INOVIO
POWERING DNA MEDICINES™

# Powering a New Decade of DNA Medicines

May 2020

Nasdaq:INO

# 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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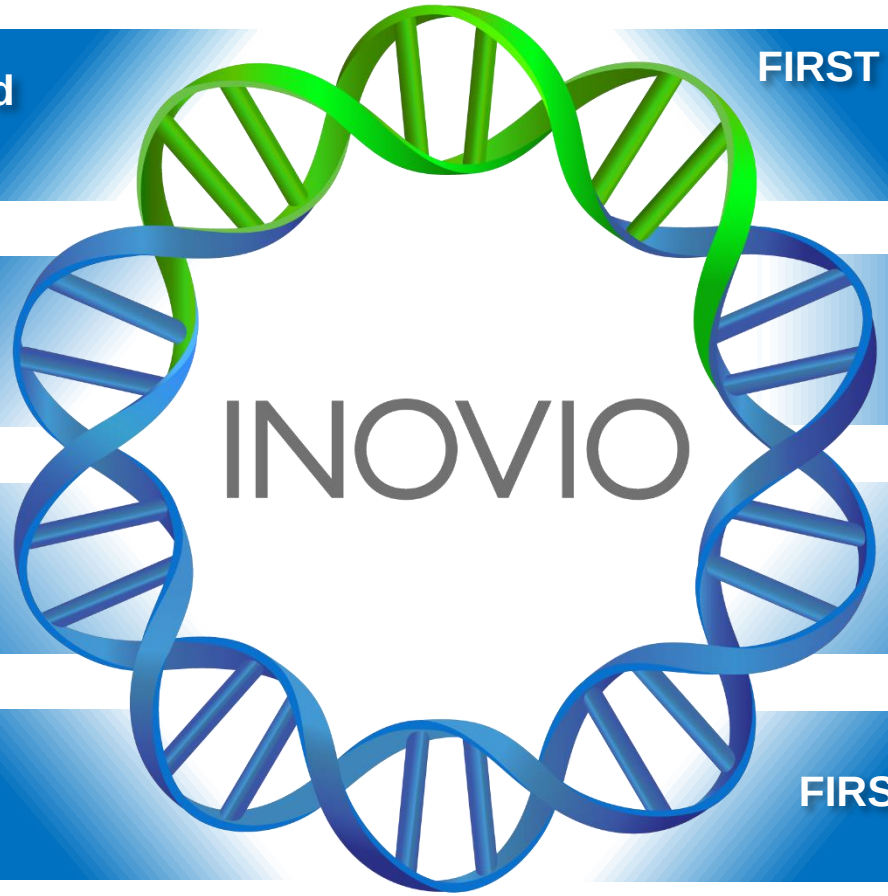
# Powering a New Decade of DNA Medicines

Precisely Designed Plasmids Delivered Through Proprietary Smart Device

Safe and Robust Immune Responses in More Than 2,000 Patients

*In Vivo* Immune Responses for "Off-the-Shelf" Speed, Efficiency

Extensive Patent Portfolio Protecting Technology Platform




FIRST DNA Medicine in Phase 3 Clinical Trials (VGX-3100) for Precancerous Cervical Dysplasia

FIRST to Show Clearance of High-Risk HPV 16/18 in Phase 2b Trial (VGX-3100)

FIRST to Show Complete Response in Phase 1 w/2 PD-1s for Head and Neck Cancer (MEDI0457)

FIRST dMAb® in Phase 1 for Zika (INO-A002)



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# INOVIO Vision to Build the Leading DNA Medicine Company

## Founding Vision

- Create **precisely designed plasmids** that **target antigens** to address **urgent medical needs**
- Develop **proprietary device** to **deliver plasmid safely** *in vivo* directly into the cell to produce **robust immune response**
- Build **scientific, medical, and commercial team** and **outstanding partnerships** to drive value

## Near-Term Execution

- **Rapidly bring to market precisely designed DNA medicines to potentially treat and prevent diseases associated with HPV, cancer, and infectious diseases**
- **Maximize value of lead candidates** worldwide

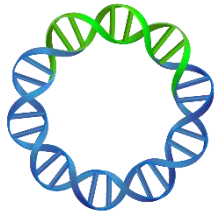
## Long-Term Strategy

- Create new market in safe, effective **DNA medicines**
- Aggressively **seek partners** to ensure **DNA medicines reach patients in need**
- **Strong financial position**
  - $270.0M cash/investments as of last reported earnings (3/31/20)
  - $121.7M net proceeds from new financing in 2Q20

# Vision Built on INOVIO Proprietary Technology

## OPTIMIZED PLASMID DESIGN AND DELIVERY TECHNOLOGY

### PRECISELY DESIGNED PLASMIDS (SynCon®)



### PROPRIETARY SMART DEVICE (CELLECTRA®)

### *IN VIVO*



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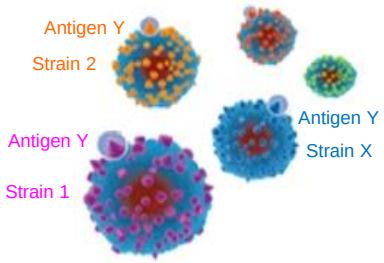
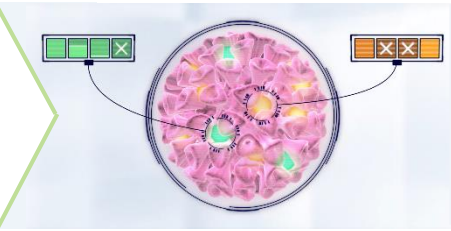
# INOVIO Technology – Powering Potent Antigen Specific Immune Responses

**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



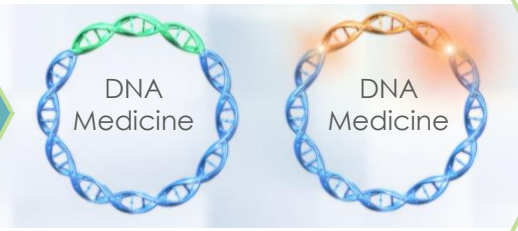

**2.** Assess gene sequence of selected antigen(s) from chosen strains/variants of the virus or cancer



**3.** Create optimal Consensus Sequence for the selected antigen

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

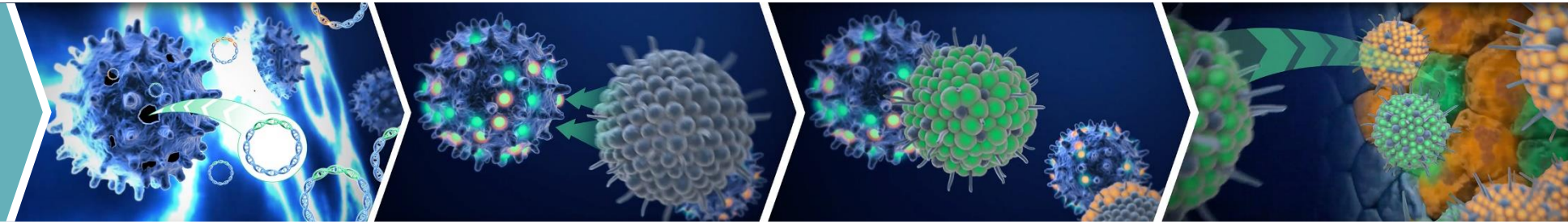
**4.** Insert SynCon sequence for each selected antigen into a separate precisely designed plasmid




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


IM ID

**6.** Protective antibodies and killer T cells produced by immune system against diverse strains of a virus or cancer





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# INOVIO's Technology Advantages

## Clinical Efficacy

- **Demonstrated clinical efficacy in Phase 2b study**
- **Lead candidate VGX-3100 in Phase 3 for cervical dysplasia**

## Safety

- **Favorable safety profile tested in over 2,000 patients in 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®
- **No anti-vector response** – allows for effective boosting

## Rapid and Scalable Manufacturing

- "Off-the-shelf" product; **no cold-chain storage issues** (room temp storage >1 yr.)
- Rapid development from concept to human in 7 months (Zika vaccine)
- Relatively inexpensive to manufacture; produce large quantities



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# INOVIO DNA Medicines Pipeline

| PRODUCT | INDICATION | ANTIGEN | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | PARTNER/COLLABORATOR/FUNDER |
|---|---|---|---|---|---|---|---|
| **HPV-TARGETED** | | | | | | | |
| VGX-3100 | Cervical HSIL | HPV 16 E6, E7/ HPV 18 E6, E7 | | | | | Apollobio (China only) |
| | Vulvar HSIL | | | | | | |
| | Anal HSIL | | | | | | |
| INO-3107 | Recurrent Respiratory Papillomatosis (RRP) | HPV 6 E6, E7/ HPV 11 E6, E7 | | | | | |
| MEDI0457 | Head & Neck Cancer | HPV 16 E6, E7/ HPV 18 E6, E7 | | | | | AstraZeneca |
| | Cervical, Anal, Penile, Vulvar Cancers | | | | | | |
| **IMMUNO-ONCOLOGY (NON HPV-ASSOCIATED)** | | | | | | | |
| INO-5401 | Glioblastoma Multiforme (GBM) | WT1, PSMA, hTERT | | | | | REGENERON |
| INO-5151 | Prostate Cancer | PSA, PSMA | | | | | Cancer Research Institute; Parker Institute for Cancer Immunotherapy |

INTERNALLY FUNDED  EXTERNALLY FUNDED



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# INOVIO DNA Medicines Pipeline (Continued)

| PRODUCT | INDICATION | ANTIGEN | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 | PARTNER/COLLABORATOR/FUNDER |
|---|---|---|---|---|---|---|---|
| **INFECTIOUS DISEASES (NON HPV-ASSOCIATED)** | | | | | | | |
| PENNVAX-GP | HIV | Gag, pol, env | | | | | NIH NIAID; HIV VACCINE TRIALS NETWORK |
| INO-4201 | Ebola | Glycoprotein | | | | | DARPA |
| INO-4700 (GLS-5300) | MERS | Spike | | | | | GEMINI; CEPI |
| INO-4600 (GLS-5700) | Zika | Glycoprotein | | | | | GEMINI |
| INO-4500 | Lassa Fever | Glycoprotein | | | | | CEPI |
| INO-4800 | COVID-19 (Coronavirus) | Spike | | | | | CEPI; BILL & MELINDA GATES foundation |
| **dMAb® (DNA-ENCODED MONOCLONAL ANTIBODIES)** | | | | | | | |
| INO-A002 | Zika | Glycoprotein | | | | | BILL & MELINDA GATES foundation |

INTERNALLY FUNDED  EXTERNALLY FUNDED

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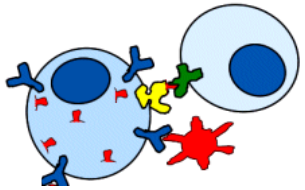
# Infectious Disease Programs

# Key characteristics of Inovio's DNA vaccine platform

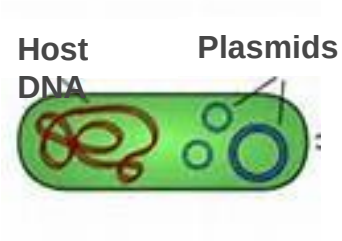
Refrigerated (2-8°C)
Storage >5 years

Robust Immune Responses
(T cell and B cell)



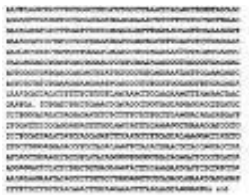
Multi-antigen Immunotherapy in Single Vial

Room Temp (25°C)
Storage >1 year;
37°C >2 months

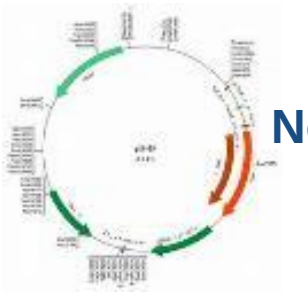




Non-replicating, Non-integrating

Rapid & Scalable Manufacture



SynCon® Rapid Design



No Anti-Vector Response (effective boosting)



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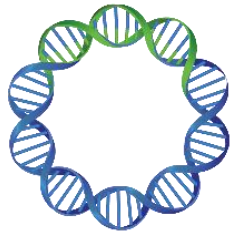
# Infectious Disease Platform:
# Positive Clinical Data and Partnering Opportunities



| Product | Indication | Data Reported (to date) | Partner/s | Next Milestone |
|---|---|---|---|---|
| **PENNVAX-GP** | **HIV** | • Phase 1: **93% (71 of 76)** evaluable vaccinated participants showed a CD4+ or CD8+ cellular immune response to at least one of the vaccine antigens<br>• **94% (62 of 66)** demonstrated an env specific antibody response | NIH NIAID<br>HIV VACCINE TRIALS NETWORK | Interim results from Phase 1/2 HIV trial study 2020 (UCSF; Deeks) |
| **INO-4201** | **Ebola** | • Phase 1: High levels of binding antibodies measured (ELISA) in **95% (170 of 179)** of evaluated subjects<br>• ***Published: The Journal of Infectious Diseases, March 2019*** | DARPA | Seeking additional grant funding for Phase 2 development |
| **INO-4700 (GLS-5300)** | **MERS** | • Phase 1: High levels of binding and neutralizing antibodies in >**90% of subjects**<br>• **98%** generated an antibody and/or T cell response against MERS | GeneOne Life Science 진원생명과학(주)<br>CEPI | Publish Phase1 data – *Lancet ID* 2019<br>Presentation at ASGCT 2020 |
| **INO-4600 (GLS-5700)** | **Zika** | • Phase 1: High levels of binding antibodies measured (ELISA) in **100% (39 of 39)** of evaluated subjects<br>• ***Published: New England Journal of Medicine, October 2017*** | GeneOne Life Science 진원생명과학(주) | Report on Puerto Rico study 2020<br>INOVIO POWERING DNA MEDICINES |

# INOVIO's COVID-19 DNA Vaccine INO-4800 Development Timeline

**DECEMBER 31, 2019**

INOVIO coronavirus experts learn about a novel coronavirus (SARS-CoV-2) which caused an outbreak of respiratory disease in Wuhan, China, now referred to as **COVID-19**

**JANUARY 10/11, 2020**

Chinese researchers share the genetic sequence of the novel coronavirus on 1/10

INOVIO designs **DNA vaccine INO-4800 in three hours** after receiving the genetic sequence late in the evening on 1/10 using its proprietary **DNA medicines platform technology**

INO-4800 was designed to precisely match the DNA sequence of the virus just after midnight on 1/11

**JANUARY 10 - JANUARY 23, 2020**

INOVIO coronavirus experts race to **manufacture INO-4800 and begin preclinical testing**

**JANUARY 23, 2020**

INOVIO receives a grant of up to **$9 million from the Coalition for Epidemic Preparedness Innovations (CEPI)** to fund ongoing preclinical and initial clinical development of INO-4800

CEPI

**JANUARY 23 - FEBRUARY 29, 2020**

**Preclinical testing continues, with immune responses generated in animal models;** initial preclinical **data submitted to peer-reviewed journal**; human clinical trial designs developed and shared with regulators

**MARCH 2020**

Ongoing preclinical studies, including challenge studies; initial preclinical data **"under consideration"** at peer-reviewed journal; **human clinical trial designs finalized; 3,000 human trial doses prepared for clinical trials in the U.S., China, and South Korea**; large-scale manufacturing plans developed

**MARCH 12, 2020**

INOVIO announces **$5 million grant from the Bill & Melinda Gates Foundation** to continue advancing the development of INO-4800, specifically to accelerate the testing and scale up of INOVIO's proprietary smart device CELLECTRA® 3PSP

BILL & MELINDA GATES foundation

**MARCH 26, 2020**

INOVIO announces the **Department of Defense (DOD)** awarded Ology Bioservices an **$11.9 million** contract to work with INOVIO on DNA technology transfer to rapidly manufacture INO-4800 for the DOD for upcoming clinical trials

**APRIL 6, 2020**

**INOVIO announces initiation of Phase 1 human clinical trial in the U.S. following authorization by the U.S. Food and Drug Administration of its Investigational New Drug (IND) application**

**U.S. study enrolled 40 healthy volunteers; study sites are the University of Pennsylvania and a clinic in Kansas City, MO**

**SPRING - SUMMER 2020**

**U.S. Phase 1 study initial immune responses and safety data** expected by late June; Phase 2/3 trial to follow*

**Human clinical trials expected to begin in China and South Korea**;* CEPI provides $6.9 million to INOVIO and International Vaccine Institute for Phase 1/2 study in South Korea with 160 participants

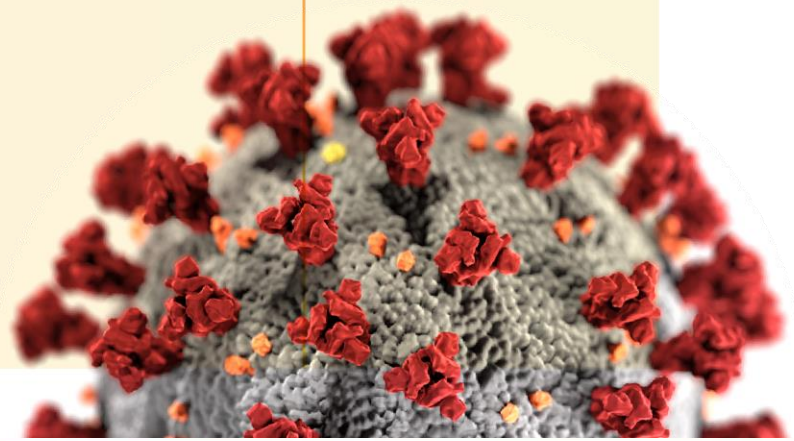
**FALL 2020**

**Human clinical trial results presented/ published**

**END OF 2020**

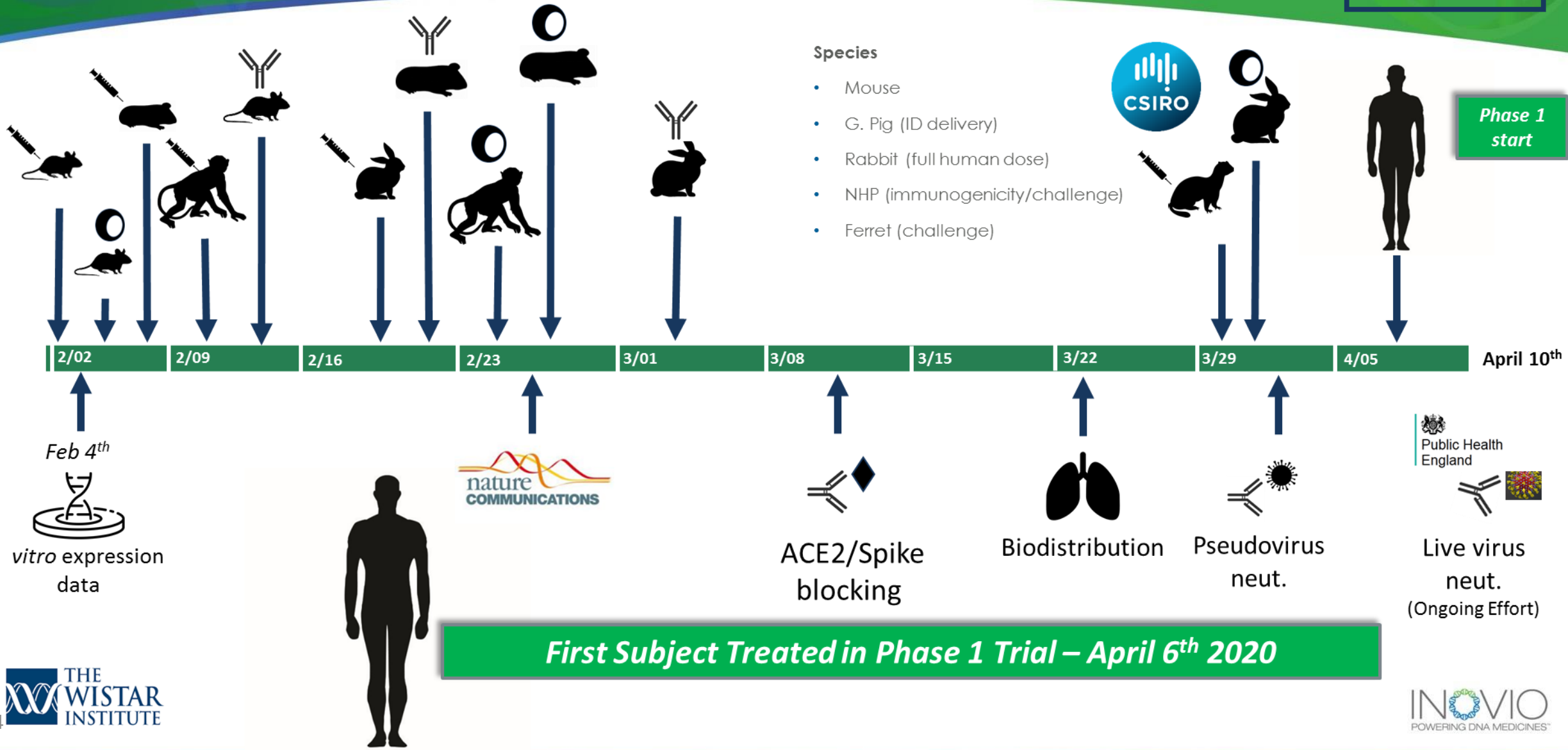
**1 million doses of INO-4800 COVID-19 DNA vaccine** planned for production*

Preclinical studies, including challenge studies, continue



*Pending appropriate regulatory guidance and external funding

# INO-4800 Rapid Response



# Clinical Development Strategy for INO-4800

## ❑ US – Phase 1 study of INO-4800 under US IND

- Initial funding of up to $9M awarded by CEPI
- Rapid start of FIH study in young, healthy population
- Preliminary safety and immune response data by late June

## ❑ Ex-US Studies in China and Korea

- Collaborations formed between INOVIO and Advaccine in China, as well as IVI in Korea to build global consortium for joint clinical development
- $7.3 million from CEPI to support the Korea Phase 1/2a trial expected to start in June 2020
- A Phase 1 study in China planned to start in June 2020

## ❑ Phase 2/3 Efficacy Study

- Study protocol being developed to assess the efficacy for prevention of COVID-19 in healthcare workers
- Ongoing preparation to start the study in July/August pending regulatory approval

# Inovio-Led Global Coalition to Advance INO-4800











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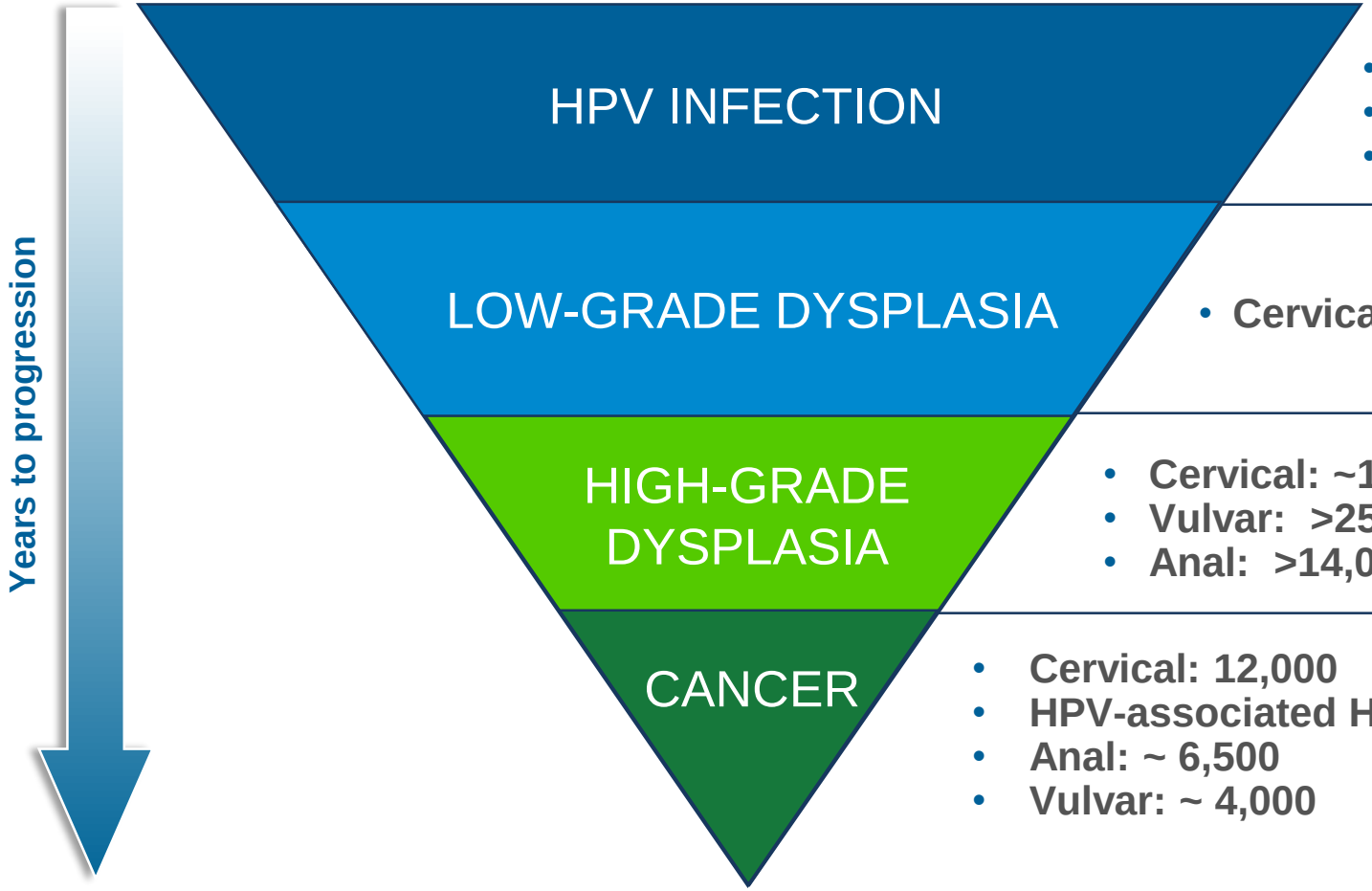
# HPV-Related Programs

# HPV-Associated Diseases Market Overview

## HPV-associated conditions per year in US:




- 80M Americans currently infected with HPV
- 14M new infections annually
- ~7M high-risk HPV infections (HPV 16/18)

- Cervical: 1.1M to 1.7M

- Cervical: ~195,000
- Vulvar: >25,000
- Anal: >14,000

- Cervical: 12,000
- HPV-associated H&N: 18,000
- Anal: ~ 6,500
- Vulvar: ~ 4,000

**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, Altekruse 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.



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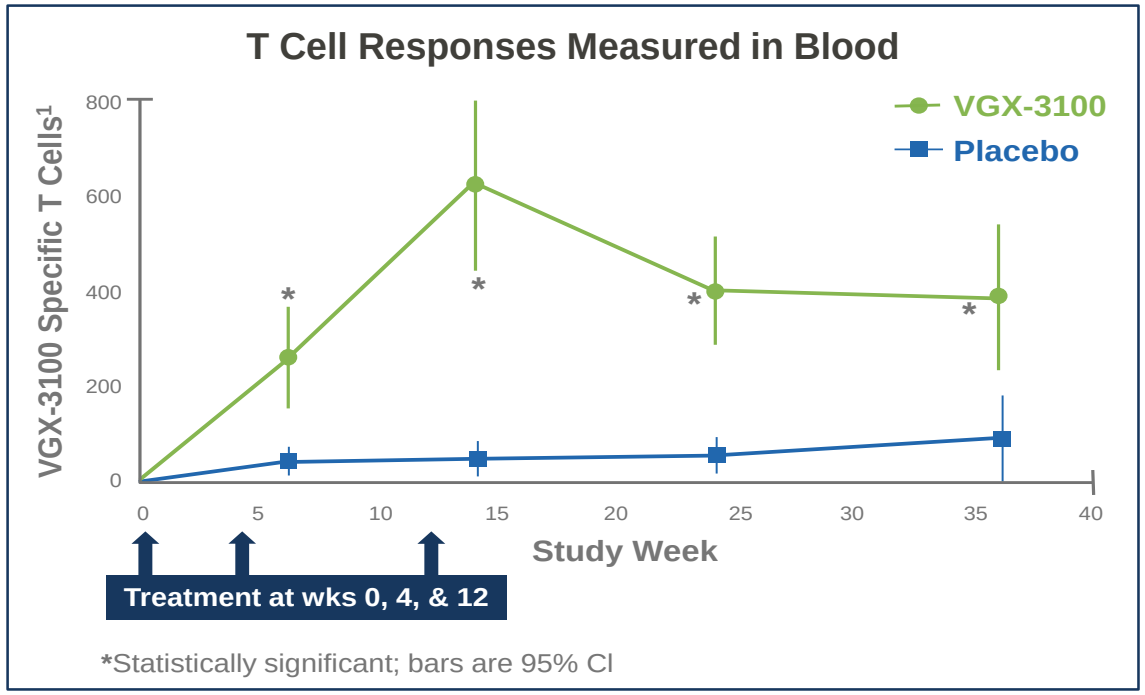
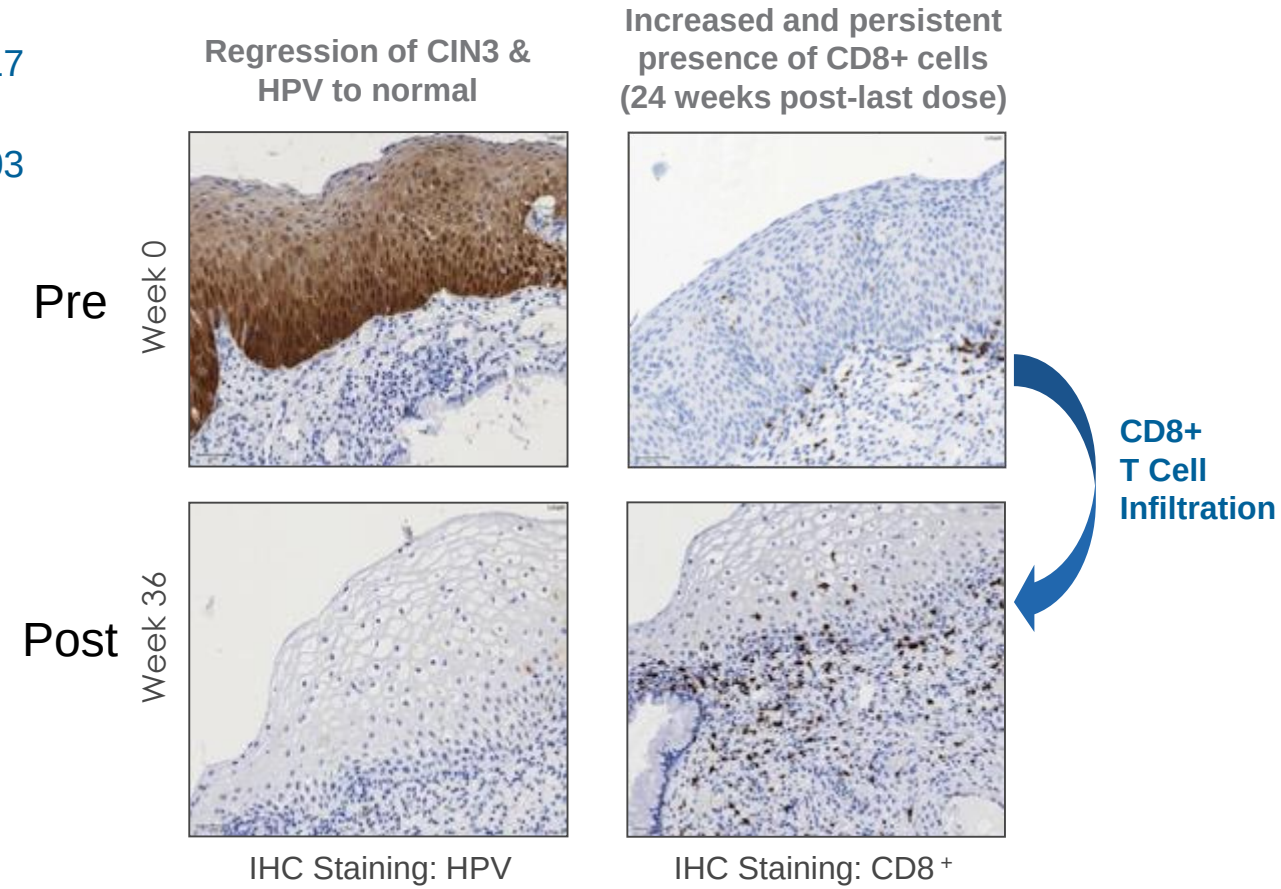
# Published VGX-3100 Phase 2b Study Achieves All Primary and Secondary Endpoints

## Phase 2b Endpoints (n=167)

| | | | |
|---|---|---|---|
| **Primary:** | Regression to CIN1 or Normal | **49.5%** | P=0.017 |
| **Secondary:** | Regression to Normal AND Virological Clearance | **40.2%** | P=0.003 |




Trimble et al. Lancet 2015

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

## TRIAL: VGX-3100

- Targets HPV 16/18 subtypes; E6/E7 oncogenes
- Treats 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 by 4Q 2020

**REVEAL2 (confirmatory) n=198 – Now Enrolling**

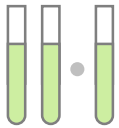
Study follow-up through week 40

**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)



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# 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)

## Precancerous Vulvar Dysplasia:

Phase 2
open-label study

x33

33 women enrolled
Interim data reported for 10

**Interim findings**
(6 months after start of treatment)

- Decrease in lesion area: 80% of patients
- Resolution of vulvar dysplasia: 20% of patients
- Non-detectability of HPV 16/18: 20% of patients

## Precancerous Anal Dysplasia:

Phase 2
open-label study

x23

23 patients enrolled
Interim data reported for 20

**Interim findings**
(6 months after start of treatment)

- Clearance of lesions: 50% of patients
- Decrease in number of lesions: 75% of patients



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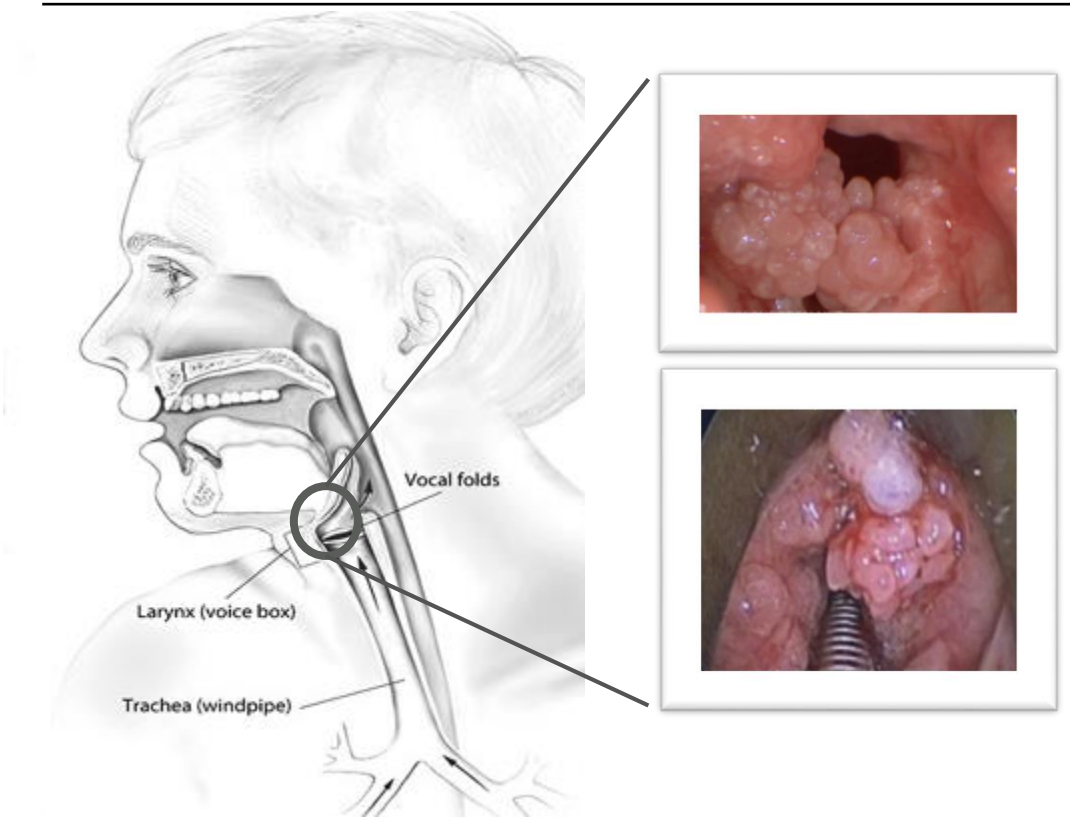
# INOVIO and QIAGEN Developing Biomarker to Optimize Patient Selection

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

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

**Areas affected by Recurrent Respiratory Papillomatosis (RRP)**




- 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.**
- HPV-associated disease; **caused by HPV 6 and 11**
- Growths can lead to life-threatening airway obstructions
- **SoC is lifelong surgery (repeated/multiple times a 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

**Sources:** RRP Foundation; Venkatesan et al. Otolaryngol Clin North Am 2013; Ivancic et al. Laryngoscope Investigative Otolaryngol; www.nidcd.nih.gov/health/recurrent-respiratory-papillomatosis; Derkay et al *Arch Otolaryngol Head Neck Surg* (1995); Armstrong et al *Arch Otolarygol Head Neck Surg* (1999); Marsico et al STDs (2014).



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# INO-3106 Pilot Study in RRP – Completed

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

Phase 1 pilot, single-site, clinical study

x2

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**

Planning potential registrational study of INO-3107 (for both HPV 6 and 11) by 1H 2020

**Published in *Vaccines* (MDPI);** entitled "Immune Therapy Targeting E6/E7 Oncogenes of Human Papillomavirus Type 6 (HPV-6) Reduces or Eliminates the Need for Surgical Intervention in the Treatment of HPV-6 Associated Recurrent Respiratory Papillomatosis"; January 23, 2020.



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# INO-3107 Phase 1/2 Study in RRP – IND Accepted

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

Phase 1/2 open-label, multicenter clinical study

x63

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

# 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**

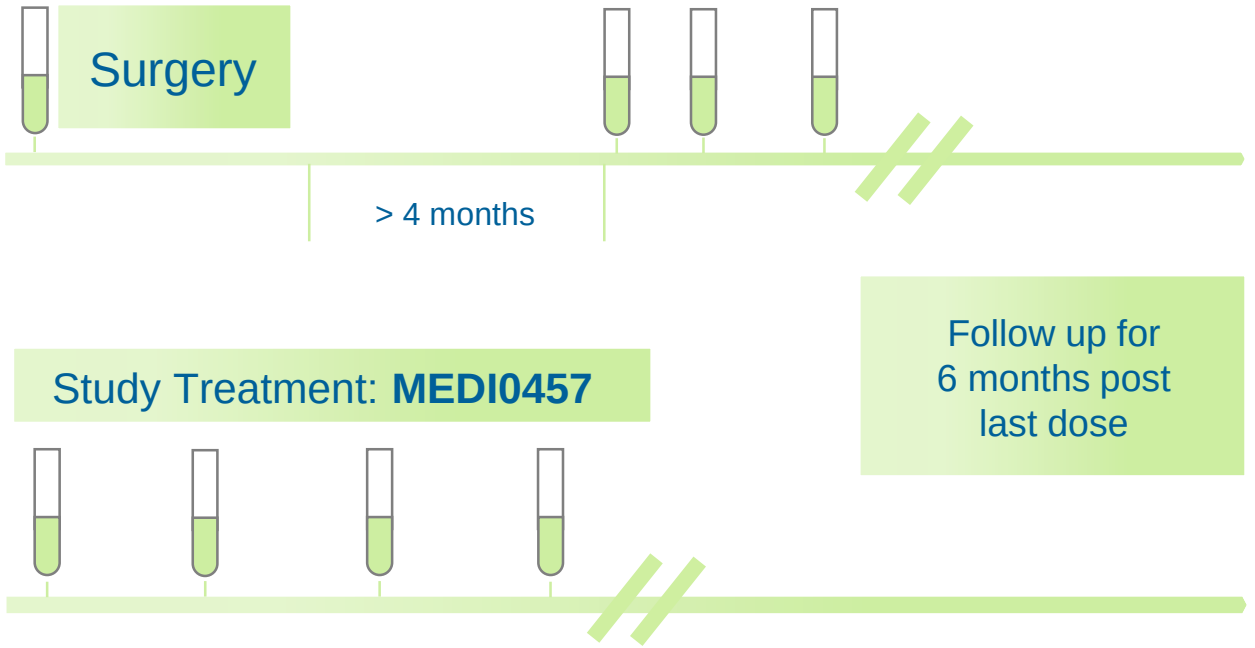
# MEDI0457 Potential to Treat Head and Neck Cancer Demonstrated in Phase 1 Trial

**Cohort 1**
HPV 16/18+ HNSCC undergoing definitive surgery (n=5)

Immunotherapy is administered before and after surgery

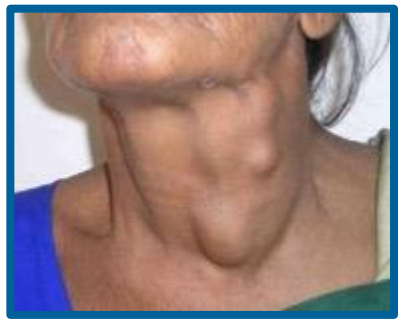
**Cohort 2**
HPV 16/18+ HNSCC undergoing definitive/adj chemoradiation (n=20)

Immunotherapy is administered 2 months after completion of chemoradiation




**MEDI0457:** 6 mg of **VGX-3100** + 1 mg of **INO-9012**

In Cohort 1, if time allows, up to 2 treatments can be administrated prior to surgery, but total 4 treatments are scheduled



**Primary:** Safety and tolerability of DNA based immunotherapy

**Secondary:** Cellular and humoral immune responses

**Exploratory:** Anti-tumor response and progression free survival



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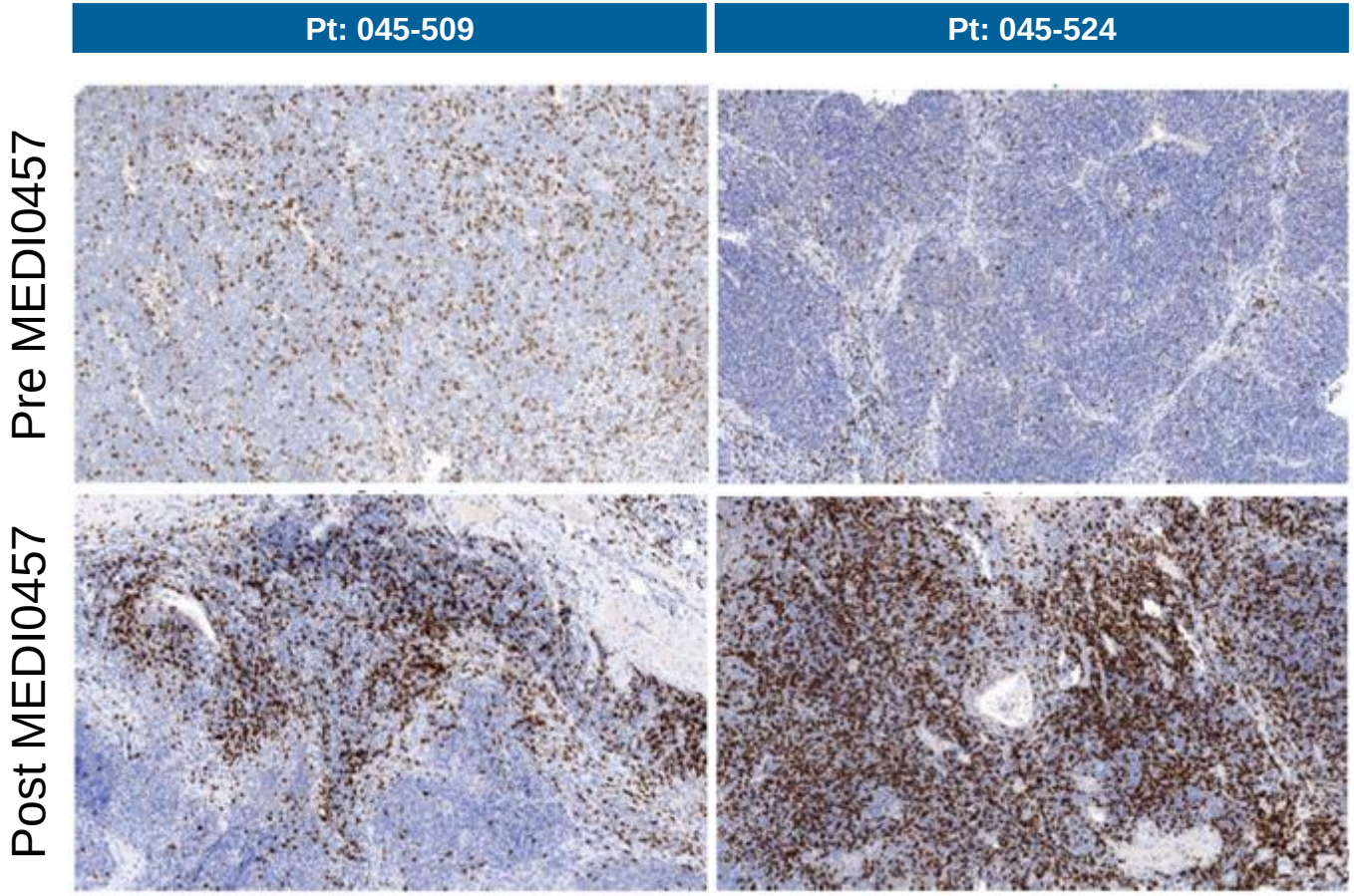
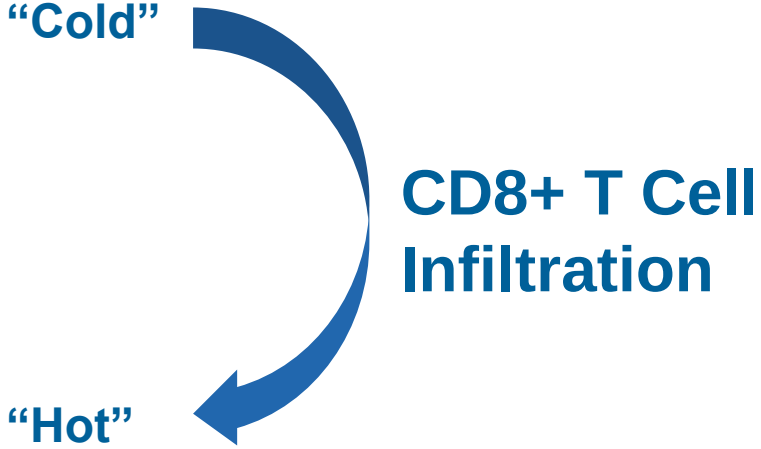
# CD8+ T Cell Infiltration into Tumor Following MEDI0457 Treatment




Robust antigen-specific CD8+ killer T cell responses observed in 20/22 – 90.1% – of patients (both tumor tissue and peripheral blood)

*Aggarwal et al Clinical Cancer Research 2018*



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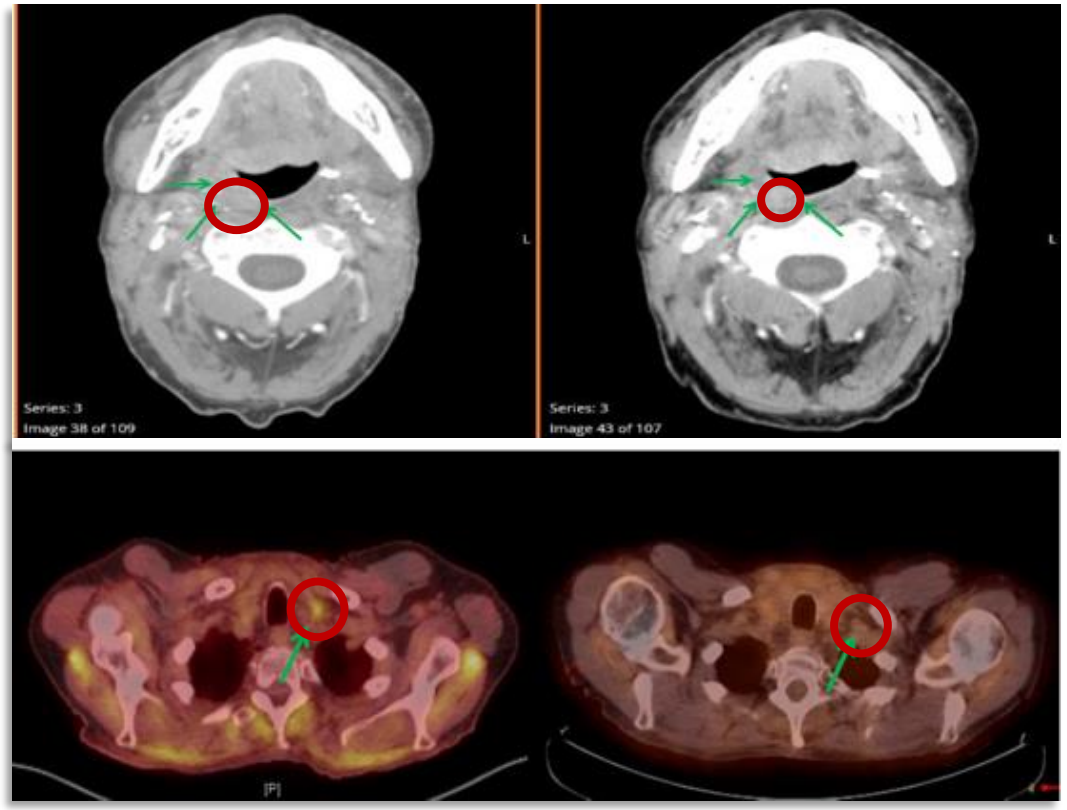
# MEDI0457 Phase 1 Study Demonstrates Complete Response




- (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)



*Published in Clinical Cancer Research (CCR) 2018*

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# MEDI0457 for HPV-Associated Head & Neck Cancer in Phase 1b/2a in Partnership with AstraZeneca

TRIAL: **MEDI0457** (VGX-3100 + IL-12) AstraZeneca

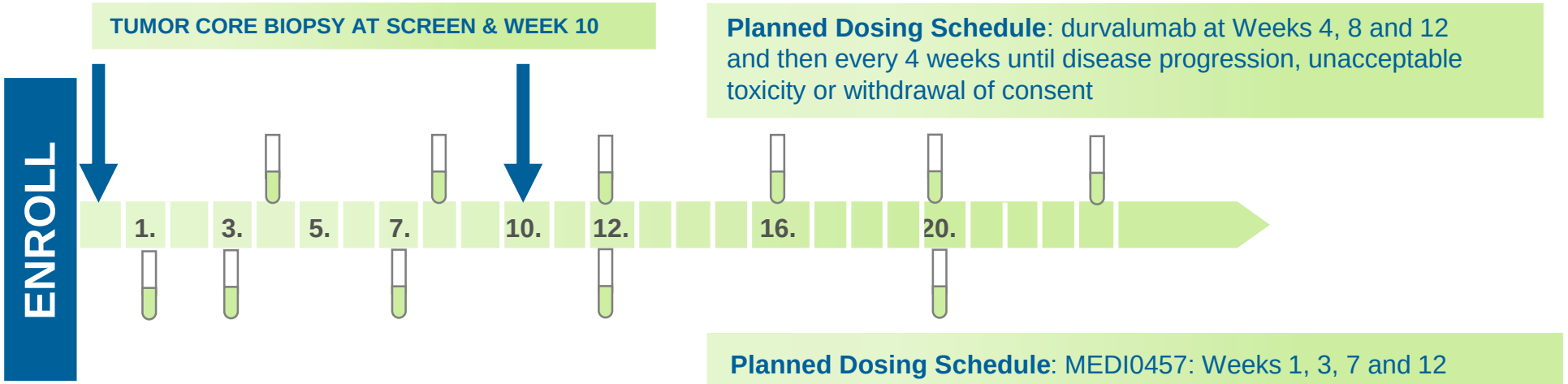
Phase 1b/2a open label study for **metastatic HPV+ HNSCC** with persistent or recurrent disease after chemotherapy treatment

Combination with AstraZeneca's PD-L1 checkpoint inhibitor (durvalumab)

**Primary Endpoints:**
Safety, tolerability
**Secondary Endpoints**:
Immunogenicity, ORR, PFS, Disease CR, OS

x35

Completed enrollment of 35 subjects in August 2019




**Planned Dosing Schedule**: durvalumab at Weeks 4, 8 and 12 and then every 4 weeks until disease progression, unacceptable toxicity or withdrawal of consent

**Planned Dosing Schedule**: MEDI0457: Weeks 1, 3, 7 and 12 and then every 8 weeks until disease progression, unacceptable toxicity or withdrawal of consent



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# Immuno-Oncology Programs
## (Non-HPV Associated)

# 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)

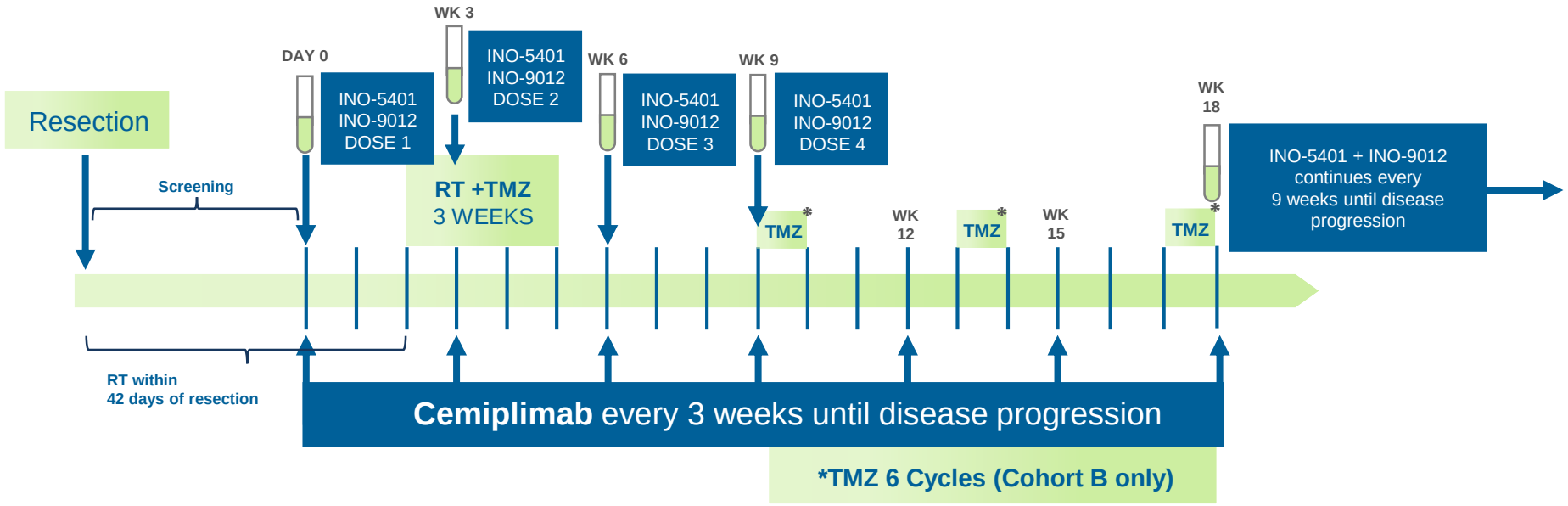
Phase 1b/2 open label study for **newly diagnosed glioblastoma (GBM)**

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

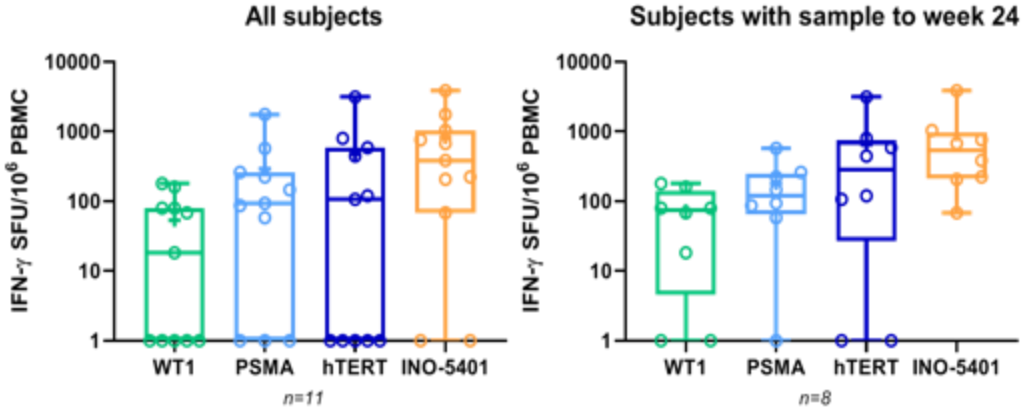
x20
**Cohort B:**
MGMT Promoter Methylated:
20 patients

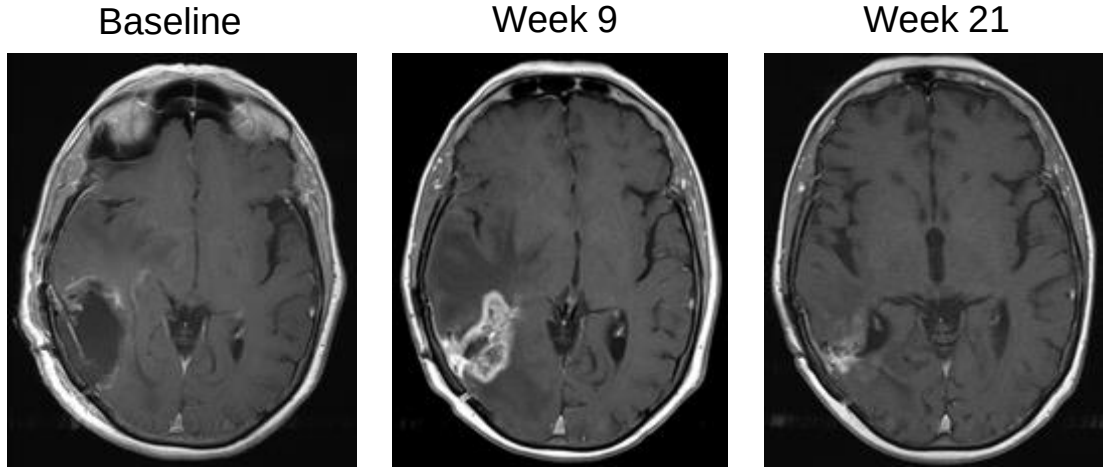


# INO-5401 Results: Promising 12-Month Overall Survival Data and 6-Month Progression-Free Survival Data; OS18 Data in 4Q2020

- **Overall survival at 12 months** (OS12) to be presented at ASCO 2020 Annual Meeting
  - **MGMT Promoter Unmethylated OS12 of 84.4%**
  - **MGMT Promoter Methylated OS12 of 85%**
  - **Compares favorably with historical value of 65%**
- Previously reported PFS6 at SITC 2019
  - MGMT Promoter Unmethylated PFS6 of 75%
  - MGMT Promoter Methylated PFS6 of 80%
  - Compares favorably with historical value of 40-60%
- **Majority of patients tested had a T cell immune response to one or more tumor-associated antigens encoded by INO-5401**
- **Combination of INO-5401 + INO-9012 with cemiplimab, with radiation and temozolomide, is promising**
- **Overall survival results (OS18) will be presented 4Q 2020**

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



Stupp et al. N Eng J Med 2005; Hegi et al. N Eng J Med 2005; Stupp et al. N Eng J Med 2009

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# 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**

x45

Three cohort, 45-patient platform study, **INO-5401 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

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CANCER RESEARCH INSTITUTE



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# 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 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



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# Strong Balance Sheet to Support Critical Milestones

NASDAQ:INO

**$270.0M**
Cash and short-term investments

**As of March 31, 2020**

**$121.7M**
Net proceeds from new financing in 2Q20

**158M**
Common stock shares outstanding

**As of May 12, 2020**

## Milestones

**VGX-3100**

- ✓ 1Q20: Report interim data from Phase 2 VIN/AIN clinical trials
- ❑ 4Q20: REVEAL 1 Phase 3 top-line efficacy & safety data
- ❑ 2H20: Report full data from Phase 2 VIN/AIN clinical trials

**MEDI0457**

- ❑ 2H20: Potential presentation from AZ on MEDI0457 Phase 2 study in HNSCC

**INO-3107**

- ✓ 1H20: Initiate Phase 1/2 trial of INO-3107 for RRP (HPV6 and 11)

**INO-5401**

- ✓ 2Q20: OS12 data from Phase 1/2 GBM clinical trial (INO-5401 plus Libtayo®)
- ❑ 4Q20: OS18 data from Phase 1/2 GBM clinical trial (INO-5401 plus Libtayo®)

**Platform Development**

- ✓ April 2020: Initiate Phase 1 trial of INO-4800 for COVID-19
- ❑ 2H20: Initiate Phase 2/3 trial of INO-4800 for COVID-19
- ❑ 2020: Advance INO-4700 against MERS into Phase 2 field study in Middle East & Africa (CEPI-funded)
- ❑ 2020: Interim Phase 1 results from first-in-human trial of dMAb candidate INO-A002 (for preventing or treating Zika virus infection)



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# INOVIO DNA Medicine Value Proposition



- **Validated Technology Platform**
  - Demonstrated **Phase 2b clinical efficacy** of lead asset VGX-3100
  - **Over 2,000 patients safety data** and consistent demonstration of high levels of T cell and antibody immune responses
  - Well-protected with over **1,000 issued and pending patents**
- **Over $210M in non-dilutive funding since 2009**
- **Partnerships with major pharma and organizations:**

CEPI · Bill & Melinda Gates Foundation · Parker Institute for Cancer Immunotherapy · AstraZeneca · Regeneron · DARPA · Department of Defense · NIH

- **Multiple catalysts in 2020**
  - VGX-3100 Phase 3 cervical precancer topline data readout
  - INO-5401 Phase 2 GBM OS18 data
  - INO-4800 Phase 1 COVID-19 safety/immunogenicity data

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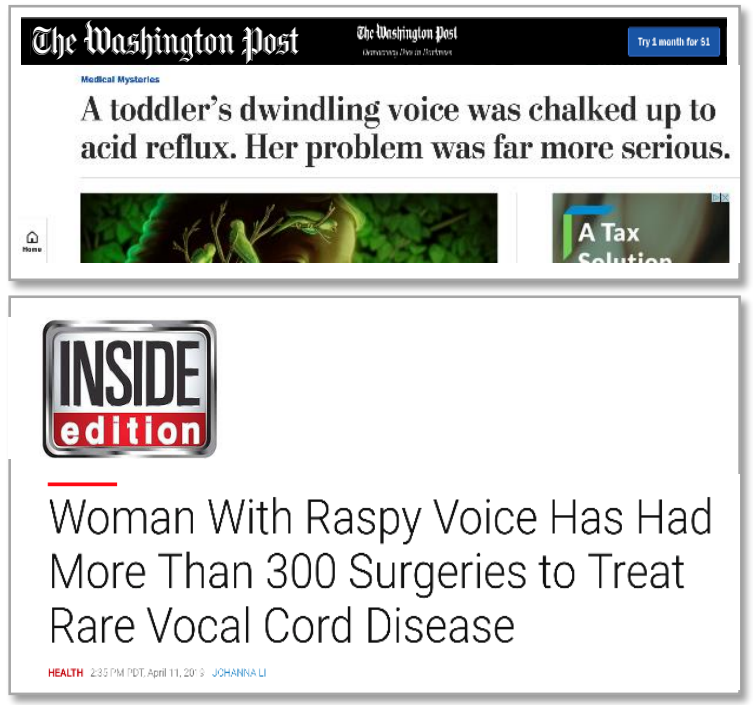
# Appendix

# INOVIO DNA Medicines Will Meet Urgent Health Needs Worldwide

## HPV-Related Diseases

- **Nearly 80M** Americans are currently **infected with HPV; ~14M become infected each year**
- **~35k** Americans get an **HPV-attributable cancer per year**, including **head and neck** and **cervical, anal, penile and vulvar cancers**
- **~23% of Americans** age18-59 have genital infections with **≥1 high-risk HPV** genotype (e.g., HPV 16, HPV 18), which can lead to cervical, anal, head and neck, and other cancers; **no current medicine to destroy/clear the virus**
    - **~4% of Americans** age 18-69 have oral infection with **≥1 high-risk HPV** genotype
- Other **HPV genotypes (6/11)** can cause debilitating conditions such as **Recurrent Respiratory Papillomatosis (RRP)**, **rare** and **potentially life-threatening in children and adults;** only current treatment is **multiple, lifelong surgeries**

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# INOVIO DNA Medicines Will Meet Urgent Health Needs Worldwide
(continued)

## Cancer (non-HPV associated)

- >11,000 people in U.S. get **glioblastoma (GBM, rare** and **most aggressive** form of brain cancer) each year; 23,000 people in U.S. have GBM

***REGENERON***

- ~3.1M men in U.S. have **prostate cancer,** the **most common** cancer among men except for skin cancer

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## Infectious Diseases (non-HPV associated)

- HIV — NIH NIAID; HIV VACCINE TRIALS NETWORK
- Ebola — DARPA
- MERS — GeneOne Life Science; CEPI
- Zika — GeneOne Life Science; BILL & MELINDA GATES foundation
- Lassa Fever — CEPI
- COVID-19 — CEPI; BILL & MELINDA GATES foundation



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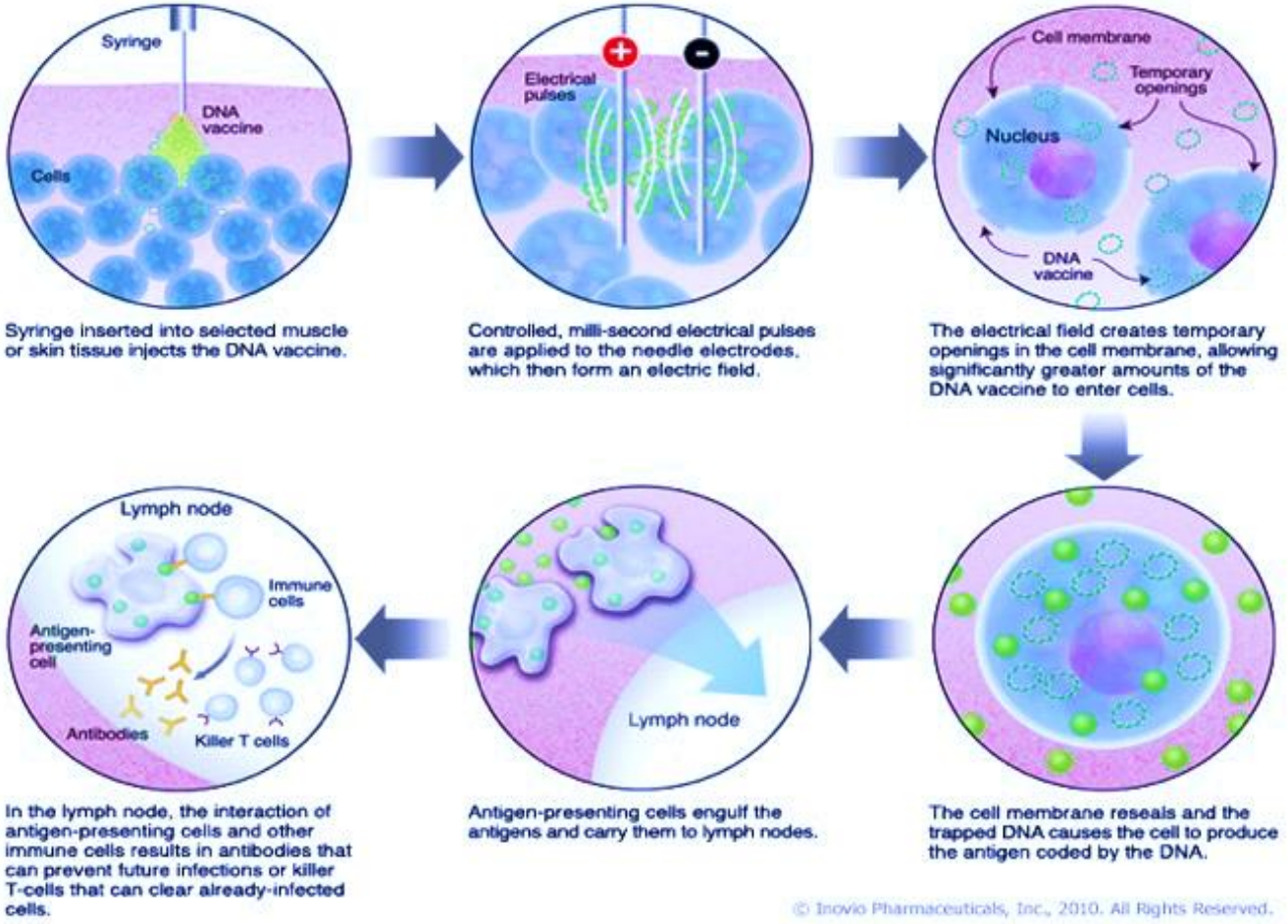
# INOVIO's Technology Delivering Precisely Designed Plasmids with Proprietary Smart Devices

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







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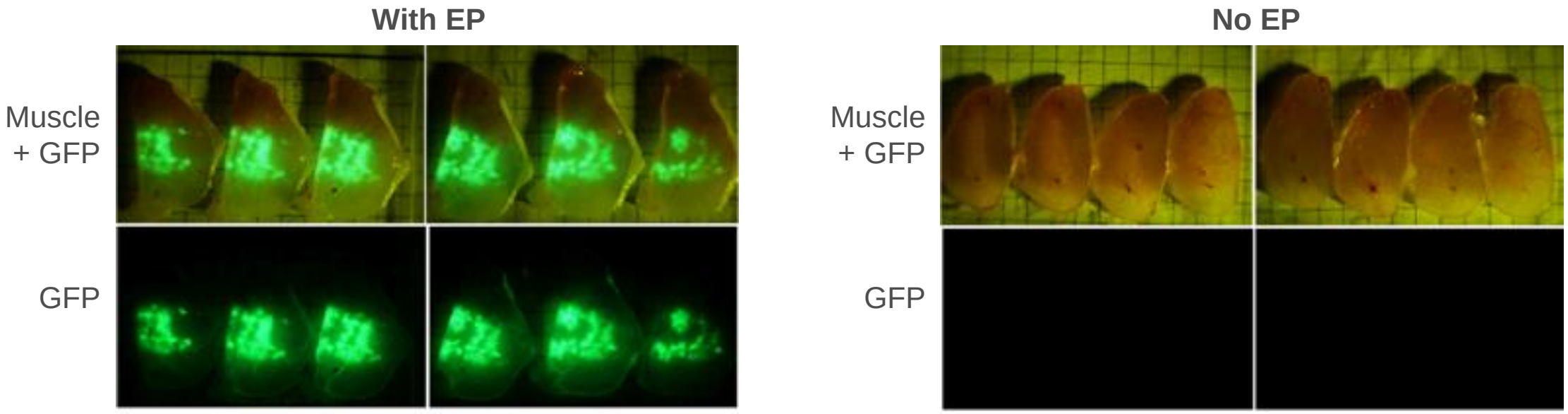
# Precise Design + Intracellular Delivery = Improved Immune Responses




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



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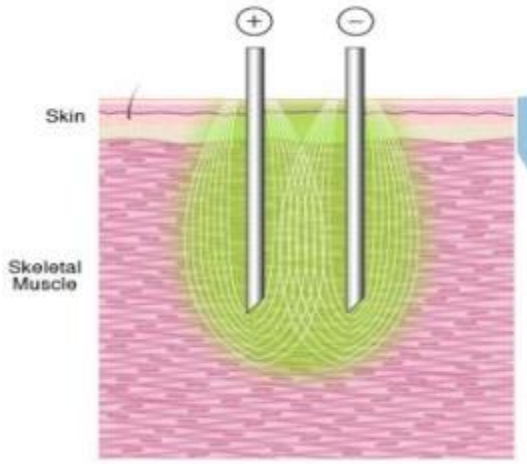
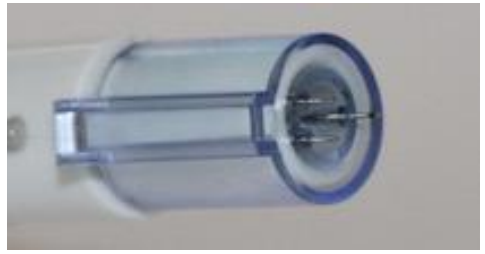
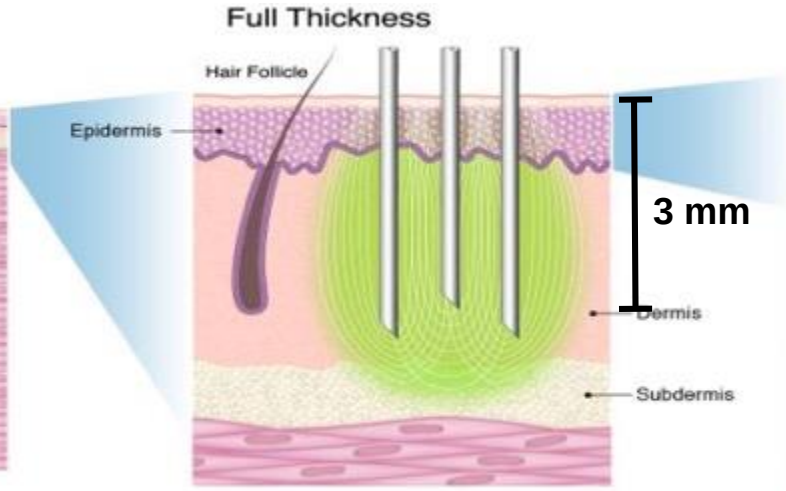
# Innovation in the Delivery of SynCon® DNA Medicine

### CELLECTRA®-5PSP
- Intramuscular
- 13, 19, 25mm electrodes
- In clinical use

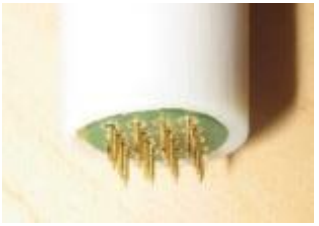


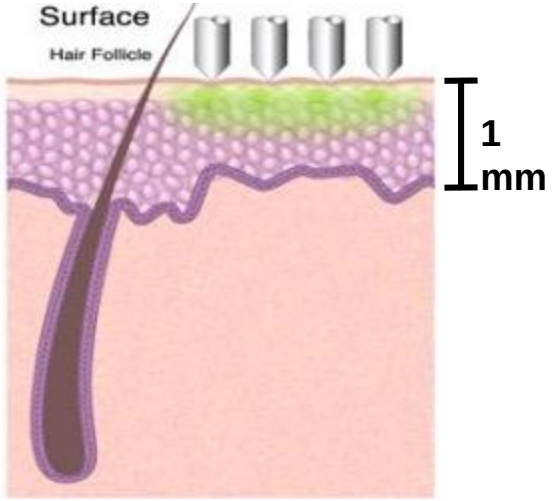

### CELLECTRA®-3P
- Intradermal – minimally invasive
- 3mm electrodes
- In clinical use






### Surface EP (SEP)
- Surface
- Noninvasive
- 4x4 electrode array
- Specifically targets epidermis
- In late-stage preclinical development





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# CELLECTRA® Platform

**CELLECTRA-5PSP**
**Intramuscular EP**

**CELLECTRA-3P**
**Intradermal EP**

**CELLECTRA-3P technology**
**in a hand-held portable device**

## CELLECTRA® 2000 EP Technology – Track record of success in the clinic

- >2000 human subjects and >6000 doses
- CELLECTRA® 5PSP device developed to support Phase 3 and commercial launch
- Phase 2 efficacy data combining DNA vaccine and EP
- Global – Regulatory approval for studies in 6 continents (including Central & Sub-Saharan Africa); both devices CE marked in Europe



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# CELLECTRA® 5PSP – INOVIO's First Commercial Smart Device

## CELLECTRA® 5PSP

- World's first commercial smart device for DNA medicine – CE Marking in Europe
- Proprietary smart device currently used in Phase 3 trials
- Simplified interaction and automated injection using prefilled cartridge
- Disposable single use array which includes used drug cartridge
- Touch screen interface, automated sensors and trigger start
- Records data file for post-treatment review
- Data files can be downloaded from system and uploaded to web-based interface
- Several rounds of Usability Testing that refined development





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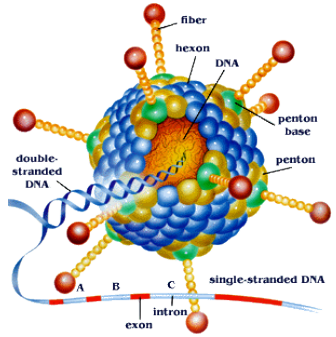
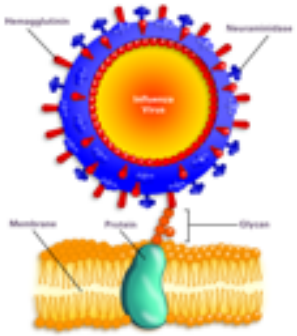
# Limitations of Other Approaches

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

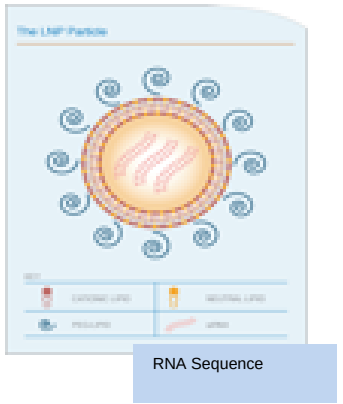
- Systemic delivery/local injection
- Preexisting or induced immunity is an issue
- Biologic variability of take
- Immune bias tuned by vector
- Hard to re-administer/tissue tropism limits and positives



## 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



RNA Sequence



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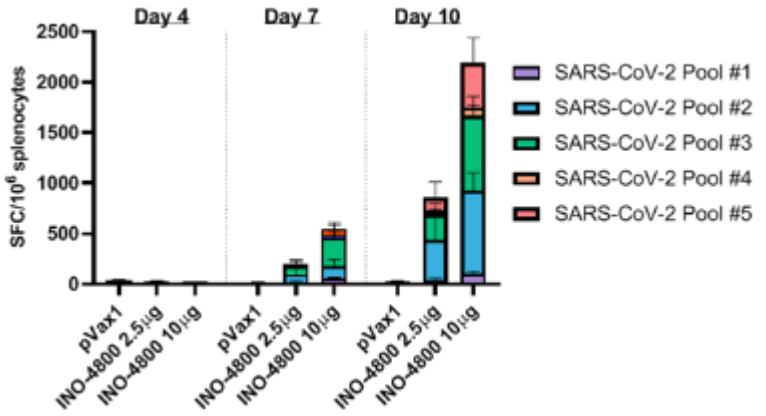
# Robust Cellular and Humoral Immune Responses Measured After Immunization with INO-4800 in Mice and Guinea Pigs

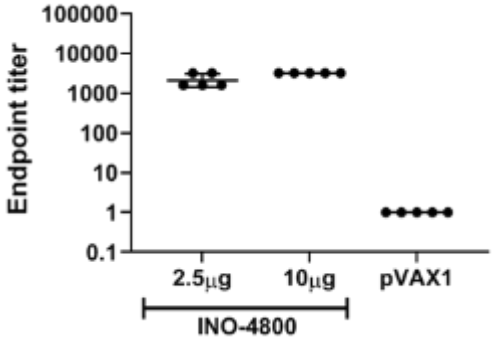
nature COMMUNICATIONS

Single dose


IFN-γ+ T cells



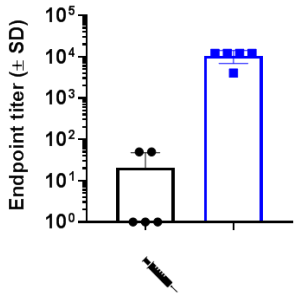

SARS-CoV-2 S protein (RBD) serum IgG binding



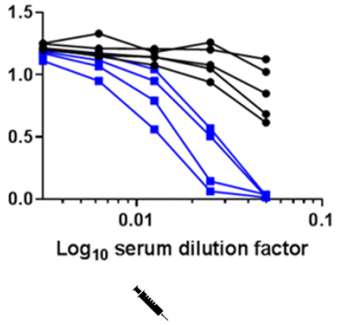


ID CELLECTRA®
delivery

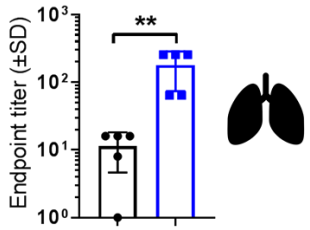
SARS-CoV-2 Spike binding



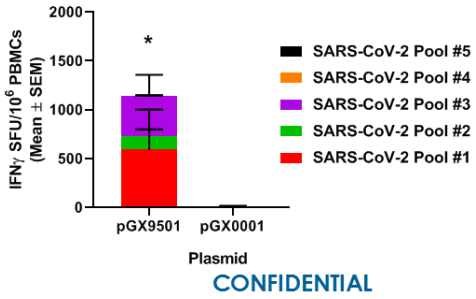

ACE2/Spike blocking



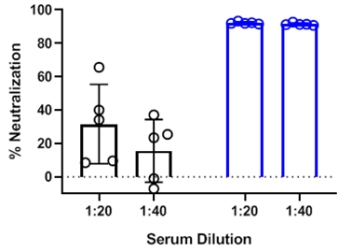

IgG biodistribution




IFN-γ+ T cell ELISpot




Pseudovirus neut.





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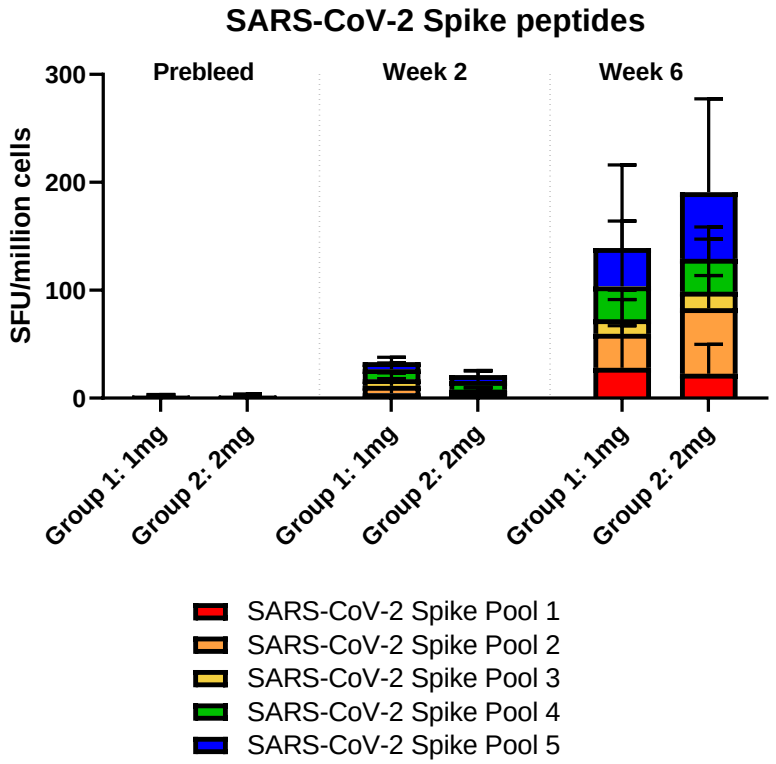
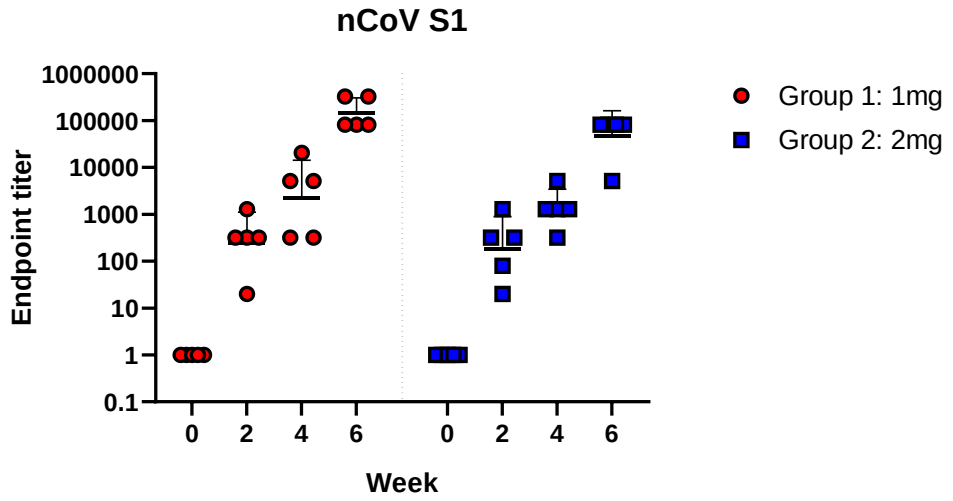
# Robust Cellular and Humoral Immune Responses following Immunization of INO-4800 in Rhesus Monkeys

**Animal:** Rhesus macaque

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

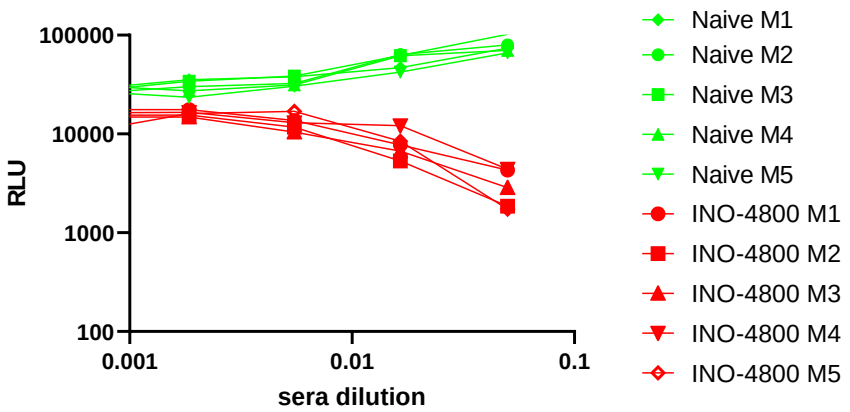
| Group | Vaccine | Delivery | Dose per immunization | n |
|---|---|---|---|---|
| 1 | pGX9501 | ID, 1 site | 1 mg | 5 |
| 2 | pGX9501 | ID, 2 sites | 2 mg | 5 |




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

# Detection of Neutralizing Antibodies




Public Health England

| Group | PRNT result (ND50) |
|---|---|
| pVAX | <1:10, 1:25, 1:20, 1:21, 1:14 |
| **INO-4800** | **>1:320, >1:320, >1:320, >1:320, >1:320** |

***Critical neutralizing antibodies detected in mice and guinea pig (NHP samples being tested) in both a pseudo and live viral neut assay***



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# 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)

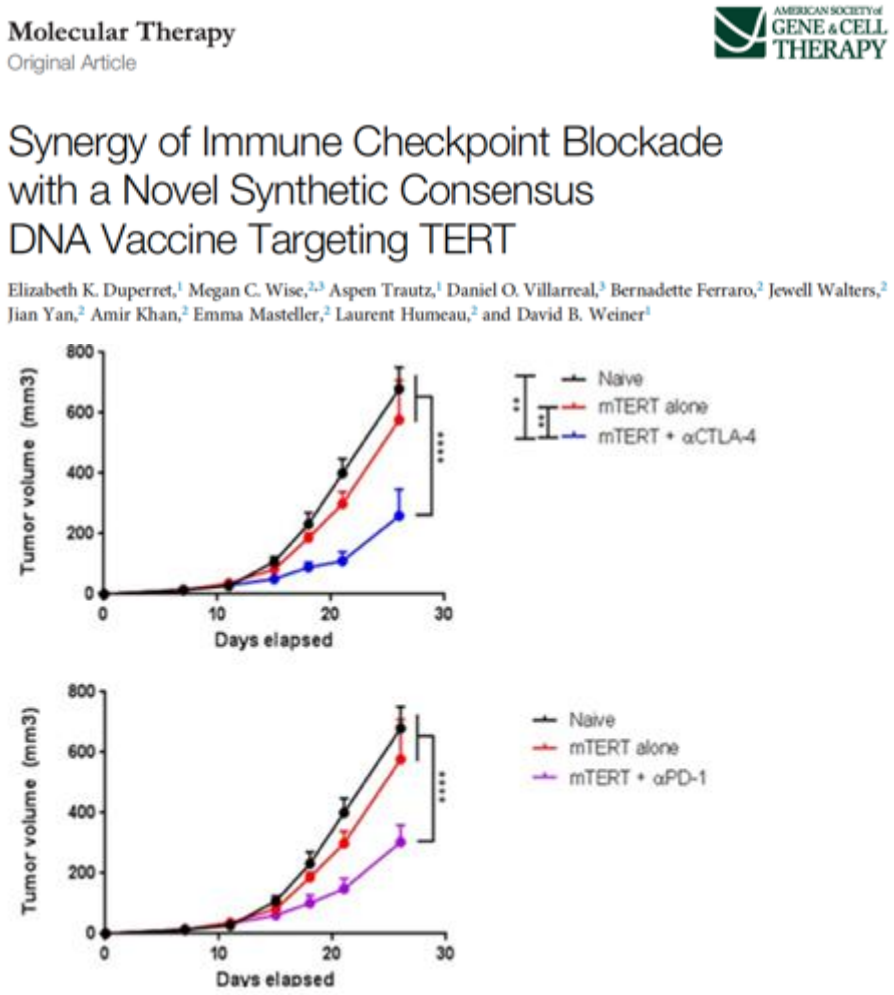
**RRP (INO-3107)**

- 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 planned

# CTLA4 or PD1 + DNA Vaccine Improves Tumor Control & Survival in Challenge Model

## Checkpoint Inhibitor Therapies Combined with INOVIO DNA Medicine

- Potential to improve response rates, without adding toxicity
- Tumor infiltration of antigen-specific, functional CD8+ T cells may prime patients for treatment with checkpoint inhibitors and increase response rates
- Combination studies initiated
  - **MEDI0457** with AstraZeneca PDL-1
  - **INO-5401** with Regeneron PD-1
  - **INO-5151** with BMS PD-1 + Celldex FTL3L (PICI Study)




**Paper published in *Molecular Therapy* 2017**



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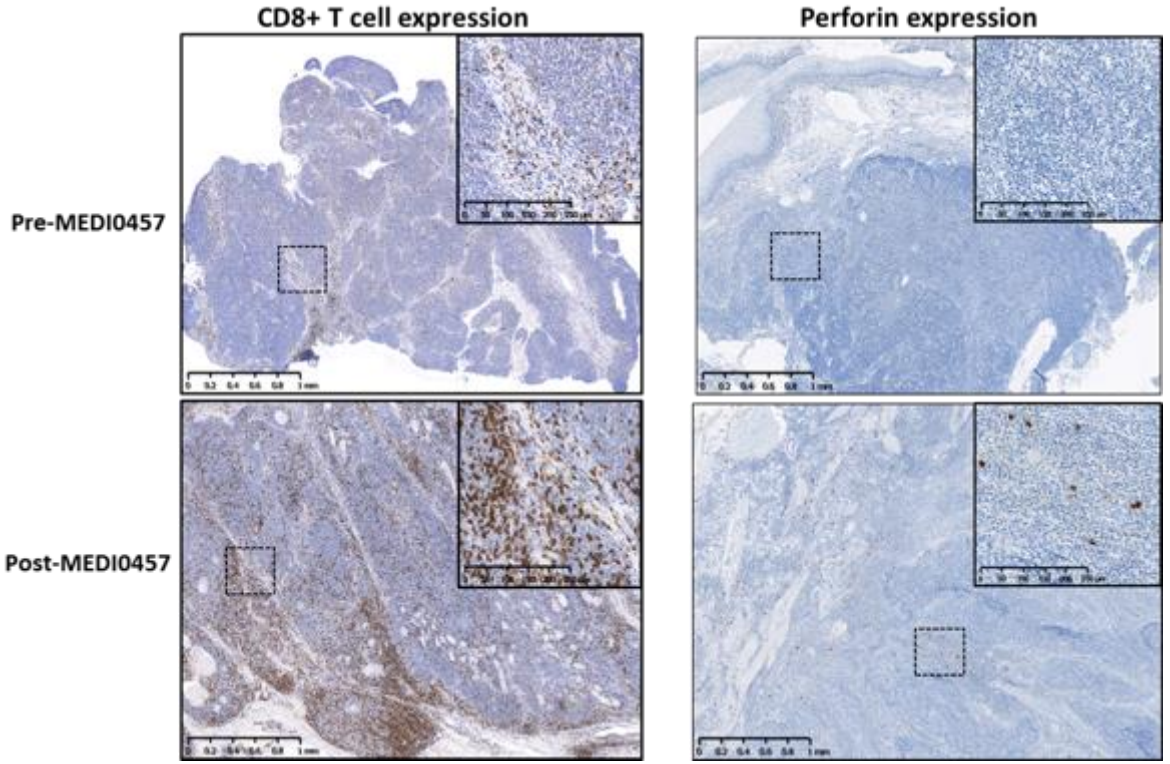
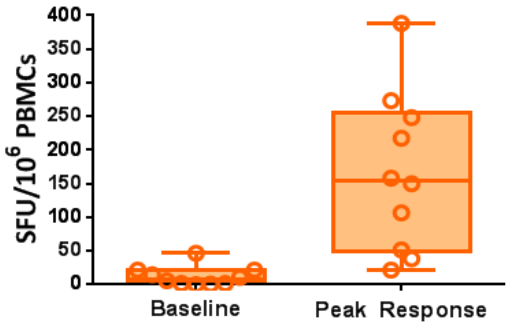
# MEDI0457 (HPV16/18) Induces Robust Anti-Tumor Immunity in Head and Neck Cancer

## Phase 1 study of MEDI0457 (INO-3112) in 22 HPV+ HNSCC Patients

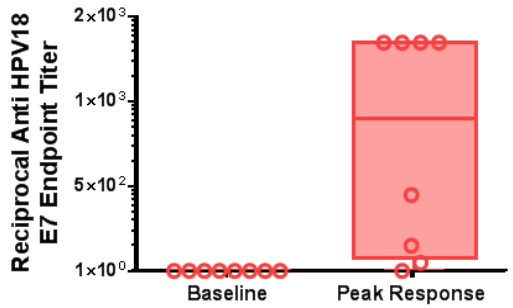
Strong invasion by CD8 T cells into tumors following immunization with MEDI0457 in HPV associated HNSCCa.




Induction of T cells:
Quantitative non-cultured ELISpots




Induction of Antibodies:
Endpoint titers to HPV18 E7




Aggarwal et al Clinical Cancer Research 2018

**Most participants respond immunologically to the vaccine**

# GBM (Newly-diagnosed) Phase 1/2 Study

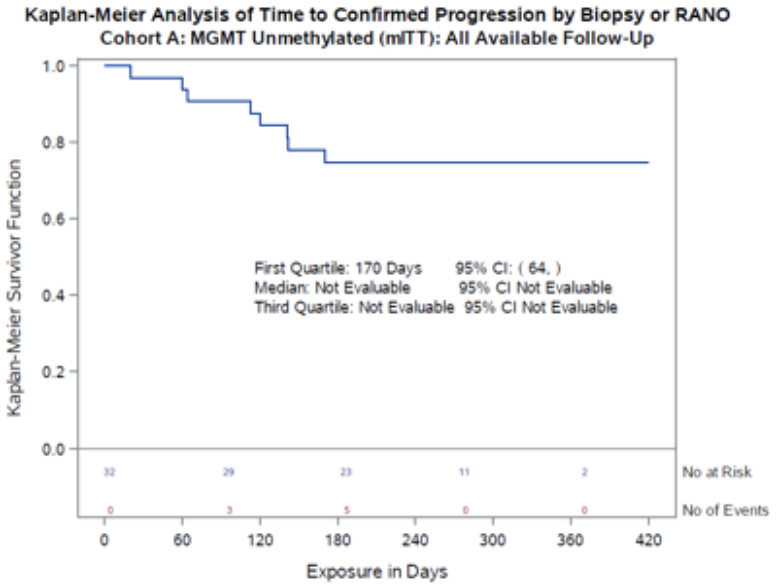
## Trial Treatment (NCT03491683)

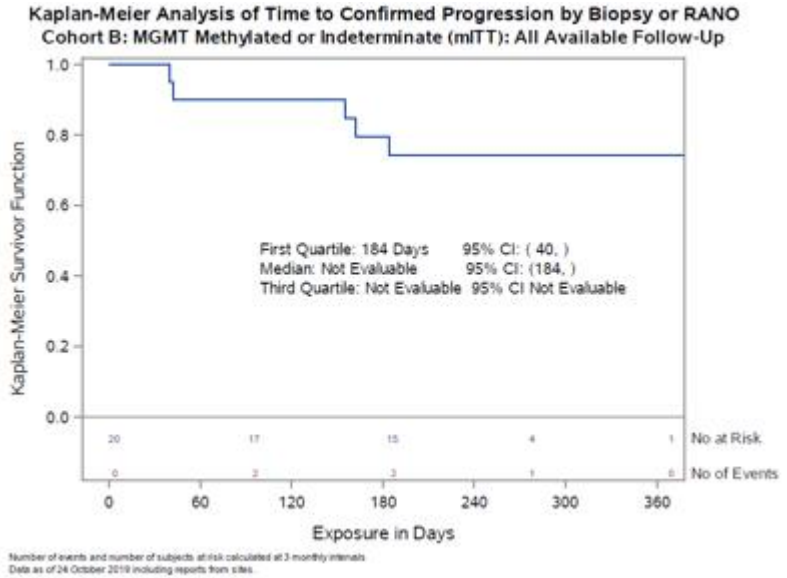
- **INO-5401** (3 mg of each WT1, PSMA and hTERT plasmids) combined with 1 mg INO-9012, (total 10 mg of DNA) IM injection followed by EP given every 3 weeks for 4 doses, then every 9 weeks; and
- **Cemiplimab (LIBTAYO®)** (350 mg/dose IV every 3 weeks)

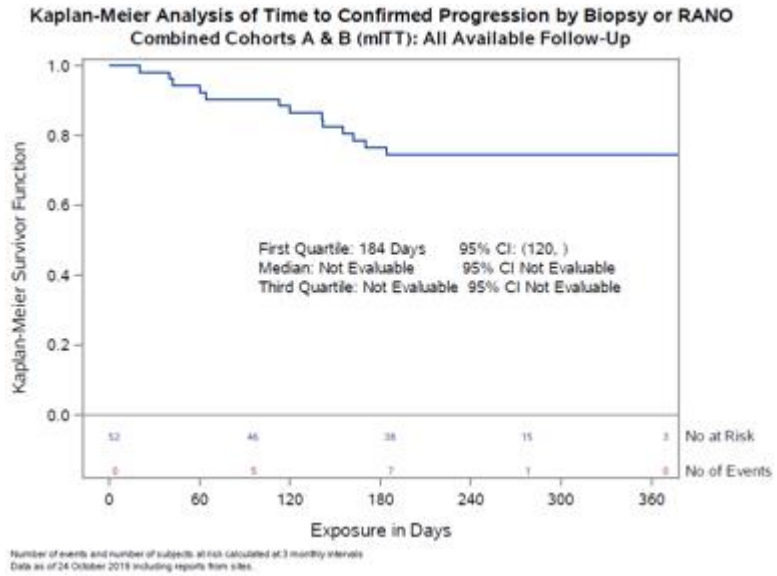
## Chemoradiation Treatment

- **Radiotherapy** (RT), given in a hypofractionated schedule (40 Gy over 3 weeks) for all patients post surgery
- **Temozolomide** (TMZ) concurrent with RT for all patients, and then following RT for 6 cycles in methylated patients only

# GBM-001 Progression-Free Survival at Six Months (PFS6)




| Cohort | N Subjects | N Event-free Subjects | PFS6 (%) | 95% CI Lower Bound | 95% CI Upper Bound |
|---|---|---|---|---|---|
| Cohort A (MGMT Unmethylated) | 32 | 24 | 75 | 56.6 | 88.5 |
| Cohort B (MGMT Methylated) | 20 | 16 | 80 | 56.3 | 94.3 |
| Both Cohorts Combined | 52 | 40 | 77 | 63.2 | 87.5 |

Confirmed PD (RANO) = confirmation by consecutive PD scan ≥4 weeks from original PD event, or progressed according to biopsy surgery. Subjects who terminated for any reason prior to 6 months other than PD included as confirmed progressive events, including two (2) subjects in Cohort B who came off-study at week three (3), and declined long-term follow-up. Note: subjects with time to events longer than 6 months included; subjects have different time on study durations.



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# Executive Team

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

- Decades of biotechnology/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 of Aeras, the leading not-for-profit organization dedicated to developing new tuberculosis vaccines
- Held management positions at Emergent BioSolutions and Microscience Ltd.

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

- Extensive R&D leadership experience 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, BOD**
- Former Senior Vice President, Merck Vaccine Division

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

**Ann C. Miller, M.D.**
- Former Head of Sanofi Oncology Global Marketing

**Jay Shepard**
- Former President & CEO, Aravive; Former Executive Partner, Sofinnova Ventures

**David B. Weiner, Ph.D.**
- Executive VP, The Wistar Institute; Director, Vaccine Center

**Wendy Yarno**
- Former Chief Marketing Officer, Merck

**Lota Zoth, CPA**
- Former CFO, MedImmune



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# 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
- ~80 FTE


## 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
- ~40 FTE


## 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
- ~70 FTE



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