

Powering a New Decade of DNA Medicines

June 2022



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, 2021 and our Form 10-Q for the quarter ended March 31, 2022, which has been filed with the Securities and Exchange Commission (SEC) and are available on the SEC's website at www.sec.gov.

In addition, the forward-looking statements included in this presentation represent INOVIO's views as of the date hereof. INOVIO anticipates that subsequent events and developments may cause its views to change. However, while INOVIO may elect to update these forward-looking statements at some point in the future, the company specifically disclaims any obligation to do so, except as may be required by law. These forward-looking statements should not be relied upon as representing INOVIO's views as of any date subsequent to the date of this presentation.

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Powering DNA Medicines

INOVIO is focused on developing and commercializing DNA medicines to help protect people from infectious diseases and help treat people with cancer and HPV-associated diseases.

Optimized DNA plasmids delivered through proprietary smart device

Extensive patent portfolio protecting technology platform

Designed to treat and prevent cancers & infectious diseases

Targets multiple antigenic sequences; combining multiple antigens into single vial



Balanced humoral and cellular immune responses to a wide range of antigen targets

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

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

No anti-vector response; ability to readminister and boost



INOVIO's Proprietary Technology

OPTIMIZED PLASMID DESIGN AND DELIVERY TECHNOLOGY

PRECISELY
DESIGNED PLASMIDS
(SynCon®)



PROPRIETARY
SMART DEVICES
(CELLECTRA®)

Intramuscular
(IM) Device for
Pre-Cancers &
Cancers



Intradermal (ID)

Device for

Vaccines

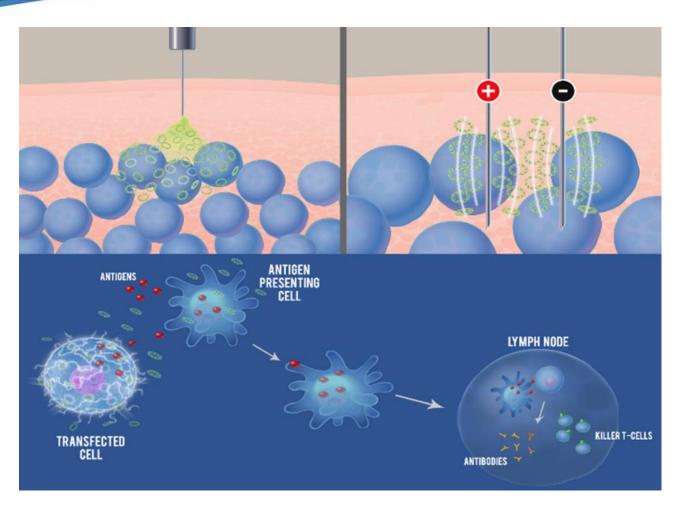


IN VIVO

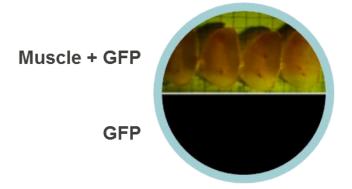




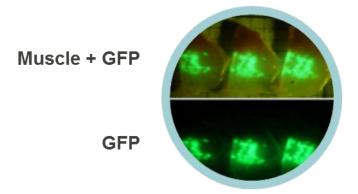
DNA Delivered with CELLECTRA Results in Improved Immune Responses



No CELLECTRA



With CELLECTRA





INOVIO DNA Medicines Pipeline







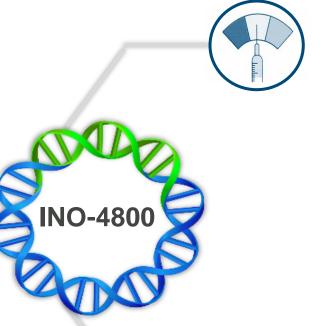
INOVIO DNA Platform Key Attributes

INOVIO's DNA platform is an important novel vaccine technology, as it provides favorable CD8 T cell response, ability to readminister, and temperature stability.

SELECT DIMENSIONS	ADVANTAGES	ONGOING AND FUTURE PANDEMIC IMPACT
CD8+ RESPONSE	Drives CD8+ responses – likely to mitigate the threat of new circulating strains	T-cell responses may be an effective countermeasure for the next pathogen
ANTIBODY RESPONSE	Binding antibodies & neutralizing antibodies at all doses and age groups	Platform can direct cross-neutralizing responses
BOOSTABILITY	Can be re-administered multiple times , leading to potentially increased CD8 response	Opportunity for homologous and heterologous boosting
SAFETY, TOLERABILITY, REACTOGENICITY	Well-tolerated in 5,000+ participants and 15,000+ doses	Immunogenic with minimal side effects and no increased reactogenicity with boosting
STORAGE AND TRANSPORTATION	Reduced reliance on cold chain - stores at 2-8° C for 5 years and at ambient for 1 year	No frozen cold chain requirement – simplified logistics for mass vaccinations and remote locations
RAPID DESIGN AND MANUFACTURE	INOVIO's DNA medicines can be designed quickly through optimized SynCon® technology	Quick response to emerging threats with clinical trials started in 3 months
COMMERCIAL READINESS	Invested in manufacturing equipment, manufacturing capacity reservations, and operational infrastructure	Prepared to manufacture volumes within a short period



COVID-19 Vaccine Candidate INO-4800 Pathways



Heterologous Boost

- HB strategy represents a greater opportunity as COVID-19 enters the endemic phase
- Currently in discussions with regulators in key countries regarding trial and pathways to licensure
- Key characteristics of INO-4800 could make it an ideal Heterologous Boost candidate
 - Cross reactive CD8 T cell response and associated durability of response
 - Ability to readminister (no anti-vector response)
 - Temperature stability
- Preliminary T cell response data from Advaccine's booster trials in China support INO-4800's potential as a booster

WHO-Sponsored Solidarity Trial Vaccines

- Global Phase 3 placebo-controlled trial will enroll 40,000 participants
- Trial represents the largest global clinical trial for COVID-19 vaccine candidates
- INO-4800 was selected by the WHO's independent vaccine prioritization advisory group



Heterologous Boost – INO-4800

Path Forward

• Evaluating the feasibility of an additional ex-US heterologous boost trial with INO-4800 as a booster in a non-inferiority clinical trial compared to viral and inactivated COVID-19 vaccines

Global Demand

 Currently licensed vaccines may not meet the global demand for boosters to address waning protection from these primary vaccinations

Key Features

- INOVIO's DNA vaccine technology make it a potential booster candidate including:
 - Cross-reactive T-cell responses
 - Tolerability of re-administration
 - Temperature stability for transport, storage, and distribution

Preliminary T Cell Data from China Homologous and Heterologous Boost Data

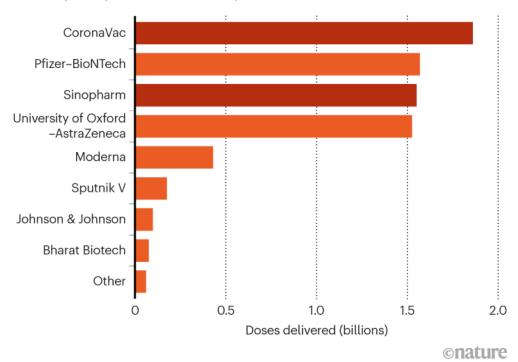
- Two doses of inactivated vaccine followed by a boost with INO-4800 resulted in an increase in the T cell immune response by 6.3 fold
- In a separate study Advaccine assessed three doses of inactivated vaccine. The cellular response was increased by 1.7 fold.



Heterologous Boost Market Potential

THE RACE TO VACCINATE

Out of the eight vaccines that account for the vast majority of COVID-19 vaccine doses delivered globally, China's CoronaVac and Sinopharm jabs account for nearly half of all doses.



Source: Data from Airfinity.

- Booster market is much larger than primary vaccine market
- Inactivated and viral vector vaccines have been administered primarily in Low- and Middle-Income countries
- About 2.4 billion doses of the Chinese vaccines have been administered in China, but almost 1 billion doses have gone to 110 other countries
- Global demand for heterologous boosters <u>may</u> <u>not be met</u> with currently licensed vaccines (EUA or full authorization) for primary series or those not currently licensed but with Phase 3 data efficacy data
- Market reset focused now on heterologous boost



Infectious Disease Pipeline Progress

INO-4500 for Lassa Fever

- Phase 1b clinical trial
- Completed enrollment of 220 participants
- Funded by CEPI
- Conducted in Ghana

INO-4700 for MERS

- Phase 2 clinical trial in approximately 500 participants
- Completed enrollment for dose-finding stage (192 participants)
- Funded by the CEPI
- Conducted at sites in Jordan, Lebanon, and Kenya

INO-4201 for Ebola

- Phase 1b clinical trial
- Completed enrollment of 46 participants
- Funded by DARPA
- Evaluating INO-4201 as a booster in participants previously vaccinated with Ervebo®

Collaborations & Partnerships for ID Programs

































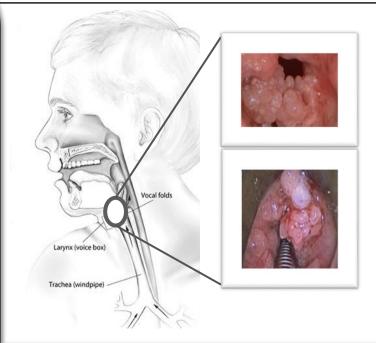


INO-3107 against Recurrent Respiratory Papillomatosis (RRP) caused by HPV 6/11

HPV-associated disease; caused by HPV 6/11

- Rare, orphan disease with ~approx. 7,330 total active cases within the U.S.¹, where virtually all of those require surgical procedures
- ~3,000 new cases per yr. in the U.S.
- Growths can lead to life-threatening airway obstructions
- Standard of care is lifelong surgery,
 repeated as needed to address symptoms
- Currently, disease is incurable and can only be treated as needed by surgery to remove tumors to temporarily restore the airway
- RRP may occur in adults as well as in children

Areas affected by Recurrent Respiratory Papillomatosis (RRP)



INO-3107 Update & Catalysts

- Granted Orphan Drug Designation in July 2020
- Completed enrollment of 32 participants in an open-label, multicenter Phase 1/2 clinical trial in participants with HPV 6/11associated RRP (1Q22)
- Immune responses and early clinical benefit data from Phase 1/2 trial in 2H22
- Phase 3 trial expected in 1H23



INO-3107 Phase 1/2 Study in RRP – Data Expected in 2H22

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

Granted Orphan Drug Designation



Phase 1/2 openlabel, multi-center clinical study



Target enrollment



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



CELLECTRA-delivered INO-3107 plasmid encoded antigens (Intramuscular)

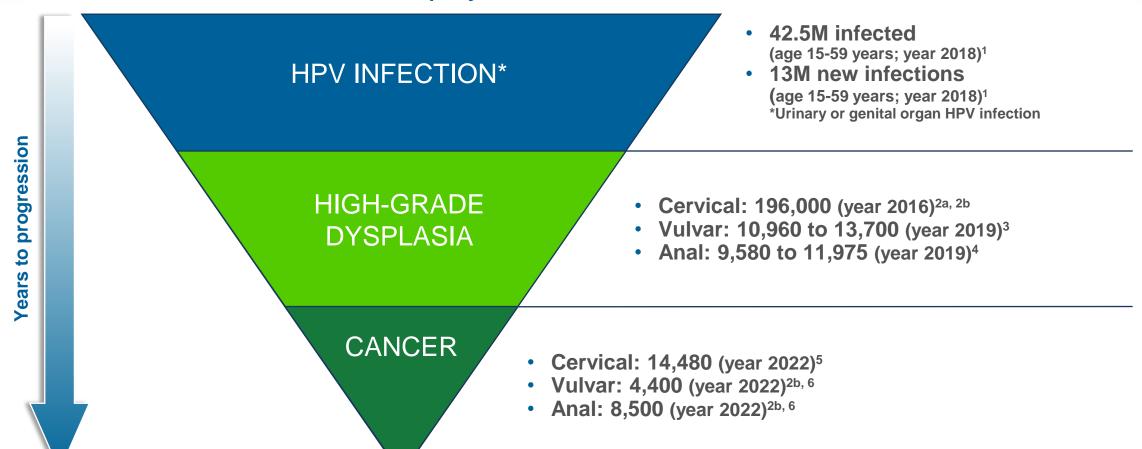
Enrollment criteria: Participants who have required at least two surgical interventions per year for the past three years for the removal of associated papilloma(s)

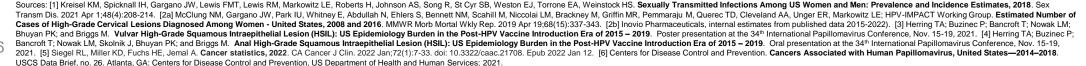
Primary endpoint: A doubling or more in the time between surgical interventions following the first dose of INO-3107 relative to the frequency prior to study therapy



HPV-Associated Anogenital Disease Burden Overview

Estimated US cases per year:







VGX-3100 Phase 3 Program: HPV-Associated Cervical HSIL

TRIAL: VGX-3100

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



Phase 3 consists of 2 studies in parallel:

REVEAL1 (primary) n=201 – Enrollment Closed Study follow-up through week 88 (as in Phase 2b) Topline efficacy data reported 1Q21 REVEAL2 (confirmatory) n=198 – Enrollment Closed
Study follow-up through week 40
Topline efficacy data expected in Q422

Primary endpoint:

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

6 mo.

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

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



Dosing: month 0, 1, 3 (as in Phase 2b)



VGX-3100: Phase 3 Program for HPV-Associated Cervical HSIL

- REVEAL1: Achieved statistical significance for primary objective in all evaluable participants: regression of cervical HSIL combined with virologic clearance of HPV subtypes 16/18, 6 months after administration
 - 23.7% (31/131) in treatment group vs. 11.3% (7/62) in placebo group
 - p=0.022; 12.4 difference in percentage, 95%CI: 0.4,22.5
 - mITT includes all participants w/ endpoint data (N=193)*
 - All secondary efficacy objectives achieved
- REVEAL2: Currently ongoing (Topline data by Q422)
 - Partnership with QIAGEN to develop pre-treatment predictive biomarker to help identify those likely to respond to VGX-3100
 - One or two additional well-controlled trials in the biomarker-positive population post REVEAL2 may be necessary to support approval of a marketing application for VGX-3100



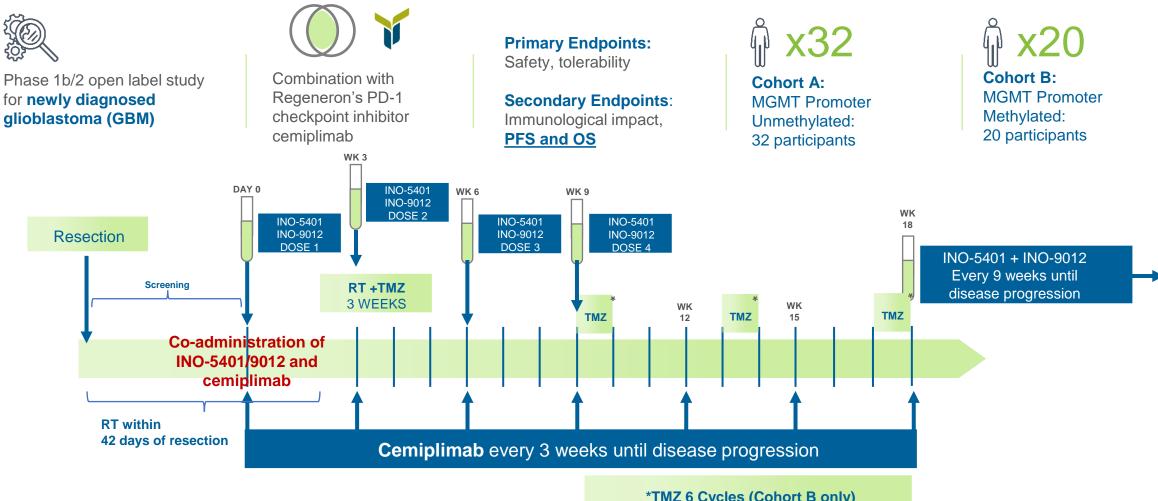


INO-5401/INO-9012 and Cemiplimab for Newly Diagnosed GBM

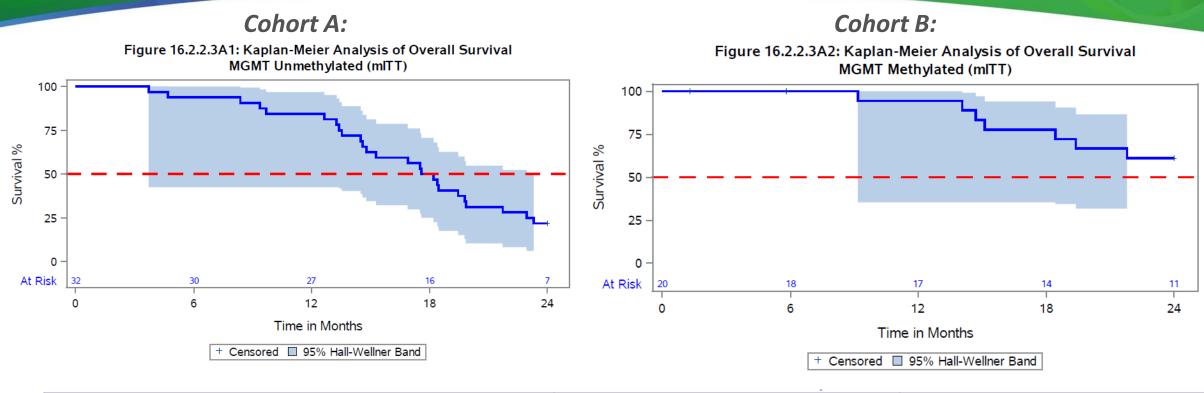
- INO-5401 is a DNA medicine composed of plasmids that encode for three tumor-associated antigens: human telomerase (hTERT), Wilms tumor-1 (WT-1), and prostate-specific membrane antigen (PSMA)
- INO-9012 is a synthetic DNA plasmid that encodes for human IL-12 designed to stimulate T cells locally without a systemic effect
- Cemiplimab is a high-affinity, highly potent, human, hinge-stabilized IgG4 monoclonal antibody to the PD-1 receptor
- In this study, INO-5401 and INO-9012 are combined with cemiplimab, in order to create an antigenspecific, activated T cell population
- INOVIO has shown that INO-5401+INO-9012 delivered intramuscularly with cemiplimab and 40 Gy radiation/TMZ have an acceptable safety profile and are immunogenic
- Abstract providing follow-up Phase 1/2 data (including OS for MGMT-methylated cohort)
 presented at 2022 ASCO Annual Meeting

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

INO-5401 (encoding tumor-associated antigens: hTERT, WT1, PSMA) plus **INO-9012**, encoding IL-12



Kaplan-Meier Survival Estimates of OS



Median OS; unmethylated (A)	17.9 mo. (14.5 – 19.8)	Historical 14.6-16 mo.
Median OS; methylated (B)	32.5 (18.4 – NR)	Historical 23.2-25 mo.
Median OS; combined (A+B)	19.5 (16.9 – 23.3)	-

NR: not reached.

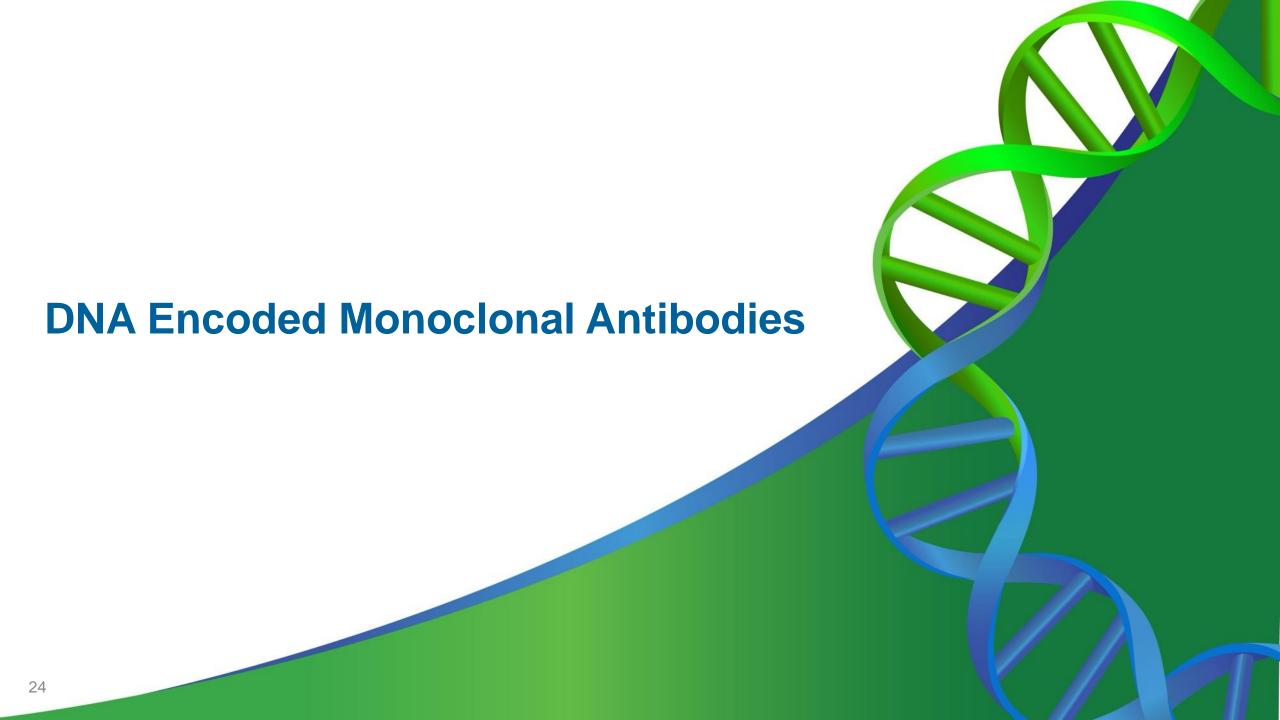
Gilbert et al. J Clin Oncol 2013; Gilbert et al. N Eng J Med 2014. Comparison is limited due to differences in study population. Data was presented at 2022 ASCO Annual Meeting.



Median OS in GBM-001 is Higher Than Historical Controls

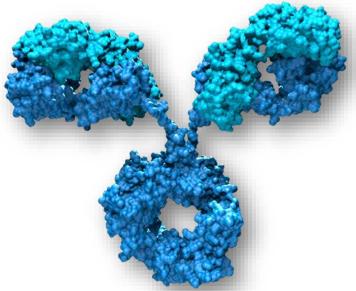
Median OS; unmethylated (A)	17.9 mo. (14.5 – 19.8)	Historical 14.6-16 mo.
Median OS; methylated (B)	32.5 (18.4 – NR)	Historical 23.2-25 mo.
Median OS; combined (A+B)	19.5 (16.9 – 23.3)	
Overall Survival at 12 Months	n Alive/N Total	OS12% (95% CI)
MGMT Unmethylated (Cohort A)	27/32	84.4 (67.2-94.7)
MGMT Methylated (Cohort B)	17/20	85.0 (62.1-96.8)
Combined	44/52	84.6 (71.9-93.1)
Overall Survival at 18 Months	n Alive/N Total	OS18% (95% CI)
Overall Survival at 18 Months MGMT Unmethylated (Cohort A)	n Alive/N Total 16/32	OS18% (95% CI) 50 (31.9 - 68.1)
		1
MGMT Unmethylated (Cohort A)	16/32	50 (31.9 - 68.1)
MGMT Unmethylated (Cohort A) MGMT Methylated (Cohort B)	16/32 14/20*	50 (31.9 - 68.1) 70 (45.7 – 88.1)
MGMT Unmethylated (Cohort A) MGMT Methylated (Cohort B) Combined	16/32 14/20* 30/52	50 (31.9 - 68.1) 70 (45.7 – 88.1) 57.7 (14.5 – 71.3)
MGMT Unmethylated (Cohort A) MGMT Methylated (Cohort B) Combined Overall Survival at 24 Months	16/32 14/20* 30/52 n Alive/N Total	50 (31.9 - 68.1) 70 (45.7 – 88.1) 57.7 (14.5 – 71.3) OS24% (95% CI)

NR: not reached. Two participants in Cohort B withdrew consent for additional follow-up at Week 3 and were considered deceased Gilbert et al. J Clin Oncol 2013; Gilbert et al. N Eng J Med 2014. Comparison is limited due to differences in study population. Data was presented at 2022 ASCO Annual Meeting.



DNA Encoded Monoclonal Antibody (dMAb™) and Bi-Specific T Cell Antibody (dBTA) Platform

- INOVIO is developing a groundbreaking DNA-encoded monoclonal antibody technology (dMAb) enabled by its smart technology platforms, with the potential to be groundbreaking
- The dMAb platform facilitates direct in vivo transfection to target tissue to produce and secrete mAbs into the blood at biologically relevant levels
- Additional DNA-encoded bi-specific T cell antibodies (dBTAs) are in development for the treatment of cancer
- dMAbs and dBTAs are a potentially transformative approach for the prevention and treatment of infectious diseases and cancer
- First-in-man Phase 1 clinical trial ongoing for Zika dMAb funded by Bill and Melinda Gates Foundation





INOVIO's dMAbs/dBTAs May Be Efficacious in Multiple Disease Models

Delivery of anti PCSK-9 in mice lowers LDL Broadly neutralizing pan-influenza A & B approach PCSK-9 Influenza A & B • Delivery of multiple antibodies (Elliott et al NJV 2017) cholesterol (Khoshnejad et al Mol Ther 2018) viruses et al. JI 20201 **Zaire Ebolavirus Cancer Antigens** Demonstrated HER2/CD3 dBTEs can reduce tumor burden in mice (Perales-Puchalt et al. JCI Insight. 2019) Delivery of anti PSMA in mice impacted tumor challenge (Muthumani et al Cancer Immuno 2017) dMAb **Checkpoint Inhibitors** Delivery of CPI in mice impacted and cured tumor challenge (Perales-Puchalt et al. Oncotarget. 20151 2019, Duperret et al. Cancer Res 2018) Multi-drug resistant Pseudomonas aeruginosa Multiple forms of DMAbs: monospecific, bispecific IgG Lowering pathogen burden and complementation in antibiotic resistant model (Patel et al Nat Comm. 2017) Lyme Disease

- Demonstrated disease protection in pia model (McNee
 - · DMAb modifications and mouse model development
 - Pre-exposure protection against highly lethal challenge in mice (Patel et al Cell Reports 2018)

Dengue virus (DENV)

• Protection against ADE (Flingai et al. Sci Rep

Zika virus – First DMAb in P1 Clinical Trial

- scFV approach
- Protection from disease in NHPs (Esquivel et al. Mol Ther. 20191

Chikungunya virus (CHIKV)

· Rapid protection & complementarity with a vaccine (Muthumani et al., JID 2016)

SARS-CoV-2

 Highly potent dMAbs expressed in vivo (candidates under preclinical development)

DMAb modifications (Yang et al JID 2019)

RSV

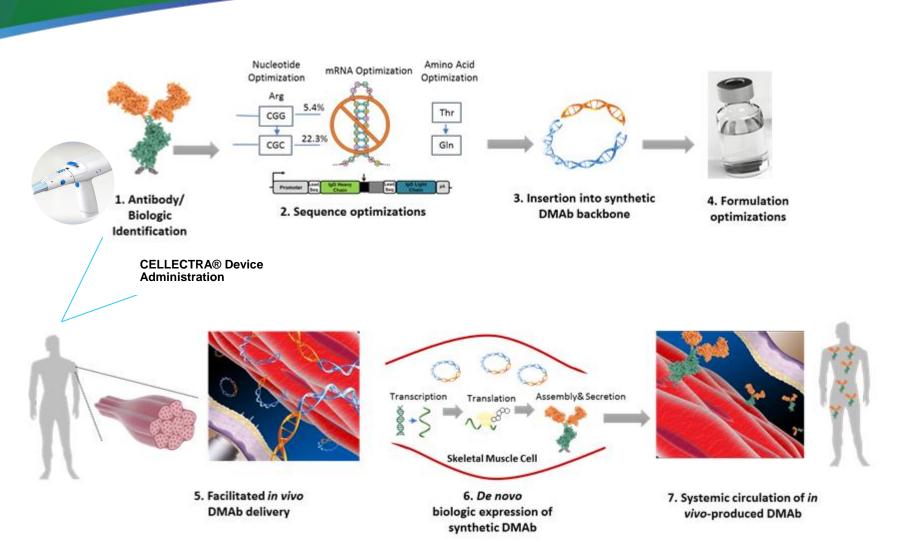
 scFV approach (Schultheis et al. HVI 2020)

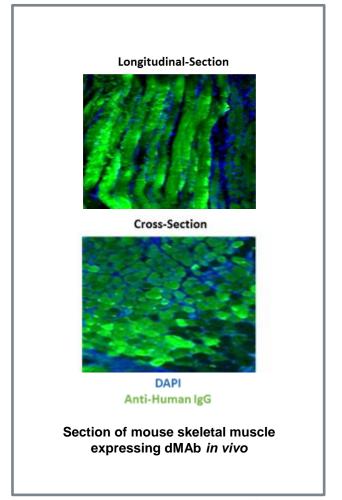
HIV

- Delivery of multiple DMabs to a single
- >10ug/ml in NHPs (Wise et al JCI 2020)
- DNA encoded post translational modifications (Xu, Wise et al EbioMed



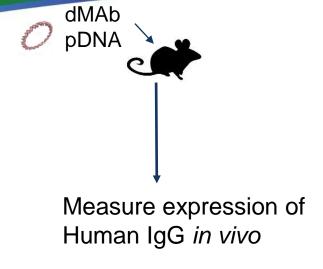
INOVIO's DNA-Encoded Monoclonal Antibody Platform



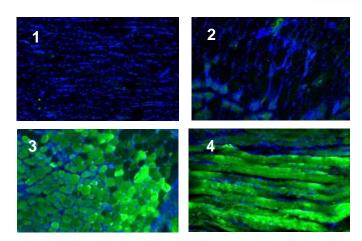




In Vivo Transfer of dMAb pDNA Into Muscle Employing Enhanced Delivery Protocol Results in Robust Levels of Functional mAbs

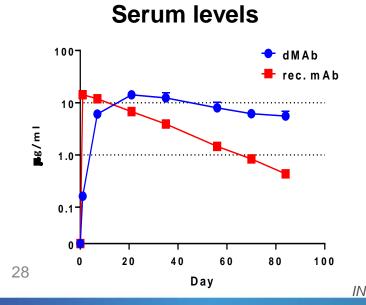


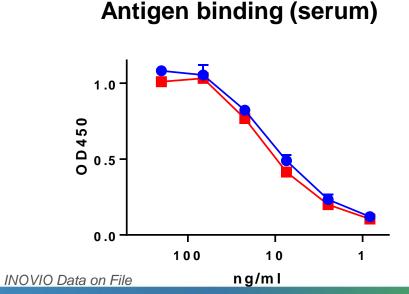
Local expression in muscle:

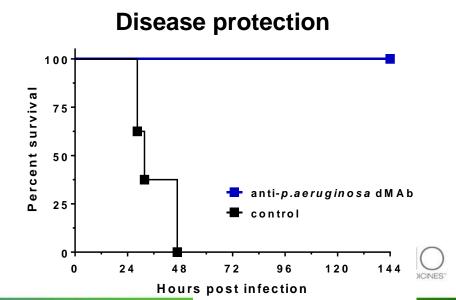


1: No Treatment
2: Empty plasmid
3: dMAb plasmid
(perpendicular)
4: dMAb plasmid
(parallel)

hlgG expression

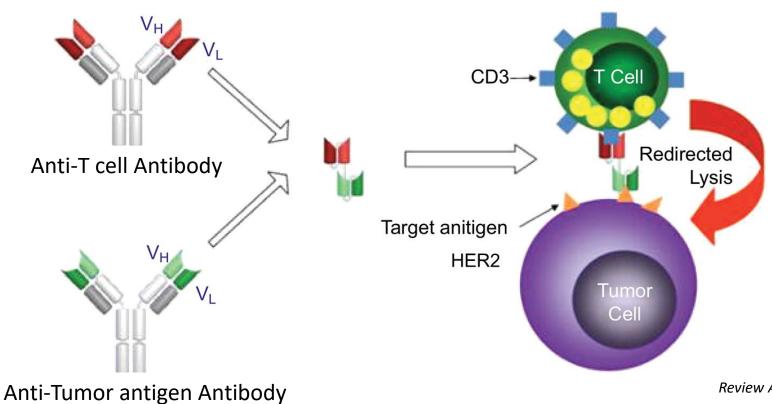


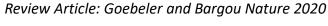




dBTA: DNA Encoded Bi-specific T Cell Antibodies: Connect Killer T Cells to Cancer Cells

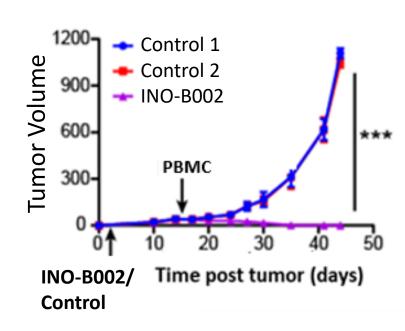
A new class of immunotherapeutic molecules for the treatment of cancer





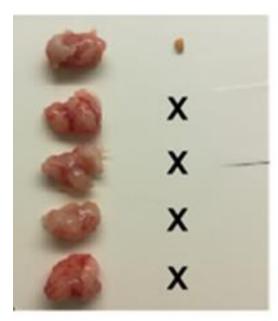


INO-B002 Treatment Prevents HER2 Tumor Growth in Preclinical Models



Tumor collection on day 45

Control INO-B002



Alfredo Perales-Puchalt et al. JCI Insight 2019



First in Human Trial Ongoing

- A clinical trial of INO-A002 in Healthy Dengue Virus-naive Adults
- Phase 1, open label, single center, dose escalation study (0.5 4 mg) to evaluate the safety, tolerability and pharmacokinetic profile of dMAb-ZK190 following delivery of INO-A002 with Hylenex® recombinant delivered IM followed by EP in healthy adult Dengue naïve volunteers ages 18-60 years.
- ClinicalTrials.gov Identifier: NCT03831503





COVID-19 dMAb Updates

- SARS-CoV-2 dMAb cocktail demonstrates
 - Durable expression
 - Activity against SARS-CoV-2 VOCs
 - Protects against disease in multiple animal models
- dMAbs targeting SARS-CoV-2 may provide a pre-exposure prophylactic option with enhanced durability
 - SARS-CoV-2 dMAbs: "A Phase 1, Open-Label, Single Center, Dose Escalation Study of the Safety and Pharmacokinetics of dMAbs in Healthy Adults" (ClinicalTrials.gov Identifier: NCT05293249)













Experienced Executive Team and Board of Directors



Jacqueline Shea, Ph.D. President & CEO

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

Simon X. Benito



Peter Kies CFO

- Ernst & Young
- Experience with growth companies



Laurent Humeau, Ph.D. CSO

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

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Former Executive VP and Chief Marketing Officer, Merck

Lota S. Zoth

Former CFO, MedImmune



NASDAQ:INO

Well-Balanced Pipeline of Milestones Supported by Strong Balance Sheet

\$360.4M

Cash and short-term investments

As of March 31, 2022

226.5M

Common stock shares outstanding

As of March 31, 2022

INO-4800

- ✓ 1Q22: Completed enrollment of heterologous and homologous boost Phase 1/2 trials with Advaccine
- □ 2Q22: Report full data set from heterologous and homologous boost Phase 1/2 trials with Advaccine

VGX-3100

□ 4Q22/1Q23: Report REVEAL2 efficacy data and safety follow-up through week 40

INO-3107

☐ 2H22: Phase 1/2 immune responses and early clinical benefit data

INO-5401

□ 2Q22: Present additional overall survival data including median OS for MGMT-methylated cohort at ASCO 2022

Platform Development

- 1H22: Initiate COVID-19 dMAb trial
- ☐ 1H22: Report INO-4500 Lassa Phase 1b data
- ☐ 2H22: Report INO-4700 MERS Phase 2 data
- □ 2H22: Report INO-4201 Ebola Phase 1b booster data

