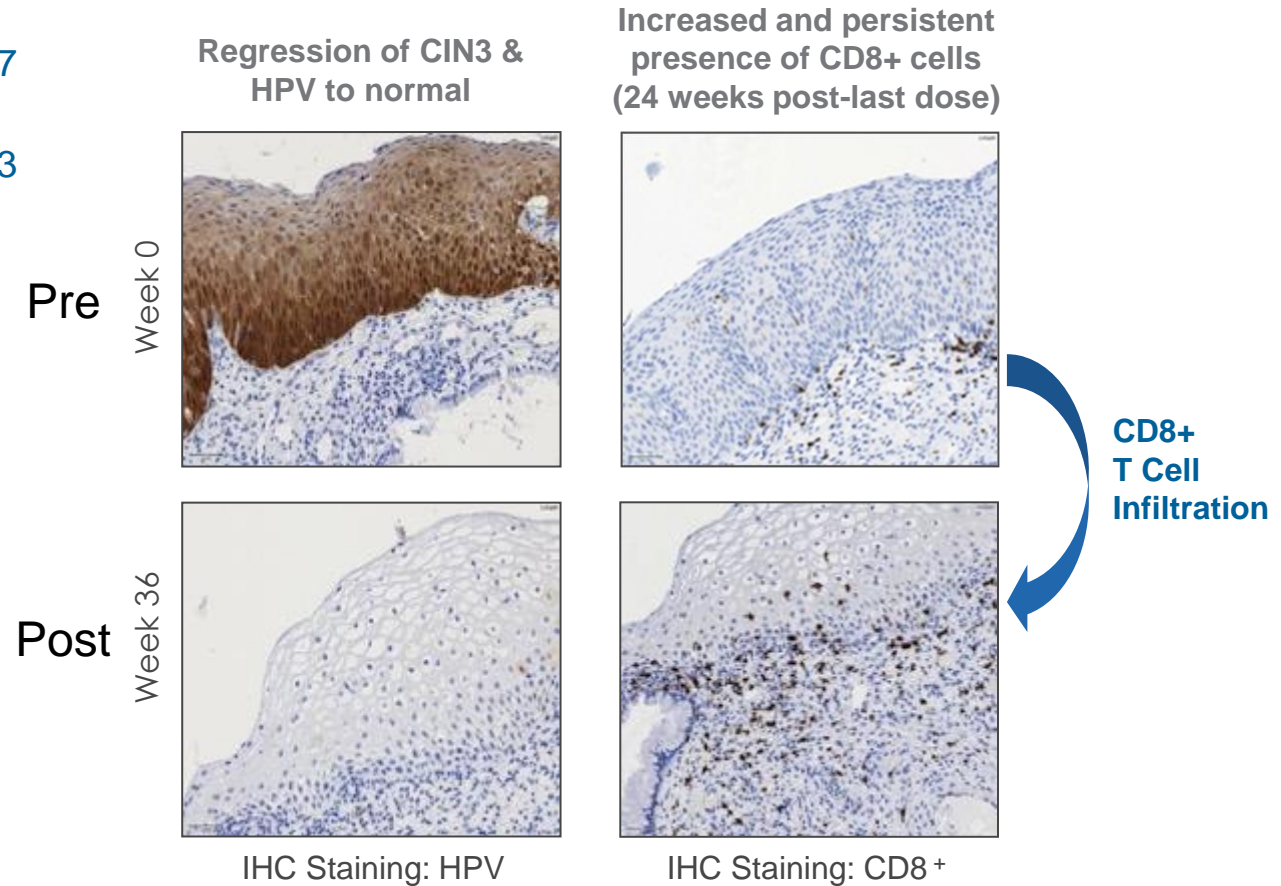
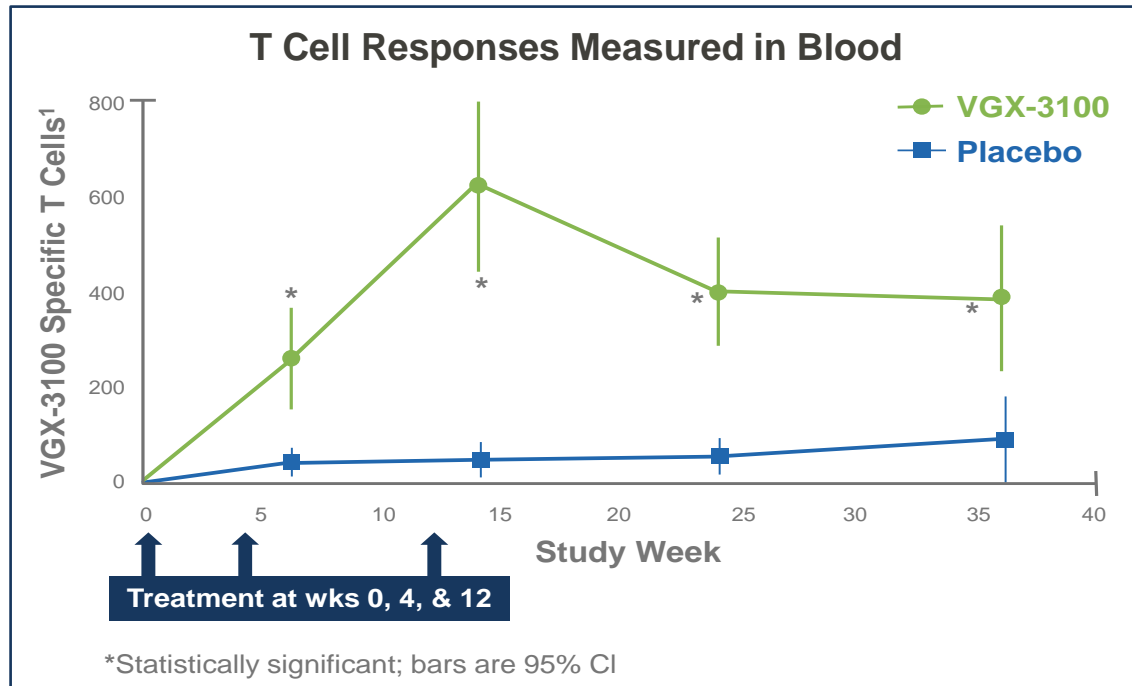


**Sources:** US CDC (2018) HPV and Cancer, available at: <https://www.cdc.gov/cancer/hpv/statistics/cases.htm> (accessed July 22, 2019); Saraiya M, Unger ER, Thompson TD, Lynch CF, Hernandez BY, Lyu CW, Steinau M, Watson M, Wilkinson EJ, Hopenhayn C, Copeland G, Cozen W, Peters ES, Huang Y, Saber MS, 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.

# Published VGX-3100 Phase 2b Study Achieved All Primary and Secondary Endpoints

## Phase 2b Endpoints (n=167)

<b>Primary:</b>	Regression to CIN1 or Normal	<b>49.5%</b>	P=0.017
<b>Secondary:</b>	Regression to Normal AND Virological Clearance	<b>40.2%</b>	P=0.003



# 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:**

**REVEAL1 (primary) n=198 – Enrollment Closed**  
Study follow-up through week 88 (as in P2b)  
Topline efficacy data expected 1H21

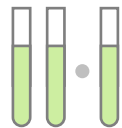
**REVEAL2 (confirmatory) n=198 – Now Enrolling**  
Study follow-up through week 40

**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



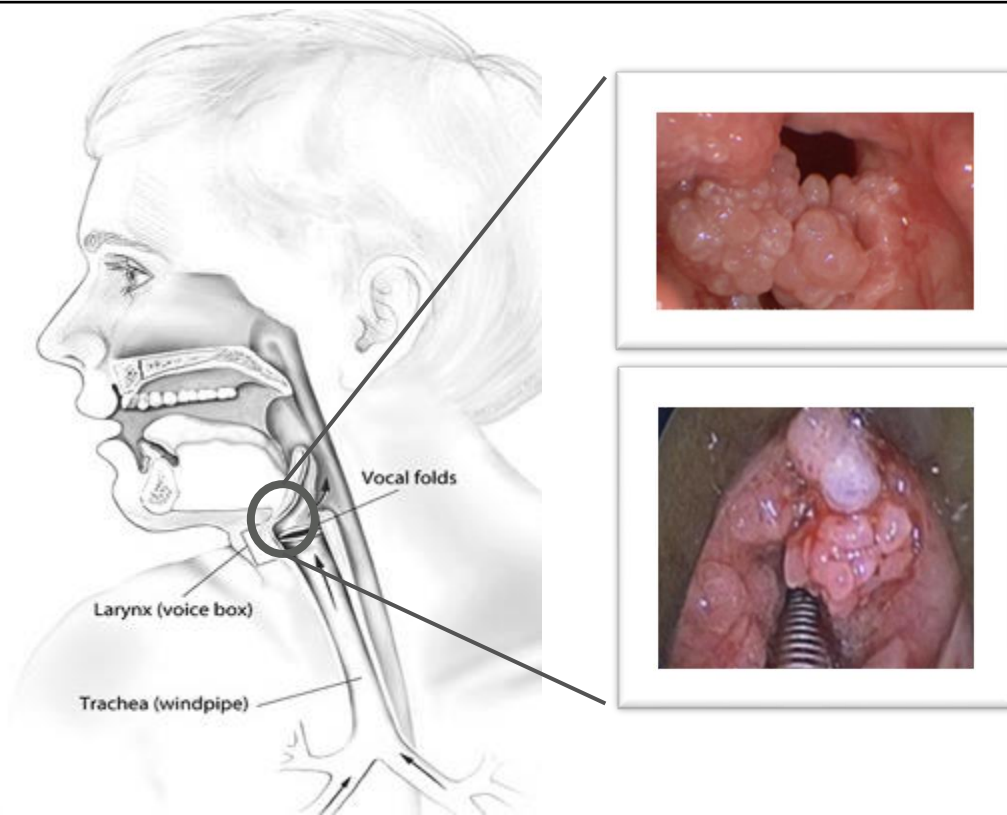
Dosing: month 0, 1, 3  
(as in P2b)

**mo.9** Primary endpoint measured at  
month 9 (as in P2b)



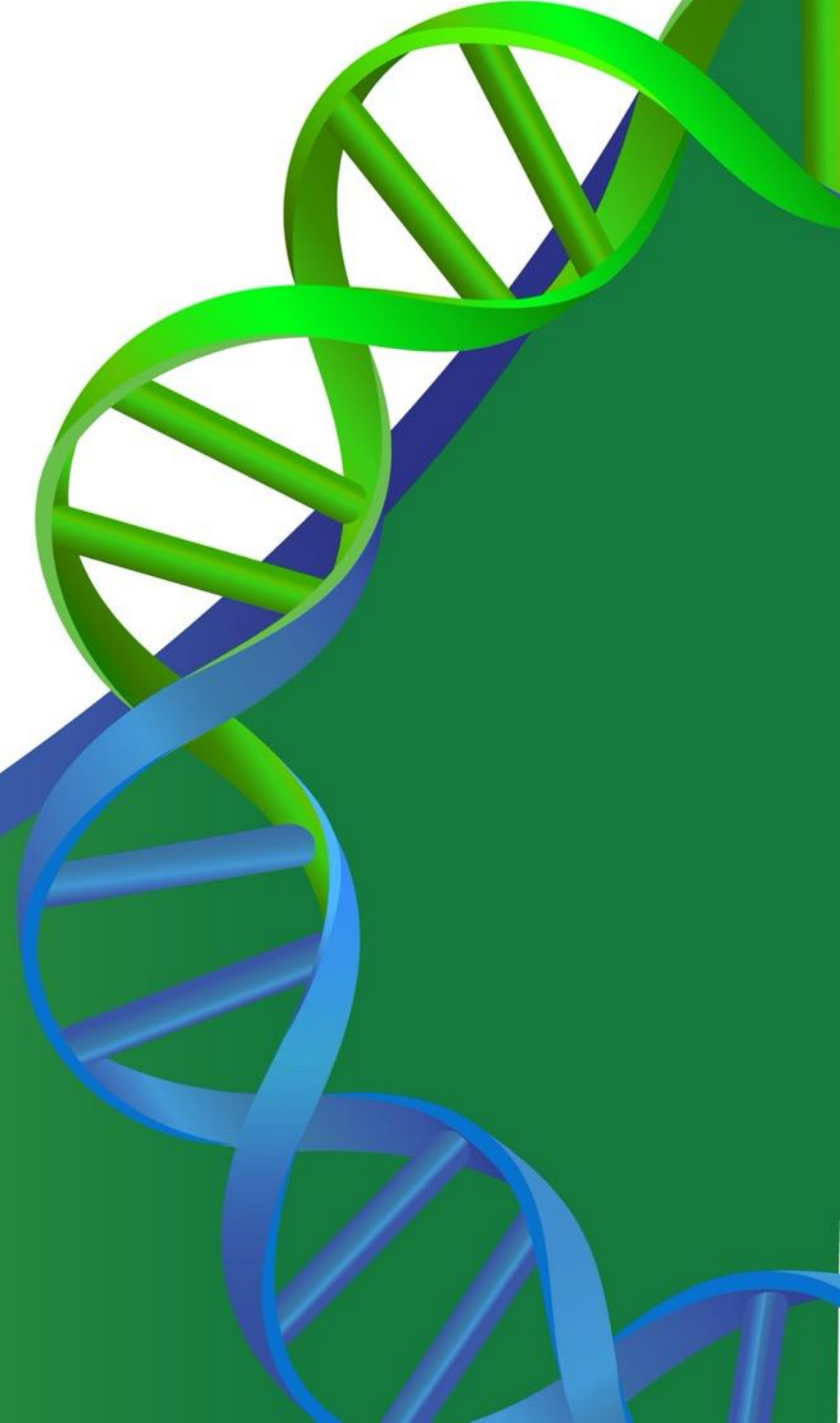
# Recurrent Respiratory Papillomatosis (RRP) Caused by HPV 6 and 11

## 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®)

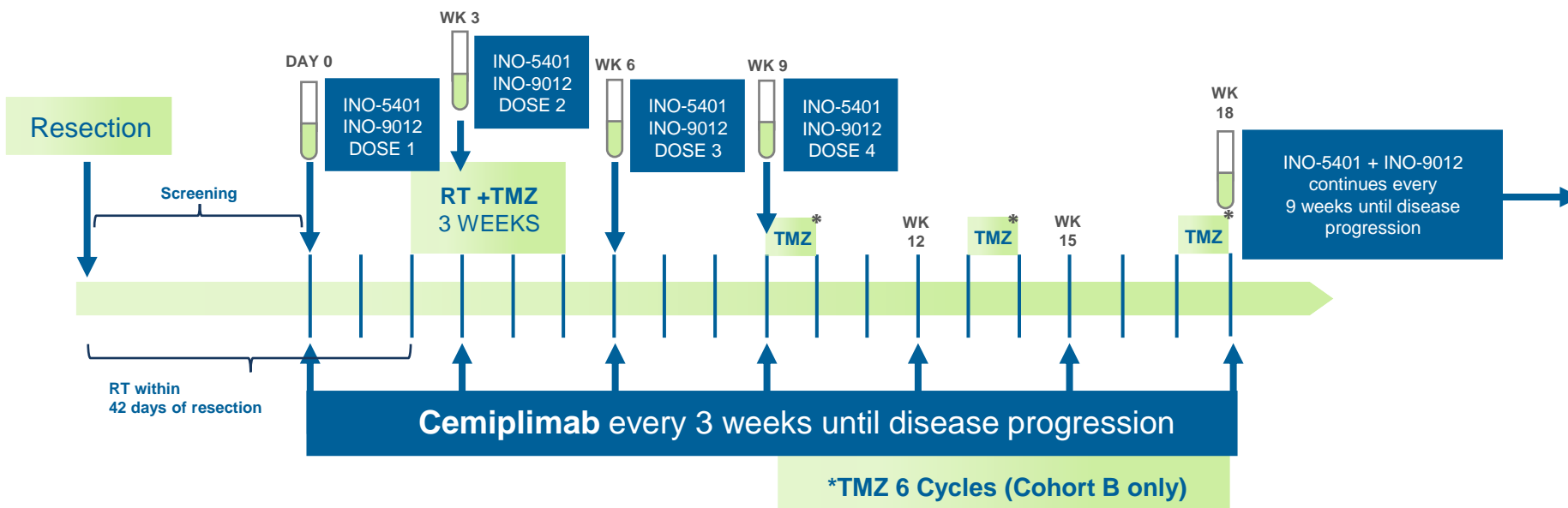
**Primary Endpoints:**  
Safety, tolerability  
**Secondary Endpoints:**  
Immunological impact, **PFS and OS**

 **x32**

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

 **x20**

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

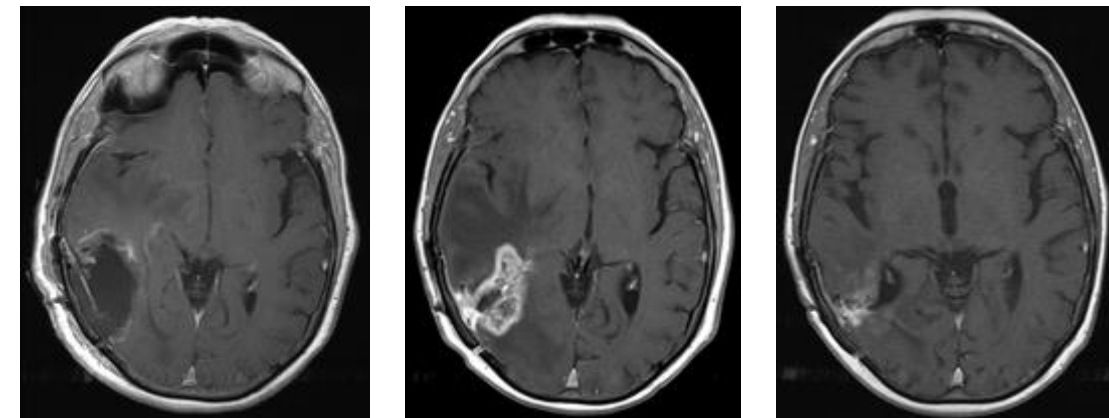
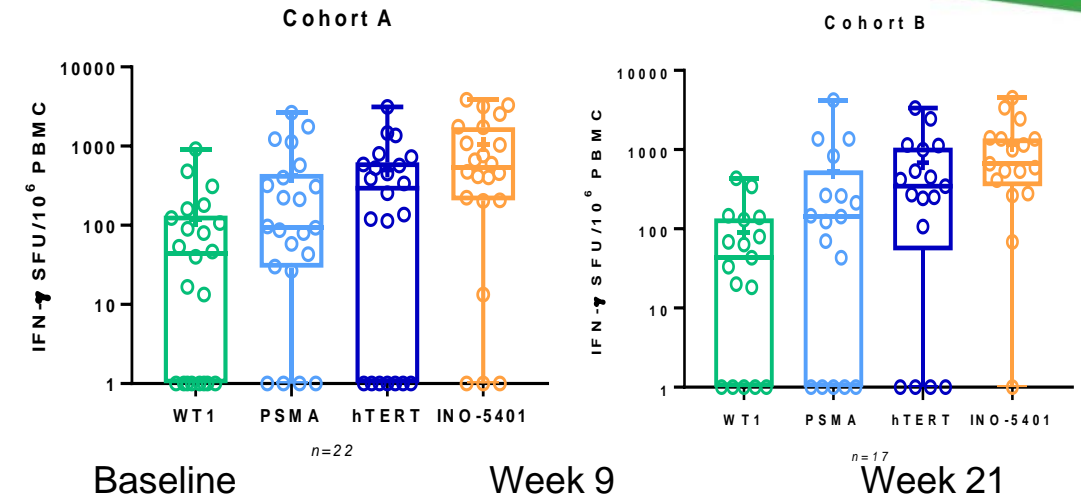


# INO-5401 Results: Interim review in newly diagnosed GBM patients

## 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
- *Additional data expected in the coming months, 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

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

<b>Overall Survival at 12 Months</b>	<b>n Alive/N Total</b>	<b>OS12% (95% CI)</b>
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)

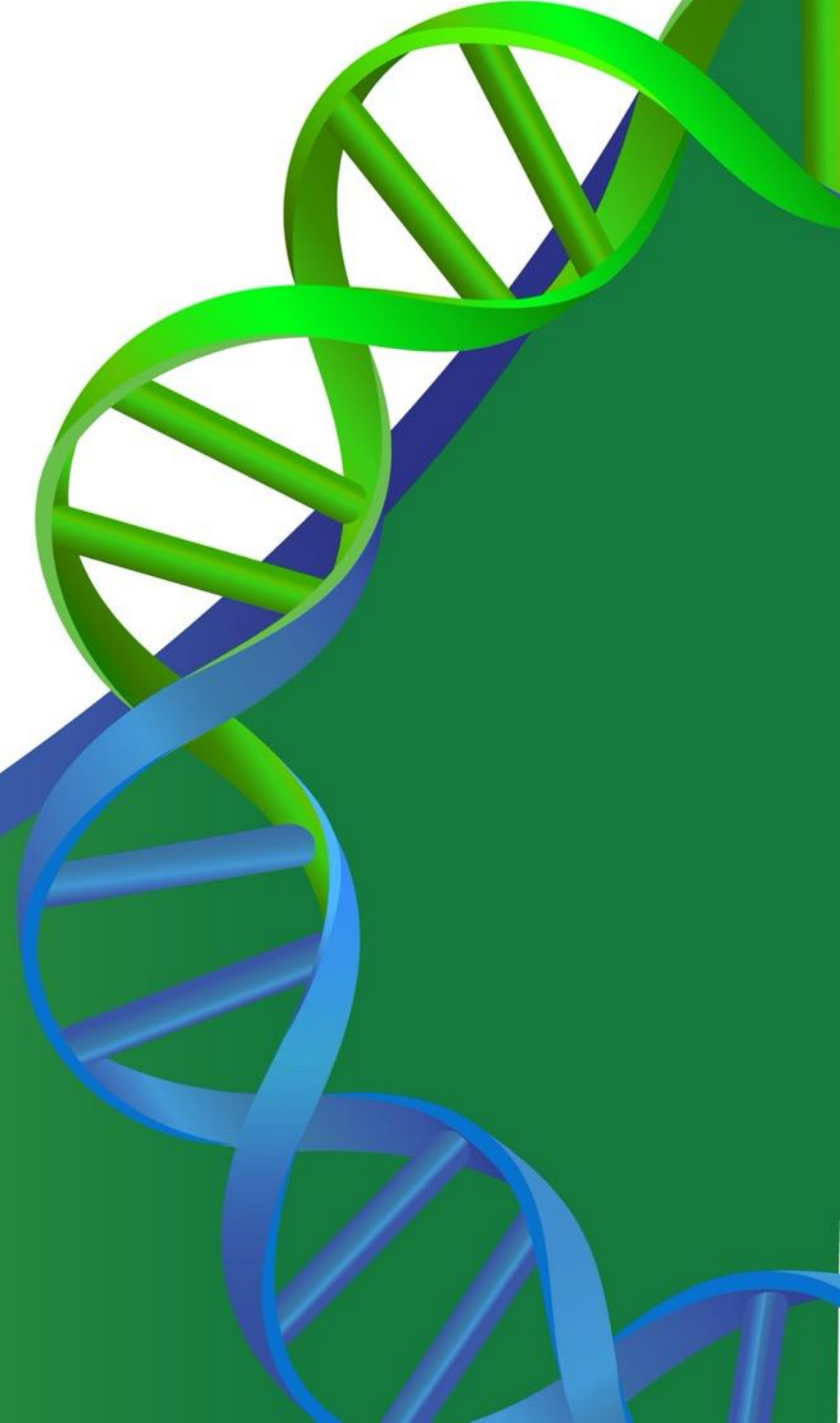
<b>Overall Survival at 18 Months</b>	<b>n Alive/N Total</b>	<b>OS18% (95% CI)</b>
MGMT Unmethylated (Cohort A)	16/32	<b>50</b> (31.9 - 68.1)
MGMT Methylated (Cohort B)	14/20*	<b>70</b> (45.7 – 88.1)
Combined	30/52	<b>57.7</b> (14.5 – 71.3)

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

# Financials & Milestones



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

NASDAQ:INO

**\$337.2M**

Cash and short-term investments

As of September 30, 2020

**168M**

Common stock shares outstanding

As of September 30, 2020

## INO-4800

- ✓ Dec. 2020: Published Phase 1 data from first cohort in The Lancet's EClinicalMedicine
- ✓ Dec. 2020: Dosed first subject in Phase 2 clinical trial called INNOVATE (INovio INO-4800 Vaccine Trial for Efficacy)
- ✓ January 2021: Fully enrolled 640 patient Phase 2 clinical trial in China
- ❑ 1Q21: Complete INNOVATE Phase 2 segment
- ❑ 2Q21: Initiate Phase 3 segment of INNOVATE trial (*pending partial clinical hold lift on Ph3*)

## VGX-3100

- ✓ Report full data from Phase 2 VIN/AIN clinical trials
- ❑ 2021: Initiate Phase 3 trials for VIN/AIN; Attain orphan drug designation
- ❑ 1H21: REVEAL 1 Phase 3 top-line efficacy & tolerability data

## INO-5401

- ✓ 4Q20: OS18 data from Phase 1/2 GBM clinical trial (INO-5401 plus Libtayo®)
- ❑ 2021: Additional survival and immunology data

## Platform Development

- ✓ 4Q20: Awarded two-year grant from DARPA to advance COVID-19 dMAb candidate
- ❑ 1Q21: Initiate Phase 2 field study for Lassa with INO-4500 funded by CEPI
- ❑ 2021: Initiate Phase 2 MERS study with INO-4700 funded by CEPI



# INOVIO

POWERING DNA MEDICINES™



# Appendix



# 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 in private biotech and mid-cap companies
- Led Translational Research, Human Therapeutics Division for Intrexon

## Board of Directors

### **Simon X. Benito**

Chairman of the Board, Former SVP, Merck Vaccine Division

### **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

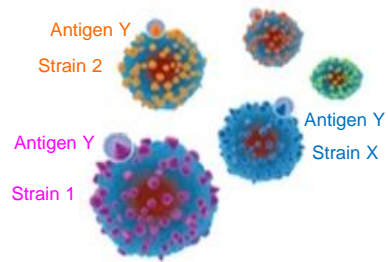
### **Lota S. Zoth**

Former CFO, MedImmune

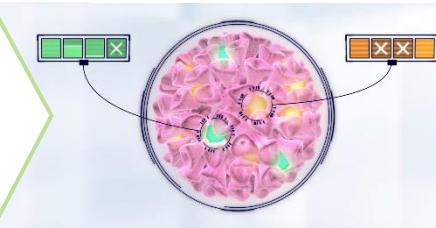
# INOVIO Technology – Powering Potent Antigen Specific Immune Responses

INOVIO DNA medicines power a patient's immune system to generate functional antibodies and killer T cells *in vivo* to fight cancer and infectious disease

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



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



3. Create optimal Consensus Sequence for the selected antigen

Sequence 1	EMEKIVLLFAIV...SL
Sequence 2	AMESIVLLFAIV...SL
Sequence X Consensus	AMEKIVLLFAIV...SK
	AMEKIVLLFAIV...SL

4. Insert SynCon sequence for each selected antigen into a separate precisely designed plasmid



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



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

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

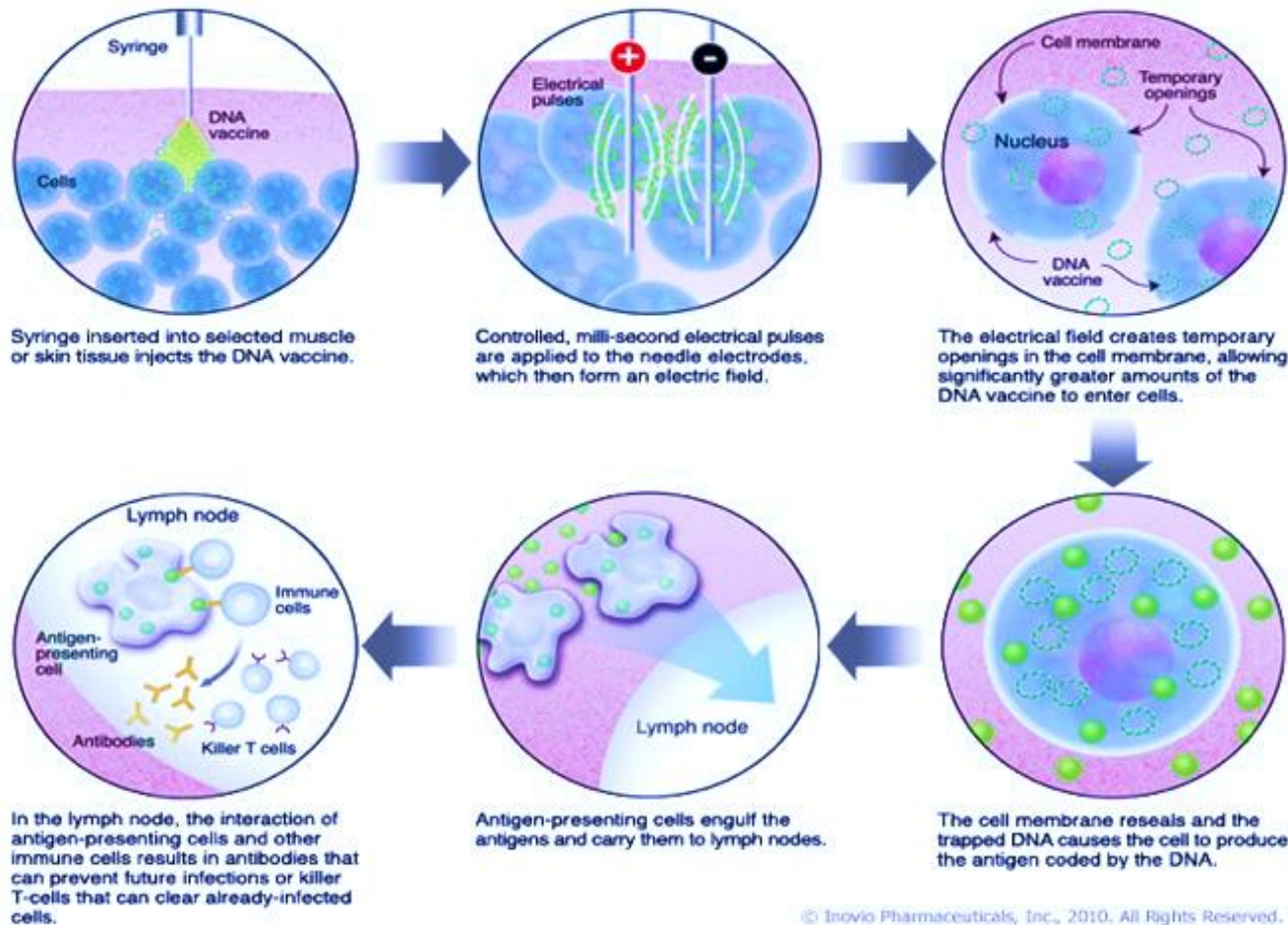


**Intradermal Device** for  
Vaccines



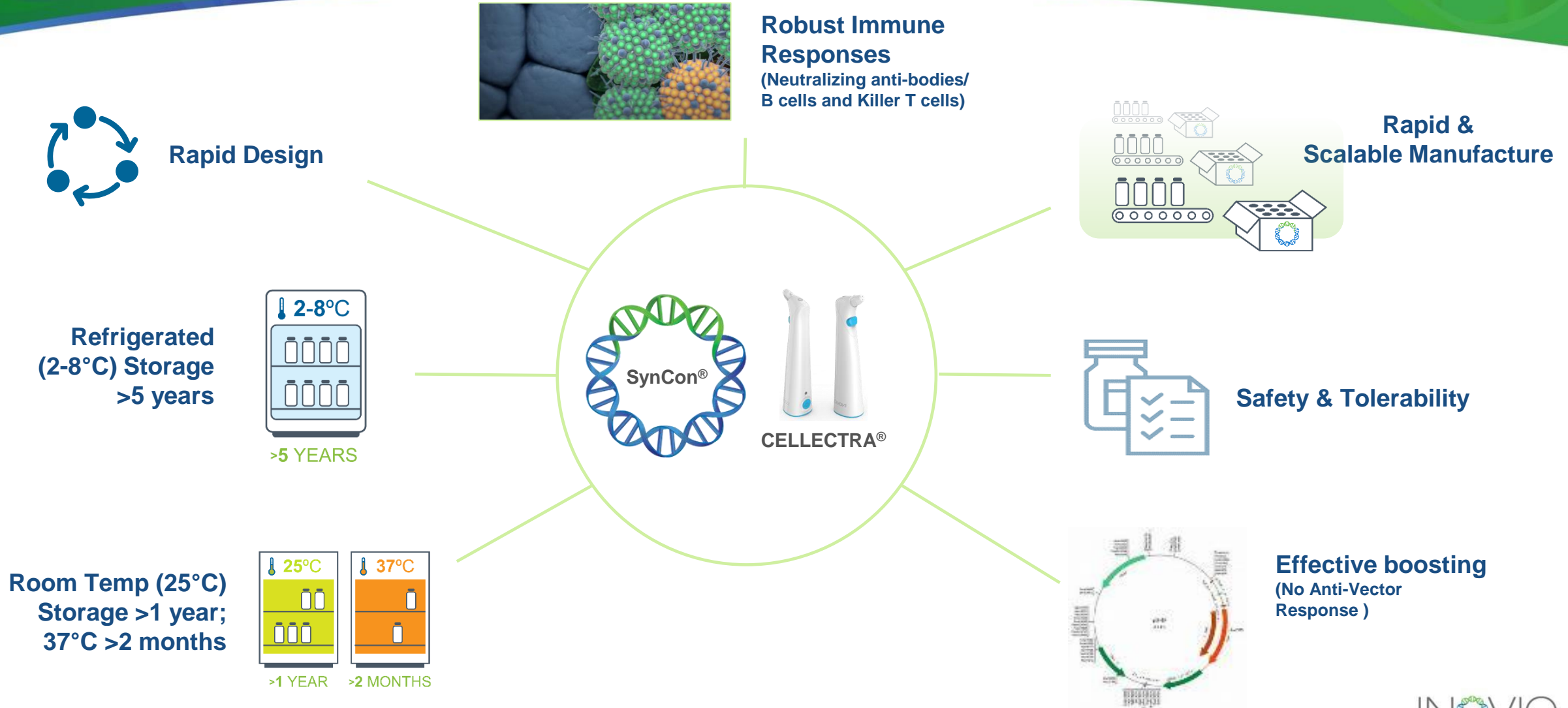
# INOVIO's Technology Delivering Precisely Designed Plasmids with Proprietary Smart Devices

**INOVIO's DNA medicine powers a patient's immune system to generate functional antibodies and killer T cells**





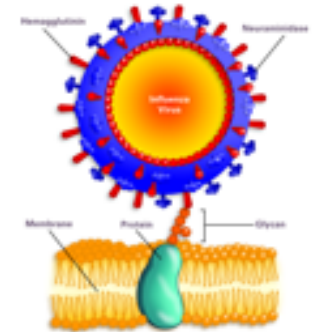
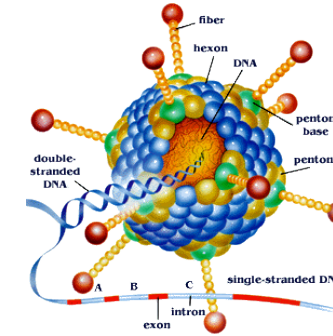
# Key Characteristics of INOVIO's DNA Medicines Platform



# Limitations of Other Approaches

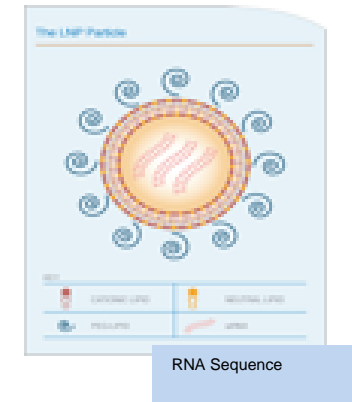
## Viral Vectors – Receptor/cell target based mediated entry

- Systemic delivery/local injection
- Preexisting or induced immunity is an issue
- Biologic variability of take
- Immune bias tuned by vector
- Hard to re-administer/tissue tropism limits and positives

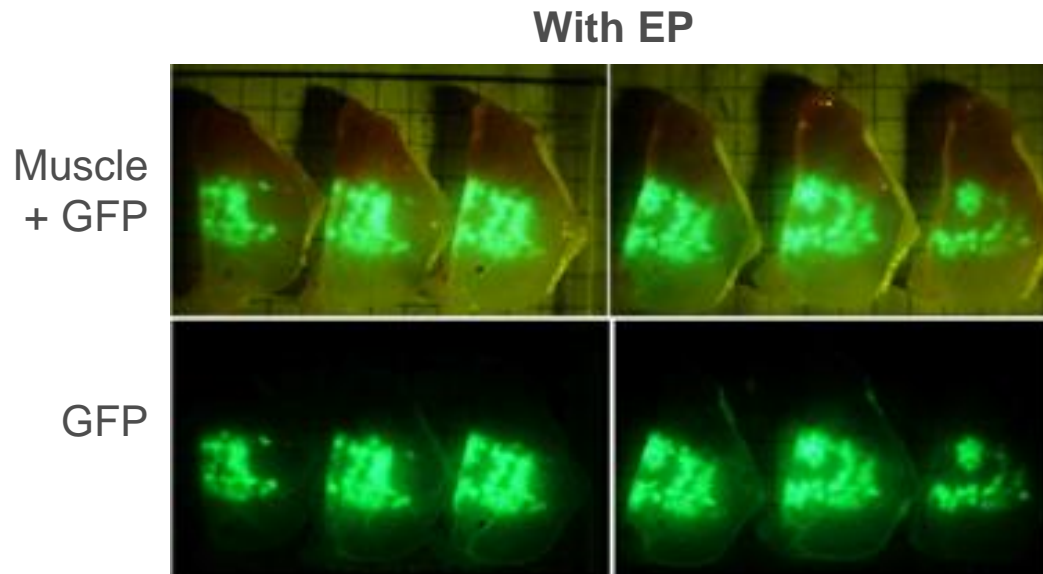


## RNA – LNP/nanoparticle delivery dependent

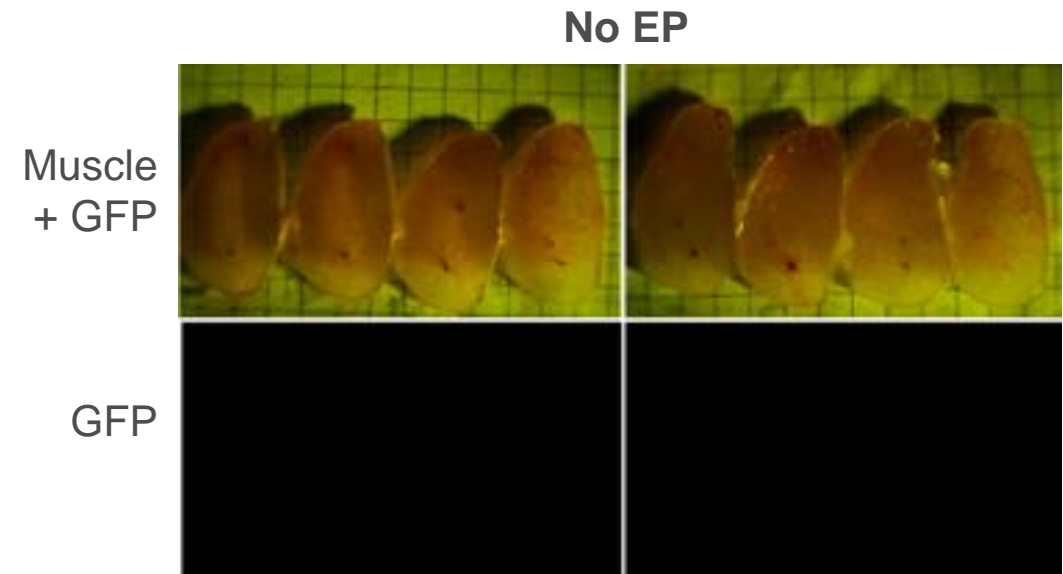
- Systemic delivery, localized expression (liver>lung or spleen)
- Process for manufacture and release work in progress
- Formulations + RNA follow tissue targeting of the particles/cold chain required, include focus on IV route
- DLT observed, low CTL induced, inflammatory
- High cost of goods



# Precise Design + Intracellular Delivery = Improved Immune Responses



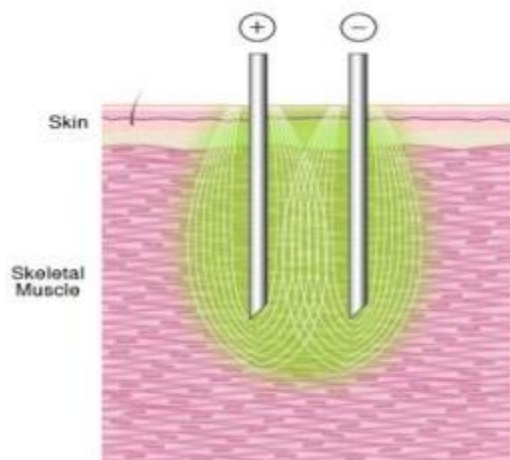
Display of GFP (green fluorescent protein)  
gene expression after CELLECTRA®  
delivery into rabbit muscle



# Innovation in the Delivery of SynCon® DNA Medicine

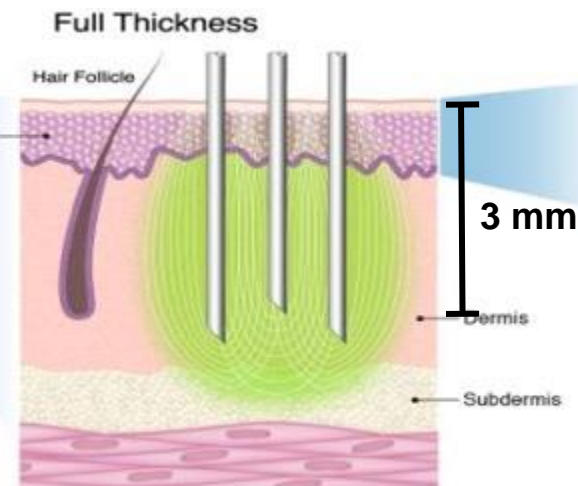
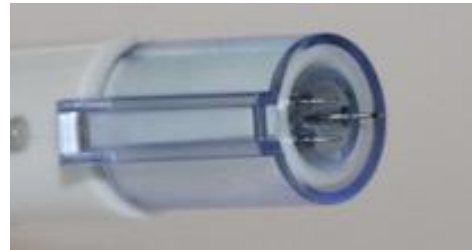
## CELLECTRA®-5PSP

- Intramuscular
- 13, 19, 25mm electrodes
- In clinical use



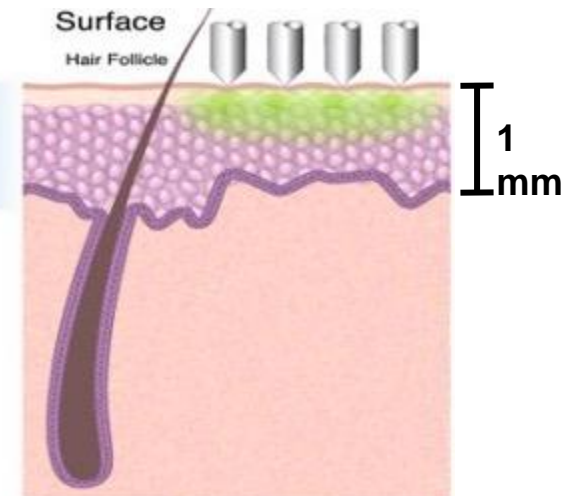
## CELLECTRA®-3P

- Intradermal – minimally invasive
- 3mm electrodes
- In clinical use



## Surface EP (SEP)

- Surface
- Noninvasive
- 4x4 electrode array
- Specifically targets epidermis
- In late-stage preclinical development





# INOVIO-Led Global Coalition to Advance INO-4800

## Funders








## Collaborators



## Manufacturers

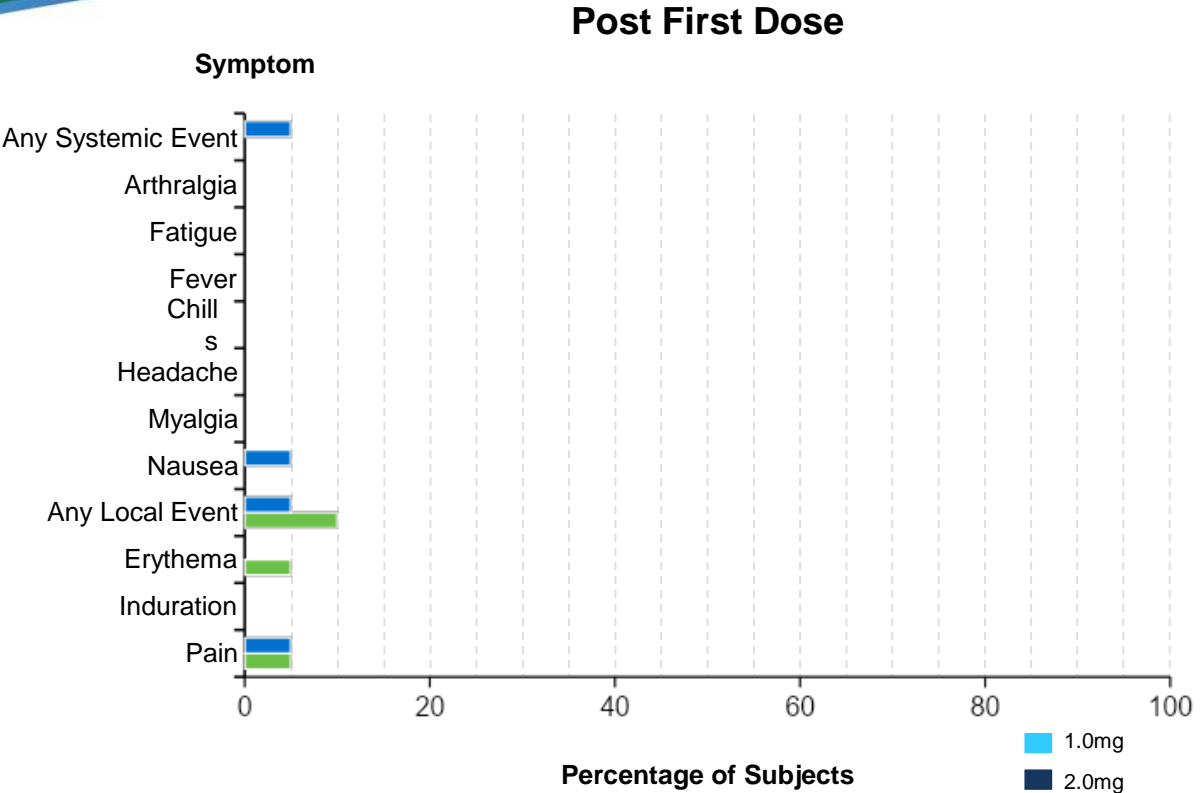


# Infectious Disease Platform: Consistency of Positive Clinical Data and Partnering Opportunities

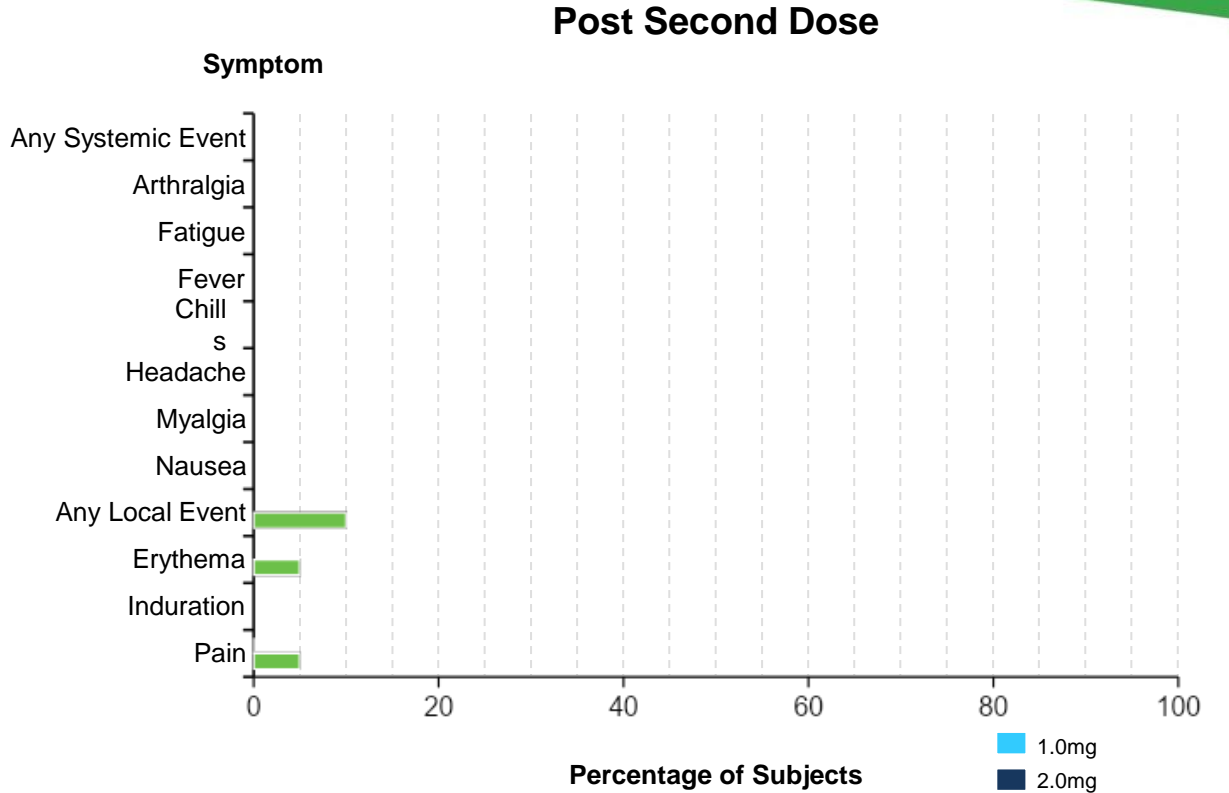
Product	Indication	Data Reported (to date)	Partner/s
PENNVAX-GP	HIV	<ul style="list-style-type: none"> <li>Phase 1: <b>93% (71 of 76)</b> evaluable vaccinated participants showed a CD4+ or CD8+ cellular immune response to at least one of the vaccine antigens</li> <li><b>94% (62 of 66)</b> demonstrated an env specific antibody response</li> </ul>	  HIV VACCINE TRIALS NETWORK
INO-4201	Ebola	<ul style="list-style-type: none"> <li>Phase 1: High levels of binding antibodies measured (ELISA) in <b>95% (170 of 179)</b> of evaluated subjects</li> <li><b>Published: The Journal of Infectious Diseases, March 2019</b></li> </ul>	
INO-4700 (GLS-5300)	MERS	<ul style="list-style-type: none"> <li>Phase 1: High levels of binding and neutralizing antibodies in <b>&gt;90% of subjects</b></li> <li><b>98%</b> generated an antibody and/or T cell response against MERS</li> <li><b>Published: The Lancet Infectious Diseases, July 2019</b></li> <li><b>Presented: ASGCT, May 2020</b></li> </ul>	 CEPI
INO-4600 (GLS-5700)	Zika	<ul style="list-style-type: none"> <li>Phase 1: High levels of binding antibodies measured (ELISA) in <b>100% (39 of 39)</b> of evaluated subjects</li> <li><b>Published: New England Journal of Medicine, October 2017</b></li> </ul>	

# U.S. Phase 1: Week 8 Safety on 40 Subjects in 18-50 year olds

Systemic and Local Adverse Events (AEs) Related to Study Drug by Dose



n=20



n=20



No serious adverse events (SAEs) reported and all adverse events (AEs) reported were mild  
No dose discontinuations due to AEs  
No tolerability concerns as per Data Safety Monitoring Board (DSMB)

# U.S. Phase 1: Week 6/8 Immunogenicity on 40 Subjects in 18-50 year age group

Induction of humoral and/or cellular responses to SARS-CoV-2 Spike Antigen

## Immune Responses

<u>Immune Assay</u>	1.0mg Cohort			2.0mg Cohort		
	All Subjects Value	Responder Value	Responder Rate <sup>‡</sup> n (%)	All Subjects Value	Responder Value	Responder Rate <sup>‡</sup> n (%)
Neutralization Week 6 GMT Reciprocal Titer [95% CI]	44.4 [14.6, 134.8]	82.4 [29.1, 233.3]	<b>15/18 (83%)</b>	34.9 [15.8, 77.2]	63.5 [39.6, 101.8]	<b>16/19 (84%)</b>
RBD Binding Antibody Week 6 GMT Reciprocal Titer [95% CI]	27.3 [4.8, 156.8]	385.6 [69.0, 2154.9]	<b>10/18 (56%)</b>	66.8 [17.4, 257.5]	222.1 [87.0, 566.8]	<b>14/18 (78%)</b>
S1+S2 Binding Antibody Week 6 GMT Reciprocal Titer [95% CI]	174.4 [59.9, 507.3]	320.0 [160.5, 638.1]	<b>17/19 (89%)</b>	136.8 [34.5, 543.1]	508.0 [243.6, 1059.4]	<b>15/19 (79%)</b>
Total Seroconversion (Response in Neutralization, RBD or S1+S2)	N/A	N/A	<b>18/19 (95%)</b>	N/A	N/A	<b>18/19 (95%)</b>
IFN-gamma ELISpot Week 8 Median SFU per [95% CI]	26.2 [10-64]	45.6 [21.1, 142.2]	<b>14/19 (74%)<sup>μ</sup></b>	71.1 [32.2-194.40]	71.1 [32.2, 194.40]	<b>19/19 (100%)<sup>μ</sup></b>

1.0mg Cohort excludes one subject with baseline positive NP ELISA

<sup>‡</sup> Response criteria: Neutralization -Week 6 PRNT IC<sub>50</sub> ≥ 10, or ≥4 if binding ELISA activity is seen RBD & S1+S2 Binding -Week 6 value >1 ELISpot – Value ≥12 SFU over Week 0

<sup>μ</sup> - Responders generated using Week 6 or Week 8 data



- 100% response observed in both 1.0 mg and 2.0 mg dosing levels
- T-cell and B-cell responses observed in both 1.0 mg and 2.0 mg dosing levels



# INO-4800 Demonstrates Durable Efficacy, Tolerability; Only COVID-19 Vaccine With No Adverse Events >Grade 1

## TRIALS: INO-4800

- Protect against SARS-CoV2 virus that causes COVID-19
- Target Spike protein

### Human Clinical Study:



Phase 1 study  
(Initial 2 cohorts reported)



x40

40 healthy volunteers age 18-50  
1 mg and 2 mg cohorts, 2 doses (Weeks 0 and 4)

**Interim findings**  
(Week 6 efficacy and  
Week 8 tolerability)

**100% (38 out of 38)** of trial  
participants demonstrated  
overall immunological  
responses through week 6

Demonstrated binding and  
neutralizing antibodies and  
T cell immune responses

Well tolerated, no SAEs  
through Week 8

Trial expanded with  
older participants, 18  
and older and added  
dose arm of 0.5 mg

### Non-Human Primate (NHP) Study:



Challenge study



x10

5 rhesus macaques received INO-4800, 5 received placebo  
2 doses (Weeks 0 and 4)  
Challenge with SARS-CoV-2 (Week 17)

**17-week findings**  
(13 weeks after  
2<sup>nd</sup> dose)

Durable antibody and T cell  
responses for >4 months  
after initial dose

Memory T and B cell  
responses → reduced viral  
loads, faster clearance in  
lungs, nasal passages

Neutralizing antibodies  
against early virus and  
dominant G614 mutant  
variant

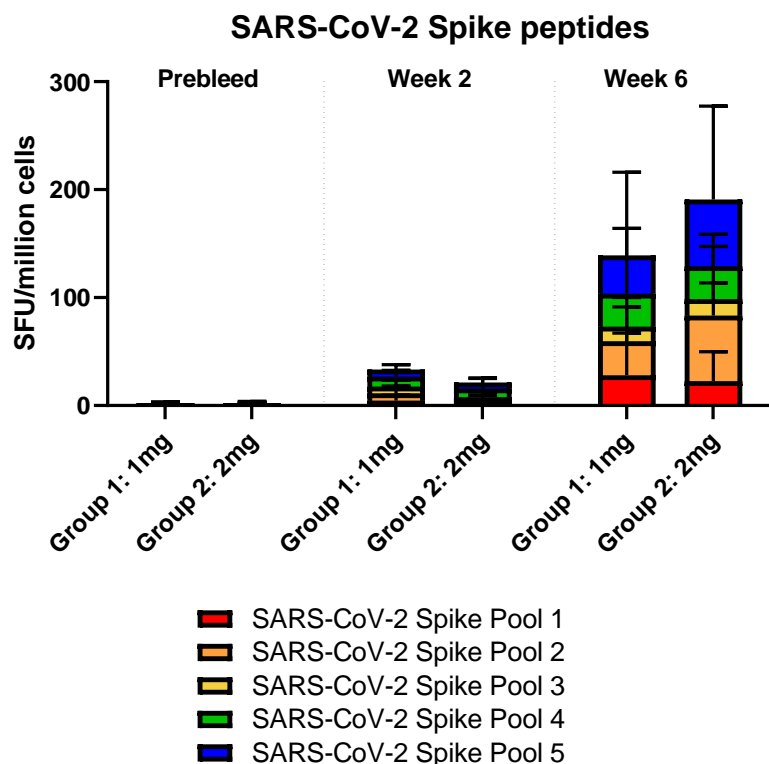
No antibody-dependent  
enhanced disease events

# Robust Cellular and Humoral Immune Responses Following Immunization of INO-4800 in Rhesus Monkeys

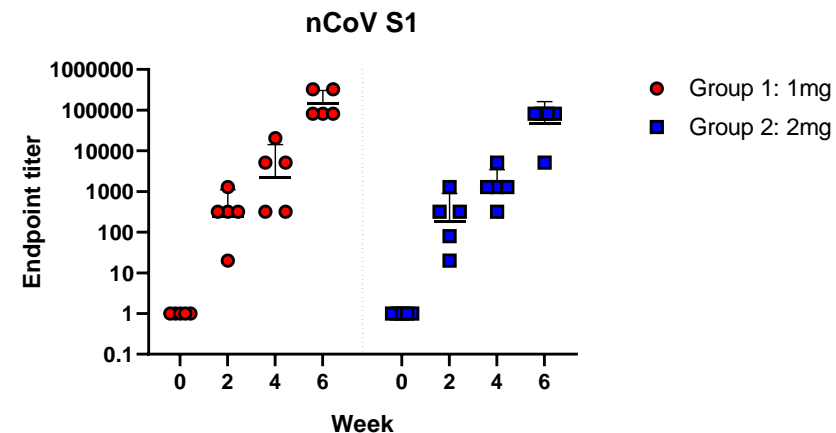


**Animal:**  
Rhesus macaque

**Treatment:**  
Day 0 and 28 ID delivery of pDNA



Group	Vaccine	Delivery	Dose per immunization	n
1	pGX9501	ID, 1 site	1 mg	5
2	pGX9501	ID, 2 sites	2 mg	5



**Robust and rapid B and T cell responses in NHPs**

# HPV-Related Clinical Program Overview

## Precancerous Dysplasias (VGX-3100)

- Cervical dysplasia: Phase 2b PoC trial demonstrated a **complete response in 43 out of 107** patients in regression of high-grade cervical lesions **and** elimination of HPV infection
- Vulvar dysplasia: Open-label Phase 2 trial showed **8 out of 10** women had **reduction in lesion area**; 2 of 10 had no virus at 6 months (interim)
- Anal dysplasia: Open-label Phase 2 trial showed **clearance of precancerous lesions in 10 out of 20** patients, decrease in lesions for 15 of 20 (interim)

## Head & Neck Cancer (MEDI0457)

- Phase 1 trial for HNSCC, **2 out of 4** patients treated with MEDI0457 and 2 different PD-1 checkpoint inhibitors **experienced a long-term complete response for >2 years**
- MEDI0457 is licensed by AstraZeneca and currently in a Phase 1b/2a study in combination with durvalumab (PD-L1 checkpoint inhibitor)

## RRP (INO-3107)

- Pilot study for Recurrent Respiratory Papillomatosis (RRP) demonstrated a clinical benefit in **2 out of 2** patients by delaying surgery due to lack of tumor recurrence
- A Phase 1/2 clinical trial for treating RRP with INO-3107, which includes both HPV 6 and HPV 11 antigens, is currently recruiting

# VGX-3100 Phase 2 Studies in HPV-Associated Vulvar and Anal HSIL/Precancerous Dysplasias

## TRIALS: VGX-3100

- Target HPV 16/18 subtypes; E6/E7 oncogenes
- Treat high-grade squamous intraepithelial lesions (HSIL)
- INOVIO plans to pursue a registrational Phase 3 clinical trial for HPV-16-/18-associated Vulvar and anal dysplasia as well as to apply for rare and orphan disease designation in 2021

### Precancerous Vulvar Dysplasia:



Phase 2  
open-label study



x24

Trial participants were 24 women between 22 and 70 years of age at entry and other than having HSIL were healthy

#### Efficacy Results

(6 months post treatment)

Decrease in lesion  
area: 63% of patients

Non-detectability of HPV 16/18 and  
lesion clearance: 15% of patients vs. a  
historical comparison of 2%

### Precancerous Anal Dysplasia:



Phase 2  
open-label study



x23

23 patients enrolled  
18 years of age or older

#### Efficacy Results

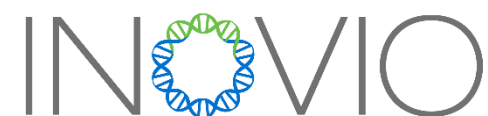
(6 months after start  
of treatment)

Decrease in number of lesions:  
78% of patients

Clearance of lesions:  
50% of patients



# INOVIO and QIAGEN Developing Biomarker to Optimize Patient Selection



In 2Q 2019, INOVIO entered into collaboration with QIAGEN to co-develop a liquid biopsy-based pretreatment commercial test kit to guide patient selection for VGX-3100:

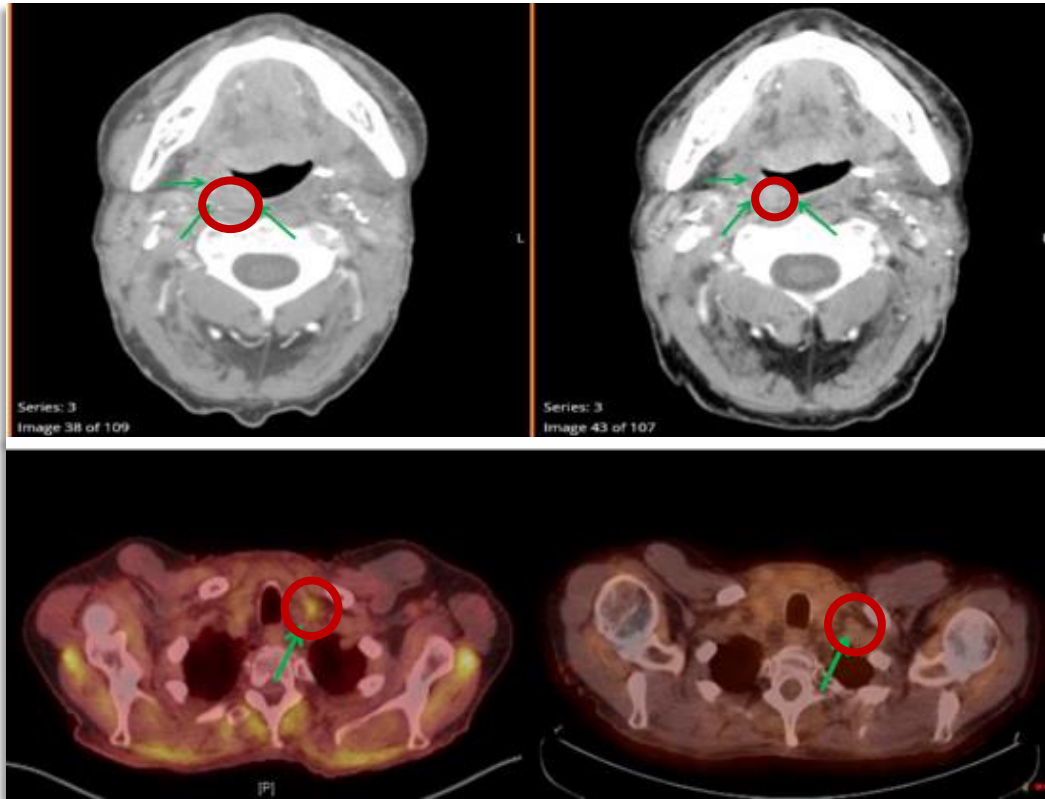
- Aimed to produce an accurate test that would **increase absolute efficacy of VGX-3100 among HPV-infected women** who have progressed to cervical HSIL (pre-cancer)
- Commercialization of a CDx test concurrently with VGX-3100 could **enhance market adoption** of this first-in-class DNA medicine

# MEDI0457 for HPV-Related Cancers in Partnership with AstraZeneca



- **MEDI0457** (formerly INO-3112) = VGX-3100 + INO-9012 (IL-12 plasmid)
- In 2015, **AstraZeneca acquired exclusive rights to MEDI0457**
  - \$27.5M upfront
  - ~\$250M in potential development and commercial milestones
  - Double-digit tiered royalties on MEDI0457 sales
- **AstraZeneca is evaluating MEDI0457 in combination with its PD-L1 checkpoint inhibitor, durvalumab, in HPV-associated cancers**

# MEDI0457 Phase 1 Study Demonstrates Complete Response



- (Top image) CT neck with IV contrast demonstrating partial response pre- and 6 weeks post-nivolumab.
- (Bottom image) PET scan images pre- and 6 weeks post-nivolumab.

## Phase 1 study of MEDI0457 (VGX-3100+IL-12) in 22 HPV+ H&N cancer patients

- Robust antigen-specific CD8+ killer T cell responses observed in **20/22 – 90.1% – of patients (both tumor tissue and peripheral blood)**
- 4 progressed over several year period exhibiting recurrence with metastatic disease; treated with PD-1
- **2/4 (50%) show complete response to PD-1 therapy and remained tumor free for 2+ years**
- 50% CR rate compares well in metastatic HPV+ H&N:
  - 4% CR rate (8/192) by KEYTRUDA alone
  - 3% CR rate (6/240) by OPDIVO alone
- AstraZeneca conducting Phase 2 studies combining MEDI0457 and durvalumab (PD-L1 inhibitor)

# INO-3106 Pilot Study in RRP – Completed

## TRIAL: **INO-3106** (for HPV 6-caused RRP)



Phase 1 pilot,  
single-site,  
clinical study



Enrolled 2 adult  
patients with RRP,  
HPV 6+



4 doses of vaccine,  
3 weeks apart on  
Day 0, Weeks 3, 6, 9



CELLECTRA-delivered  
INO-3106 (only for HPV 6)  
plasmid encoded antigens

Two RRP patients  
had prior surgeries  
every 6 months

**After receiving 4 doses, 1 patient  
has gone >915 days without  
surgery, and the second went  
584 days without surgery**

Open-label Phase 1/2 study to  
evaluate efficacy, tolerability,  
and immunogenicity of INO-  
3107 (for HPV 6 and 11)



# INO-3107 Phase 1/2 Study in RRP – Granted Orphan Drug Designation Phase 1/2 Currently Enrolling

## TRIAL: **INO-3107** (for HPV 6 and/or 11-caused RRP)

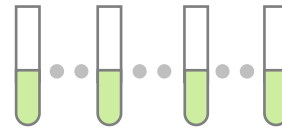
*Granted Orphan Drug Designation*



Phase 1/2 open-label, multicenter clinical study



Target enrollment



4 doses of vaccine,  
3 weeks apart on  
Day 0, Weeks 3, 6, 9



CELLECTRA-delivered  
INO-3107 plasmid  
encoded antigens

**Enrollment criteria:** Subjects who have required at least two surgical interventions per year for the past three years for the removal of associated papilloma(s)

**Primary endpoint:** A doubling or more in the time between surgical interventions following the first dose of INO-3107 relative to the frequency prior to study therapy

# INO-5151 Phase 2 Prostate Cancer Combination Study

TRIAL: **INO-5151** (encoding tumor-associated antigens: **PSA, PSMA**)



Phase 2 study (PORTER) for **metastatic castration-resistant prostate cancer**



Three cohort, 45-patient platform study, **INO-5151 in Cohort C**

## Cohort C – 15 patients



**INO-5151** (DNA immunotherapy)  
**CDX-301** (FLT3 ligand) from Celldex Therapeutics  
**Nivolumab** (anti-PD-1) from Bristol-Myers Squibb

**PICI/CRI** will fund & execute the clinical study



# Scientific Advisory Board



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

- “Father of DNA vaccines”
- Executive VP, The Wistar Institute; Director, Vaccine Center



**Anthony W. Ford-  
Hutchinson, Ph.D.**

- Former SVP, Vaccines R&D, Merck
- Oversaw development: Singulair®, Januvia®, Gardasil®, Zostavax®, Proquad® and Rotateq®



**Stanley A. Plotkin, M.D.**

- Developed rubella and rabies vaccines
- Oversaw Sanofi flu vaccine
- Emeritus Professor, Wistar Institute & University of Pennsylvania



**Rafi Ahmed, Ph.D.**

- Professor, Department of Microbiology and Immunology, Emory University School of Medicine

# INOVIO Fully Integrated Capabilities Poised for Rapid Production



## Philadelphia Corporate and Operations Site

- Corporate, Clinical, Regulatory, Compliance, Biostatistics, and Data Management functions



## San Diego Research Center

- Molecular biology, cell biology, and clinical immune monitoring
- Research-grade DNA manufacture capabilities
- 6,000 sf dedicated BSL-2 research lab (wet lab and cell culture)
- 5,000 sf cGLP labs to process, store, and analyze human clinical trial samples
- Well established QA capability



## San Diego Device Engineering and Manufacturing Facility

- Electroporation delivery device and consumable design, engineering, and manufacturing
- Delivery device testing and distribution
- 53,000 sf facility opened in July 2017
- ISO 13485 and MDD certified by TÜV America in San Diego