



#### **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 March 31, 2020, which have been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at <u>www.sec.gov</u>.

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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<sup>™</sup> Plasmid in Phase 1 for Zika (INO-A002)



# **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®)



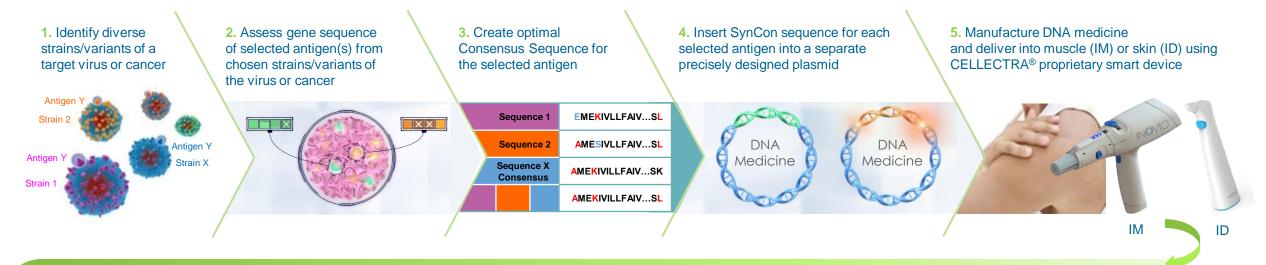
IN VIVO



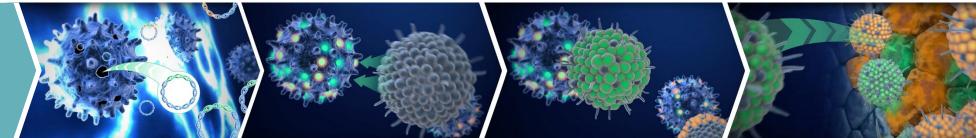


#### INOVIO Technology – Powering Potent Antigen Specific Immune Responses

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



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





# **INOVIO's Technology Advantages**

#### **Clinical Efficacy**

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

#### Safety

- Favorable safety profile tested in over 2,000 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<sup>™</sup> plasmid
- No anti-vector response allows for effective 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)</li>
- Relatively inexpensive to manufacture; produce large quantities



# **INOVIO DNA Medicines Pipeline**

PRODUCT	INDICATION	ANTIGEN	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER/COLLABORATOR/FUNDER
<b>IPV-TARGETED</b>							
	Precancerous Cervical Dysplasia (HSIL)						6
VGX-3100	Precancerous Vulvar Dysplasia (HSIL)	HPV 16 E6, E7/ HPV 18 E6, E7					Apollobio
	Precancerous Anal Dysplasia (HSIL)						(China; INOVIO maintains global rights)
INO-3107	Recurrent Respiratory Papillomatosis (RRP)	HPV 6 E6, E7/ HPV 11 E6, E7					
	Head & Neck Cancer						
MEDI0457	Cervical, Anal, Penile,	HPV 16 E6, E7/ HPV 18 E6, E7					AstraZeneca
	Vulvar Cancers						

#### IMMUNO-ONCOLOGY (NON HPV-ASSOCIATED)

INO-5401	Glioblastoma Multiforme (GBM)	WT1, PSMA, hTERT		REGENERON
INO-5151	Prostate Cancer	PSA, PSMA		CANCER RESEARCH PICIFICATION CANCER INSTITUTE

INTERNALLY FUNDED



## **INOVIO DNA Medicines Pipeline** (Continued)

PRODUCT	INDICATION	ANTIGEN	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNER/COLL	ABORATOR/FUNDE
ECTIOUS DISEAS	ES (NON HPV-ASSOCIATED)							
PENNVAX-GP	HIV	Gag, pol, env						HIV VACCINE
INO-4201	Ebola	Glycoprotein					D	ARPA
INO-4700 (GLS-5300)	MERS	Spike					GENE	CEP
INO-4600 (GLS-5700)	Zika	Glycoprotein						ENE
INO-4500	Lassa Fever	Glycoprotein					C	E P I
INO-4800	COVID-19 (Coronavirus)	Spike						EPI

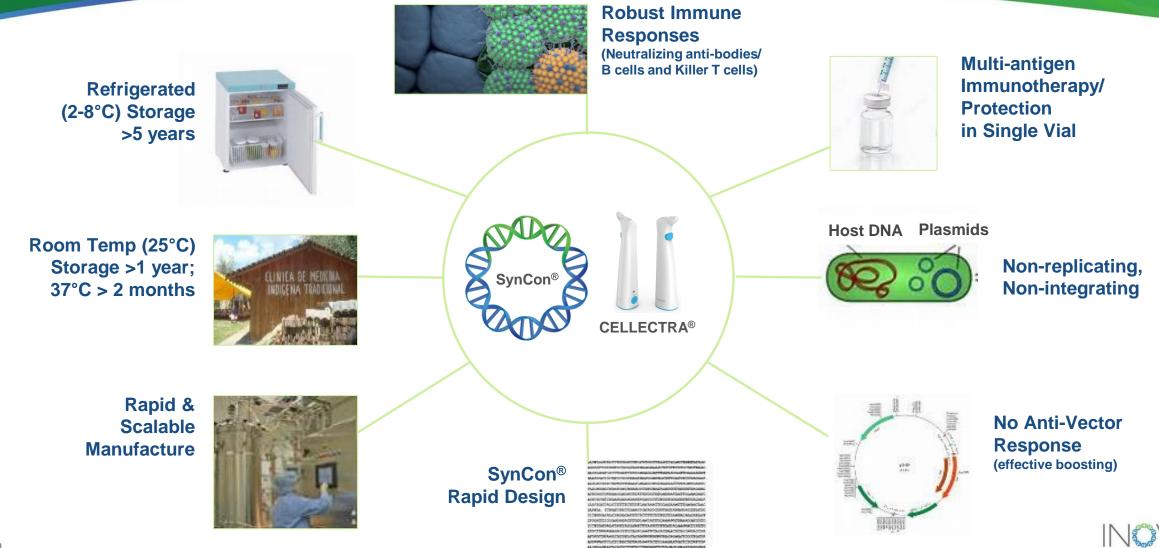
#### **dMAb<sup>™</sup> (DNA-ENCODED MONOCLONAL ANTIBODIES)**

INO-A002	Zika	Glycoprotein				BILL&MELINDA GATES foundation
			INTER	NALLY FUND	ED	EXTERNALLY FUNDED



# **Infectious Disease Programs**

# **Key Characteristics of INOVIO's DNA Vaccine Platform**



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

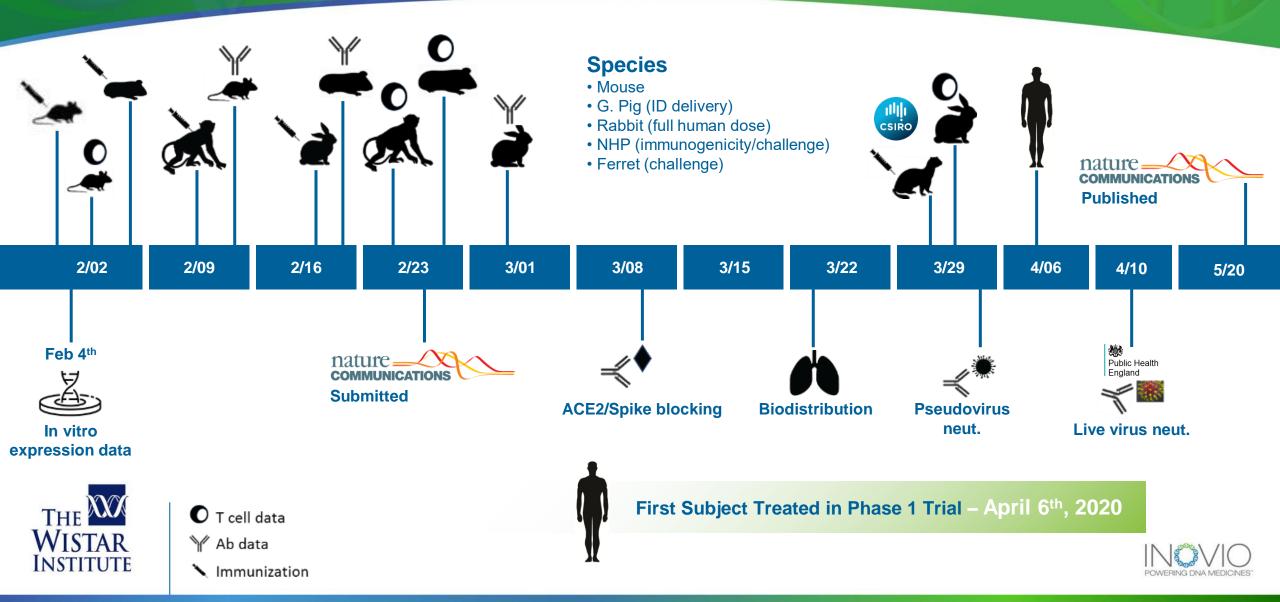


Product	Indication	Data Reported (to date)	Partner/s	Next Milestone
PENNVAX-GP	HIV	<ul> <li>Phase 1: 93% (71 of 76) evaluable vaccinated participants showed a CD4+ or CD8+ cellular immune response to at least one of the vaccine antigens</li> <li>94% (62 of 66) demonstrated an env specific antibody response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

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

DECEMBER 2019	JANUARY 10/11, 2020	JANUARY 10 - JANUARY 23, 2020	JANUARY 23, 2020	JANUARY 23 - FEBRUARY 29, 2020	MARCH 2020
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	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	INOVIO coronavirus experts race to manufacture INO-4800 and begin preclinical testing and clinical trial design	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	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	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	MARCH 26, 2020	APRIL 6 - APRIL 23, 2020	MAY 2020	JUNE - JULY 2020	ONGOING
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	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	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 fully enrolled 40 healthy volunteers; study sites are the University of Pennsylvania and a clinic in Kansas City, MO	Preclinical data published in peer-reviewed journal Nature Communications	In June, U.S. Phase 1 trial results to be announced Phase 2/3 trial expected to begin Human clinical trials expected to begin in China and South Korea*	INO-4800 COVID-19 DNA vaccine production and scale up underway*

### **INOVIO 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 pending regulatory approval



# **INOVIO-Led Global Coalition to Advance INO-4800**



# BILL& MELINDA GATES foundation















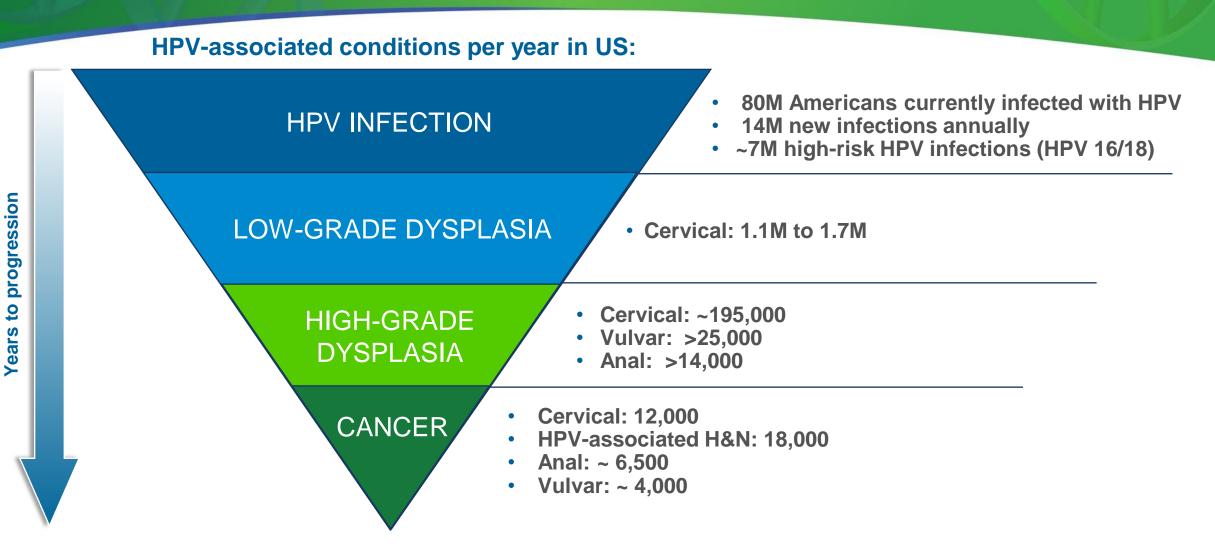






# **HPV-Related Programs**

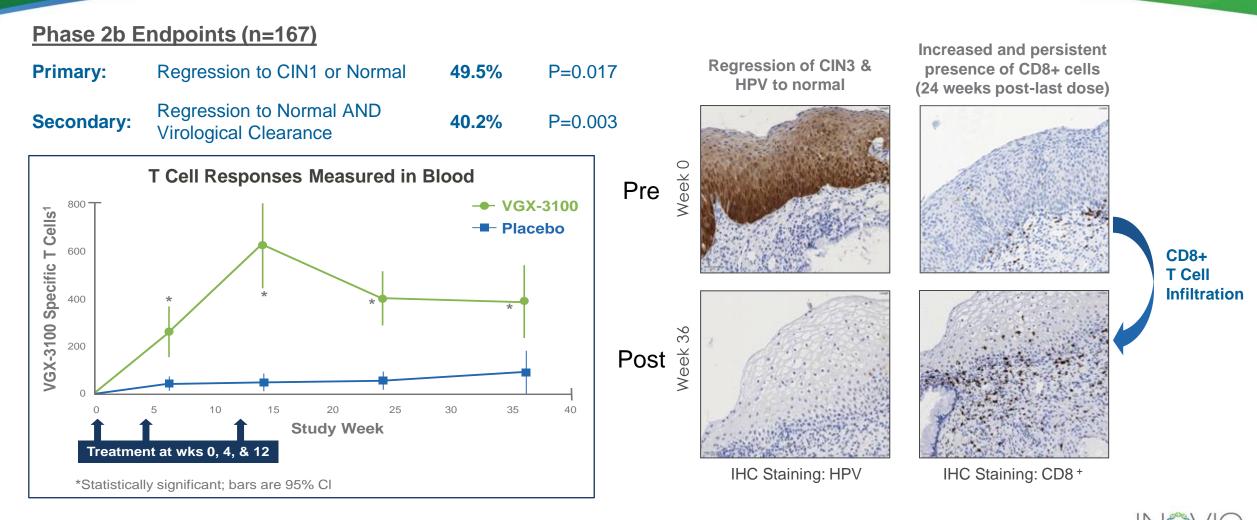
### **HPV-Associated Diseases Market Overview**



Sources: US CDC (2018) HPV and Cancer, available at: <a href="https://www.cdc.gov/cancer/hpv/statistics/cases.htm">https://www.cdc.gov/cancer/hpv/statistics/cases.htm</a> (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, Alteknues 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 – <a href="https://seer.cancer.gov/statfacts">https://seer.cancer.gov/statfacts</a> (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 Achieves All Primary and Secondary Endpoints





#### 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), doubleblind, placebo-controlled



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



Primary endpoint measured at month 9 (as in P2b)



### 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



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

Interim findings (6 months after start of treatment) Clearance of lesions: 50% of patients ∯ <mark>x23</mark>

23 patients enrolled Interim data reported for 20

Decrease in number of lesions: 75% of patients



### **INOVIO and QIAGEN Developing Biomarker to Optimize Patient Selection**



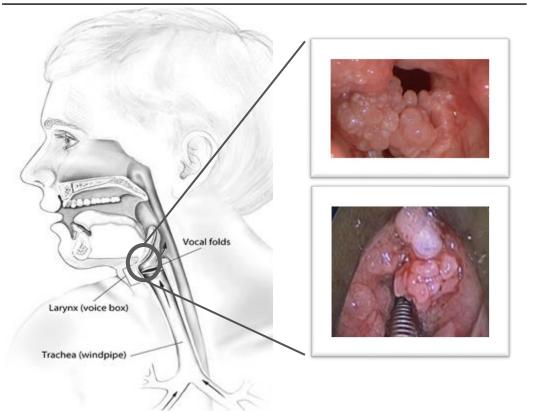
In 2Q 2019, INOVIO entered into collaboration with QIAGEN to co-develop a liquid biopsy-based pretreatment commercial test kit to guide patient selection for VGX-3100:

- 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



## 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).

## **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 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.

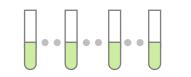
## **INO-3107** Phase 1/2 Study in RRP – IND Accepted

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



Phase 1/2 openlabel, multicenter clinical study **x63** 

Target enrollment



4 doses of vaccine, 3 weeks apart on Day 0, Weeks 3, 6, 9 1 all com

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



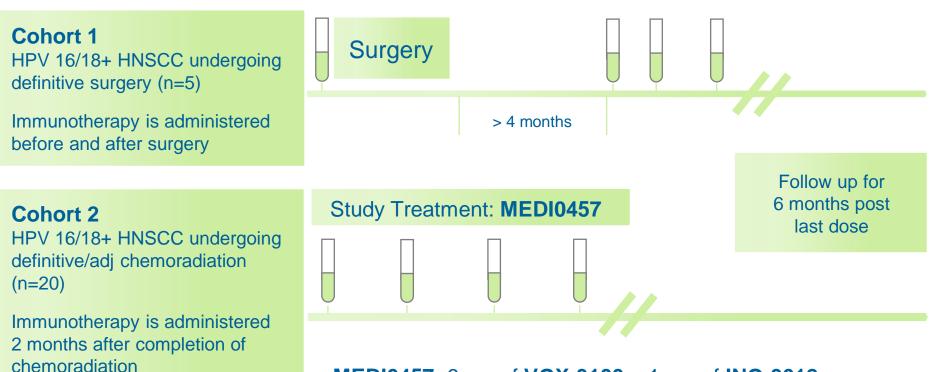
# MEDI0457 for HPV-Related Cancers in Partnership with AstraZeneca



- **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





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

Secondary: Cellular and humoral immune responses

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

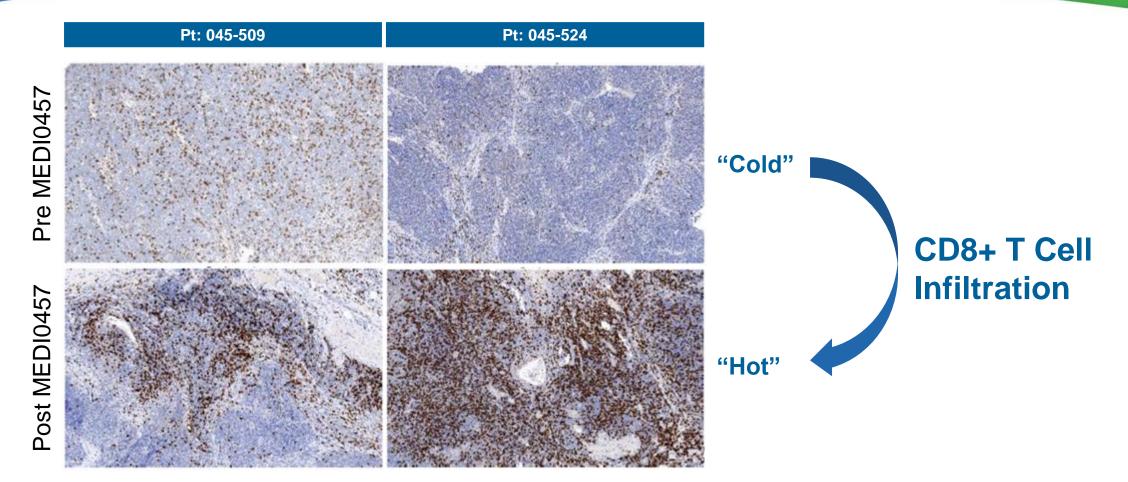


#### MEDI0457: 6 mg of VGX-3100 + 1 mg of INO-9012

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

#### 27

# **CD8+ T Cell Infiltration into Tumor Following MEDI0457 Treatment**

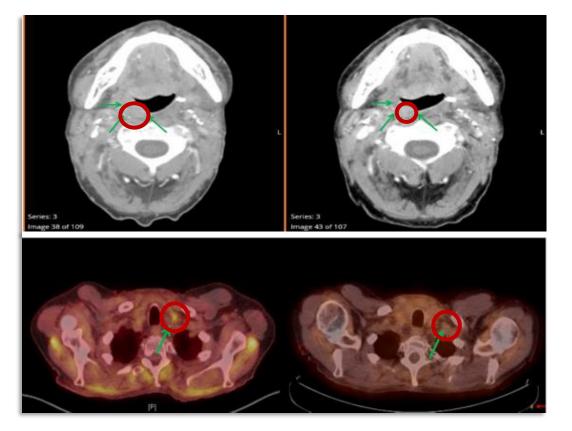


Robust antigen-specific CD8+ killer T cell responses observed in 20/22 - 90.1% – of patients (both tumor tissue and peripheral blood)



Aggarwal et al Clinical Cancer Research 2018

## 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)



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

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



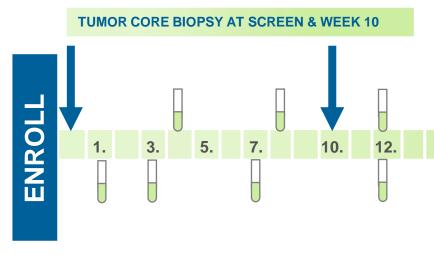
Phase 1b/2a open label study for metastatic HPV+ HNSCC with persistent or recurrent disease after chemotherapy treatment



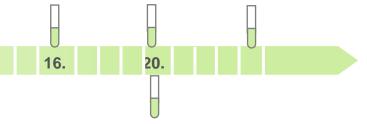
Combination with AstraZeneca's PD-L1 checkpoint inhibitor (durvalumab) Primary Endpoints: Safety, tolerability Secondary Endpoints: Immunogenicity, ORR, PFS, Disease CR, OS

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



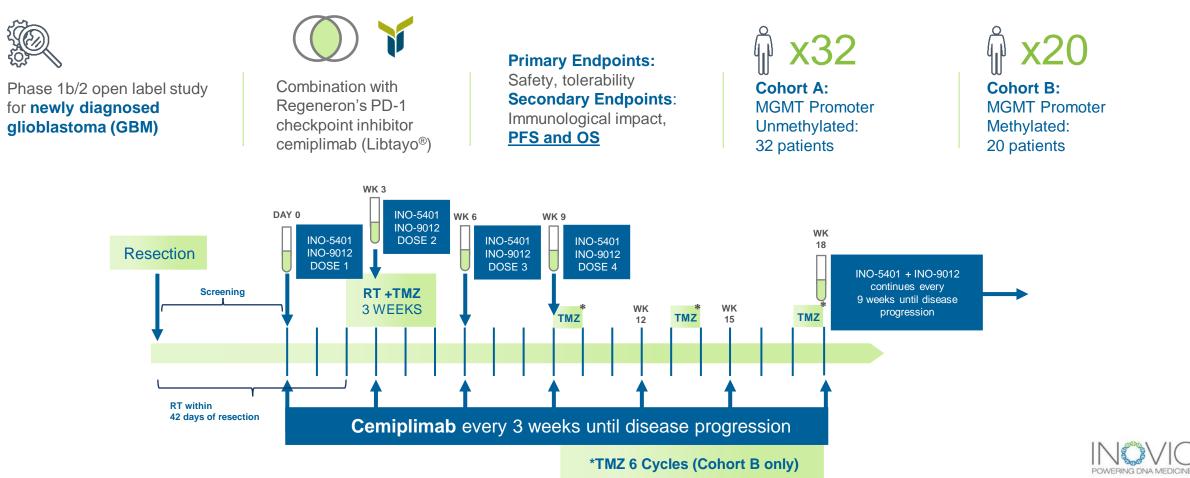
**Planned Dosing Schedule**: MEDI0457: Weeks 1, 3, 7 and 12 and then every 8 weeks until disease progression, unacceptable toxicity or withdrawal of consent



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

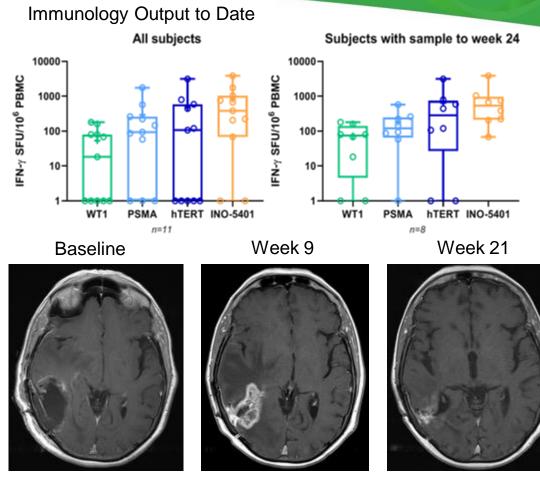
# INO-5401 for Newly Diagnosed GBM in Phase 1/2 Study in Collaboration with Regeneron

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



#### 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



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



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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



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 TherapeuticsNivolumab (anti-PD-1) from Bristol-Myers Squibb

PICI/CRI will fund & execute the clinical study

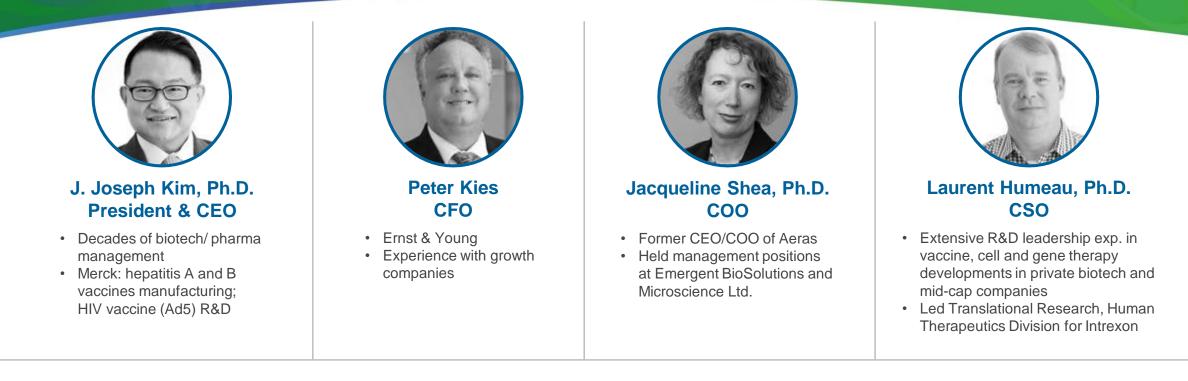






# **Management & Financials**

#### **Experienced Executive Team and Board of Directors**



# 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



# **Strong Balance Sheet to Support Critical Milestones**

## \$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)
- Question 2020: Interim Phase 1 results from first-in-human trial of dMAb<sup>™</sup> plasmid candidate INO-A002 (for preventing or treating Zika virus infection)



**NASDAQ:INO** 

# **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** ۲
- **Partnerships with major pharma and organizations:**
- 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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BILL&MELINDA



NASDAQ:INO



# POWERING DNA MEDICINES<sup>™</sup>



# 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

#### HealthDay

#### **HPV Blamed for Rising Rates of Anal Cancer**

OURNAL of the









Anal cancer rates and deaths are climbing in the US, study says



#### The Washington Post The Washington Post

A toddler's dwindling voice was chalked up to acid reflux. Her problem was far more serious.





Woman With Raspy Voice Has Had More Than 300 Surgeries to Treat Rare Vocal Cord Disease

HEALTH: 2:35 PM PDT, April 11, 2019. JOHANNA LI



Try 1 month for SI

## **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



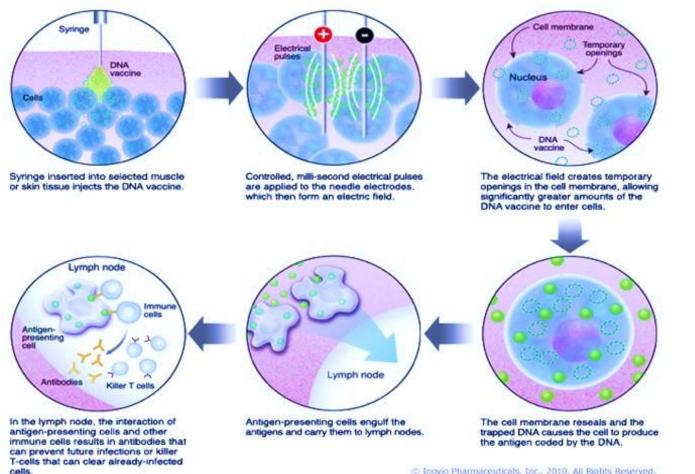
## Infectious Diseases (non-HPV associated)





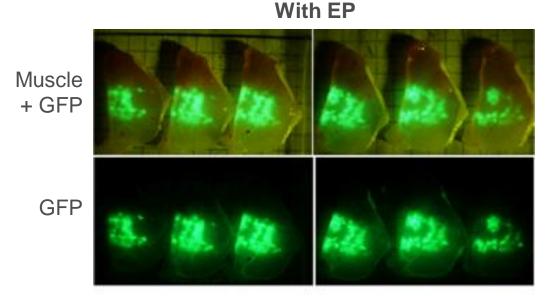
## **INOVIO's Technology Delivering Precisely Designed Plasmids with Proprietary Smart Devices**

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

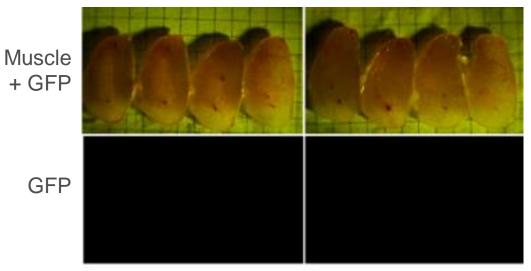




## Precise Design + Intracellular Delivery = Improved Immune Responses



Display of GFP (green fluorescent protein) gene expression after CELLECTRA® delivery into rabbit muscle No EP



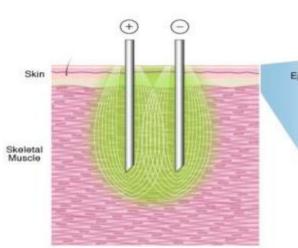


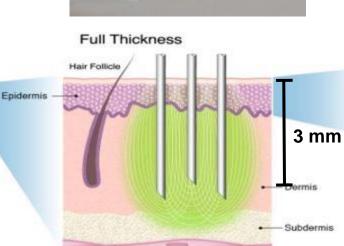
# Innovation in the Delivery of SynCon<sup>®</sup> DNA Medicine

#### **CELLECTRA®-5PSP**

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







#### **CELLECTRA®-3P**

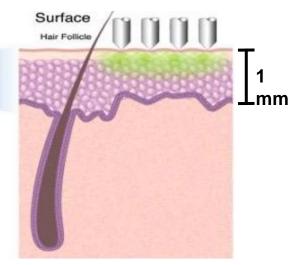
- Intradermal minimally invasive
- 3mm electrodes
- In clinical use



#### Surface EP (SEP)

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







# **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



# **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





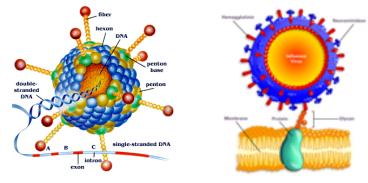
# **Limitations of Other Approaches**

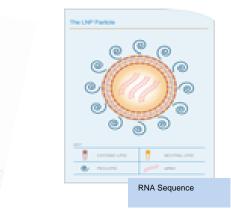
## Viral Vectors – Receptor/cell target based mediated entry

- 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**

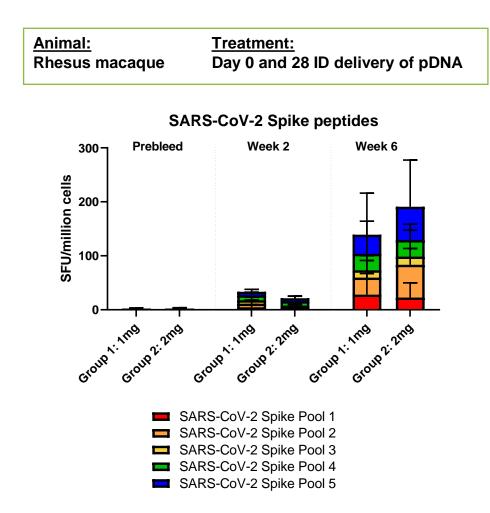
- Systemic delivery, localized expression (liver>lung or spleen)
- Process for manufacture and release work in progress
- Formulations + RNA follow tissue targeting of the particles/cold chain required, include focus on IV route
- DLT observed, low CTL induced, inflammatory
- High cost of goods



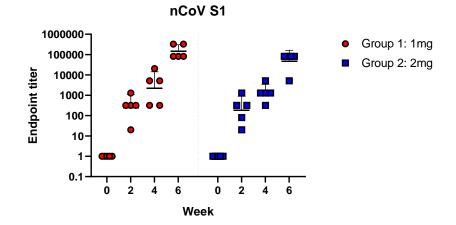




# Robust Cellular and Humoral Immune Responses Following Immunization of INO-4800 in Rhesus Monkeys



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	<ul> <li>Cervical dysplasia: Phase 2b PoC trial demonstrated a complete response in 43 out of 107 patients in regression of high-grade cervical lesions <i>and</i> elimination of HPV infection</li> <li>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)</li> </ul>			
(VGX-3100)	<ul> <li>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)</li> </ul>			
Head & Neck Cancer (MEDI0457)	<ul> <li>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 &gt;2 years</li> <li>MEDI0457 is licensed by AstraZeneca and currently in a Phase 1b/2a study in combination with durvalumab (PD-L1 checkpoint inhibitor)</li> </ul>			
RRP (INO-3107)	<ul> <li>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</li> <li>A Phase 1/2 clinical trial for treating RRP with INO-3107, which includes both HPV 6 and HPV (11 antigana, is planned)</li> </ul>			

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

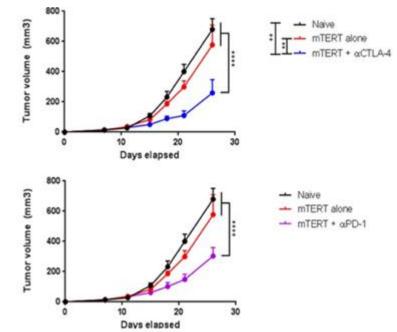
- Potential to improve response rates, without adding toxicity
- Tumor infiltration of antigen-specific, functional CD8+ T cells may prime patients for treatment with checkpoint inhibitors and increase response rates
- Combination studies initiated
  - MEDI0457 with AstraZeneca PDL-1
  - INO-5401 with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

Molecular Therapy Original Article



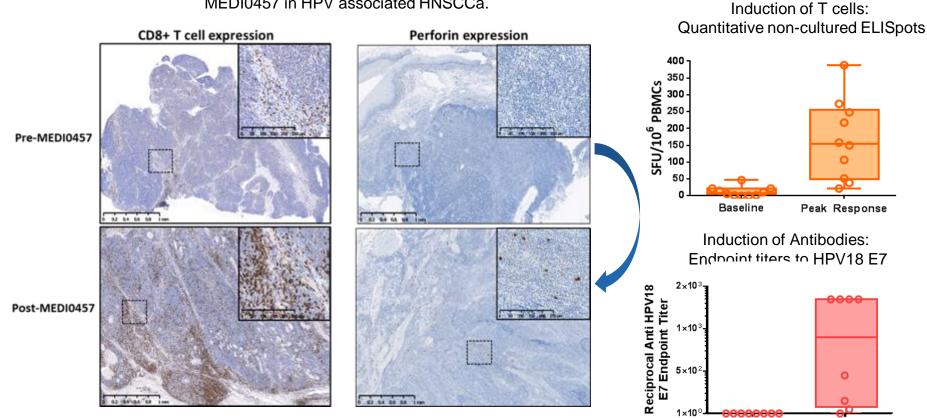
#### Synergy of Immune Checkpoint Blockade with a Novel Synthetic Consensus DNA Vaccine Targeting TERT

Elizabeth K. Duperret,<sup>1</sup> Megan C. Wise,<sup>2,3</sup> Aspen Trautz,<sup>1</sup> Daniel O. Villarreal,<sup>3</sup> Bernadette Ferraro,<sup>2</sup> Jewell Walters,<sup>2</sup> Jian Yan,<sup>2</sup> Amir Khan,<sup>2</sup> Emma Masteller,<sup>2</sup> Laurent Humeau,<sup>2</sup> and David B. Weiner<sup>1</sup>





# 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.

Aggarwal et al Clinical Cancer Research 2018

Most participants respond immunologically to the vaccine







Baseline

Peak Response



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

## Trial Treatment (NCT03491683)

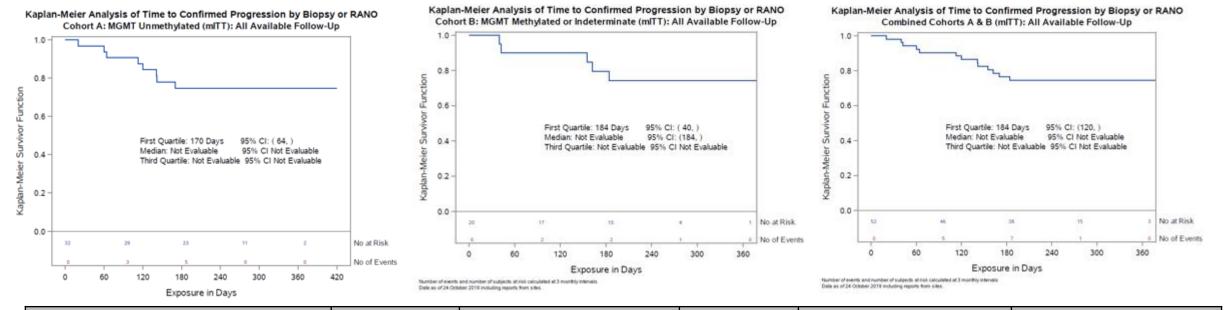
- INO-5401 (3 mg of each <u>WT1, PSMA and hTERT plasmids</u>) combined with 1 mg INO-9012, (total 10 mg of DNA) IM injection followed by EP given <u>every 3 weeks</u> for 4 doses, then <u>every 9 weeks</u>; and
- Cemiplimab (LIBTAYO<sup>®</sup>) (350 mg/dose IV every 3 weeks)

## **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 <u>methylated patients only</u>



# **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  $\geq$ 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.



## **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



## **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<sup>®</sup>, Januvia<sup>®</sup>, Gardasil<sup>®</sup>, Zostavax<sup>®</sup>, Proquad<sup>®</sup> and Rotateq<sup>®</sup>



#### 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

