INOVIO
POWERING DNA MEDICINES™

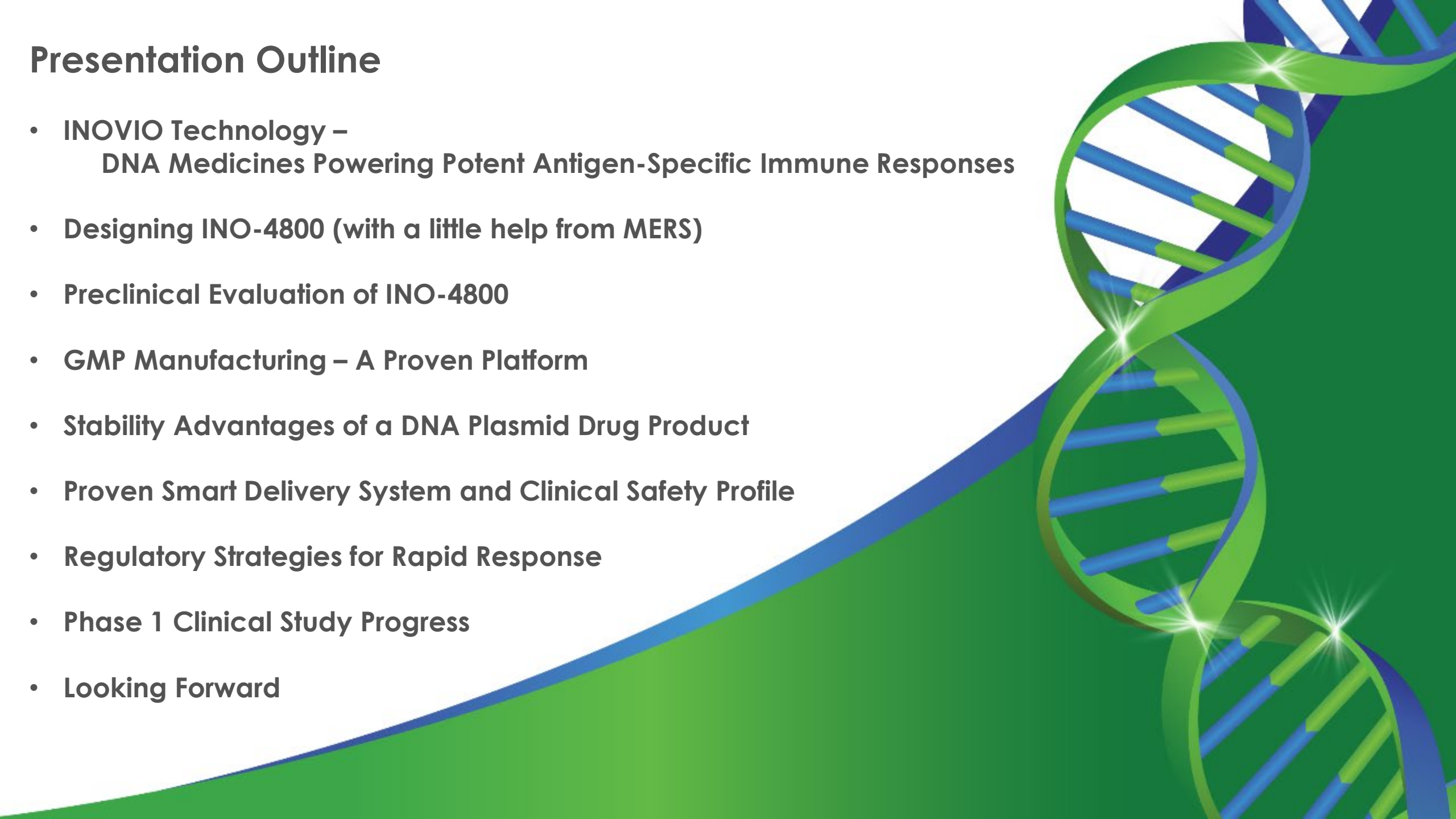
INO-4800: One SARS-CoV-2 Vaccine, One Decade of Innovation

Cell & Gene Therapy Products, June 8, 2020
Robert J. Juba Jr.

Nasdaq:INO

Presentation Outline

- INOVIO Technology –
  DNA Medicines Powering Potent Antigen-Specific Immune Responses
- Designing INO-4800 (with a little help from MERS)
- Preclinical Evaluation of INO-4800
- GMP Manufacturing – A Proven Platform
- Stability Advantages of a DNA Plasmid Drug Product
- Proven Smart Delivery System and Clinical Safety Profile
- Regulatory Strategies for Rapid Response
- Phase 1 Clinical Study Progress
- Looking Forward



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™ plasmid in Phase 1 for Zika (INO-A002)

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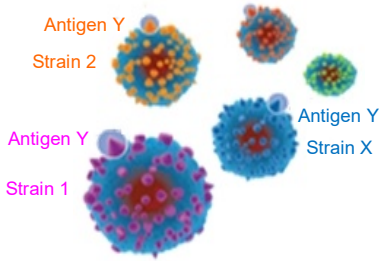
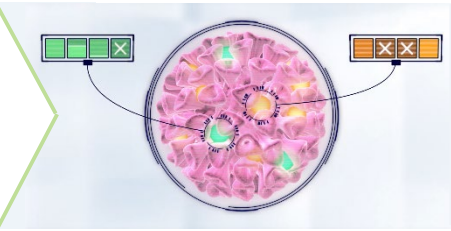
INOVIO Technology – DNA Medicines Powering Potent Antigen Specific Immune Responses

INOVIO DNA medicines power a subject'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



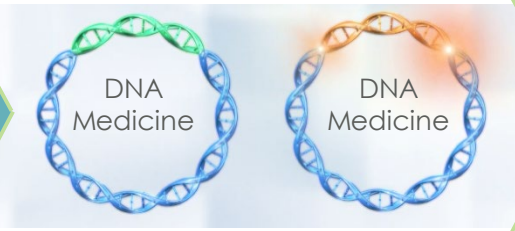
2. Assess gene sequence of selected antigen(s) from chosen strains/variants of the virus or cancer



3. Create optimal Consensus Sequence for the selected antigen

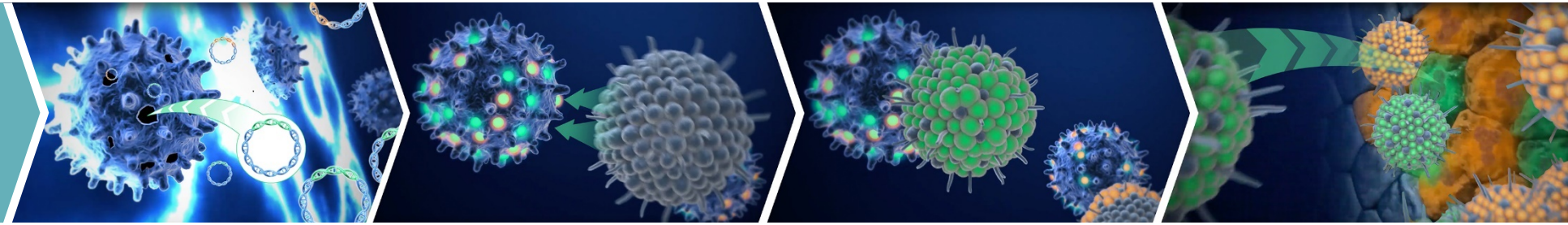
Sequence 1	EMEKIVLLFAIV…SL
Sequence 2	AMESIVLLFAIV…SL
Sequence X Consensus	AMEKIVILLFAIV…SK
	AMEKIVILLFAIV…SL

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



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

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



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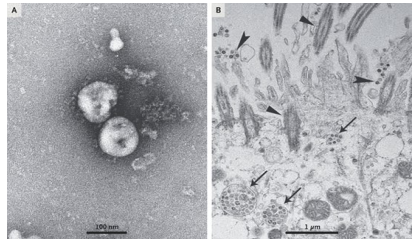
INO-4800: Synthetic DNA vaccine targeting SARS-CoV-2 Spike Glycoprotein

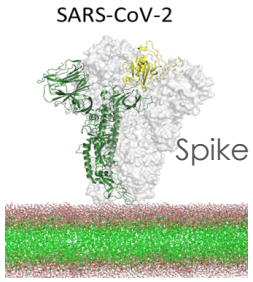
Rapid design of INO-4800

Isolation of virus



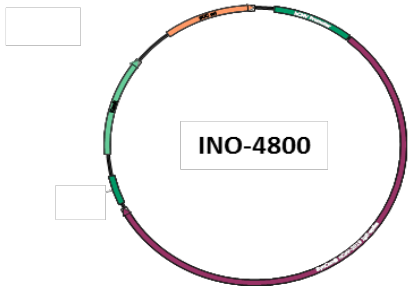
Zhu, N et al. 2020 NEJM

Virus sequence published



Gene Optimization Algorithm

Cloned into expression vector

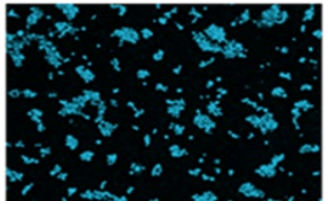


INO-4800 instructs expression of Spike protein

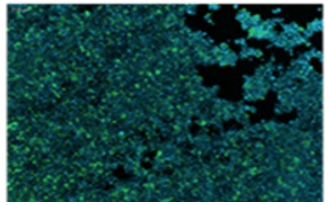
Spike protein is the main target of **neutralizing antibodies**

- Considered a key component for vaccines
- Codon and RNA optimized

Control



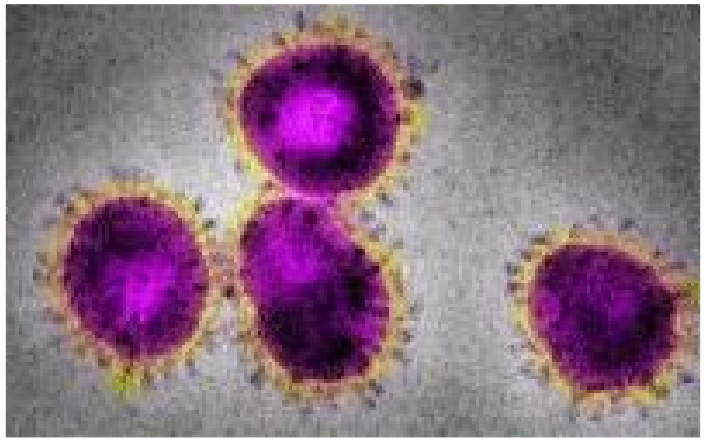
INO-4800



INOVIO Response to Novel Coronavirus COVID-19 Outbreak Builds Upon Prior Experience in Developing a MERS Vaccine

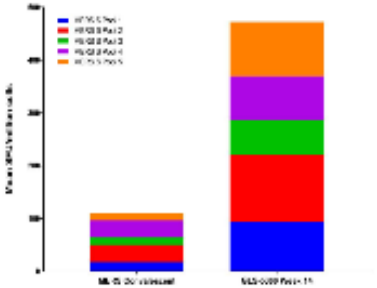
We designed our COVID-19 vaccine candidate, named INO-4800, based upon studies **targeting the MERS coronavirus family members**.

CEPI



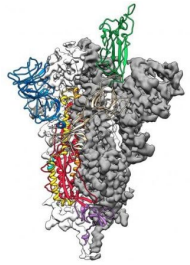
Track Record of Success with MERS DNA Vaccine – Preclinical

- **100% protection** from clinical disease in primate model after 2 immunizations
- **75% protection** after a single immunization
- Strong cellular and humoral responses after **1 or 2 doses** (NHP, camels and mice)



Track Record of Success with MERS DNA Vaccine – Clinical

- **Phase 1 (US) and Phase 2 (Korea)** data generated
- **76% seroconversion** after single immunization
- Over **80% seroconversion** after two immunizations
- **Strong and broad cellular responses** noted at all time points



Spike protein is the main target of **neutralizing antibodies**

- Considered a key component for vaccines
- Codon and RNA optimized

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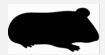
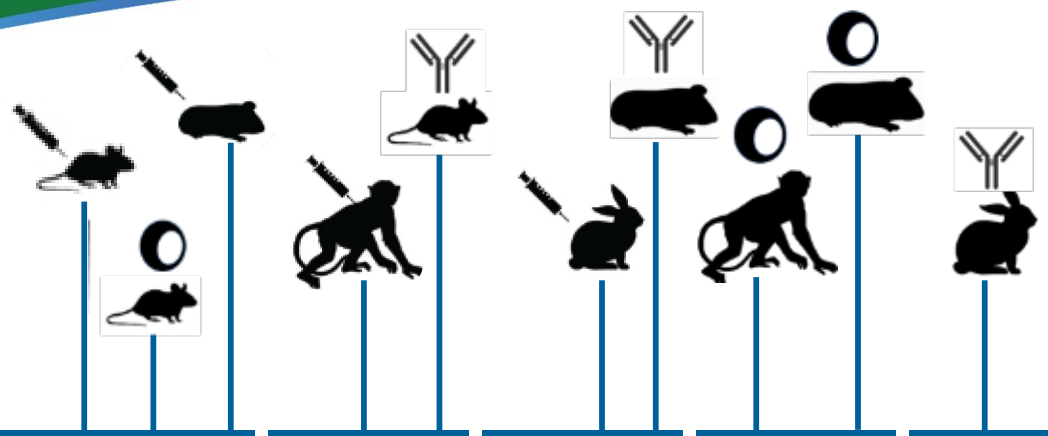
INO-4800 Preclinical Studies – Summary of Data

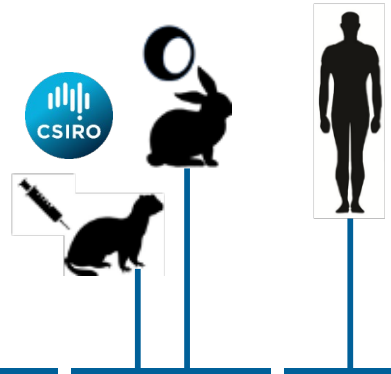
Species	T cell Responses	Binding antibody Responses	ACE2/Spike blocking	Biodistribution	Pseudovirus neut.	Live virus neut.
	✓	✓	✓	✓	✓	✓
	✓	✓	✓	✓	✓	✓
	✓	✓	✓	Study planned	✓	Study planned
	Study initiated	Study initiated	Study planned (awaiting sample shipment)	Study initiated	Study planned (awaiting sample shipment)	Study initiated
	✓	✓	✓	Study initiated	✓	Study initiated

INOVIO INO-4800 Preclinical Rapid Response Timeline



Species

- Mouse
- G. Pig (ID delivery)
- Rabbit (full human dose)
- NHP (immunogenicity/challenge)
- Ferret (challenge)



nature COMMUNICATIONS
Published

2/02	2/09	2/16	2/23	3/01	3/08	3/15	3/22	3/29	4/06	4/10	5/20

Feb 4th
In vitro expression data

nature COMMUNICATIONS
Submitted

ACE2/Spike blocking

Biodistribution

Pseudovirus neut.

Public Health England
Live virus neut.

THE WISTAR INSTITUTE

T cell data
Ab data
Immunization

First Subject Dosed in Phase 1 Trial – April 6th, 2020

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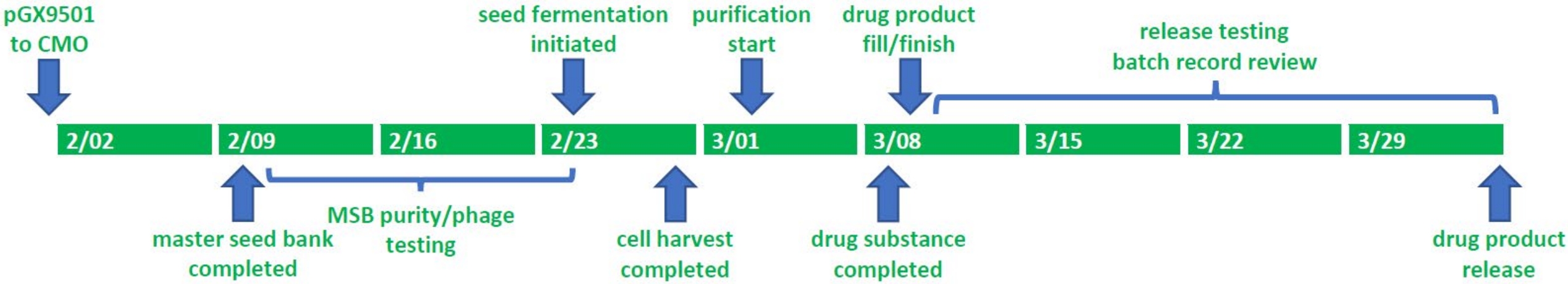
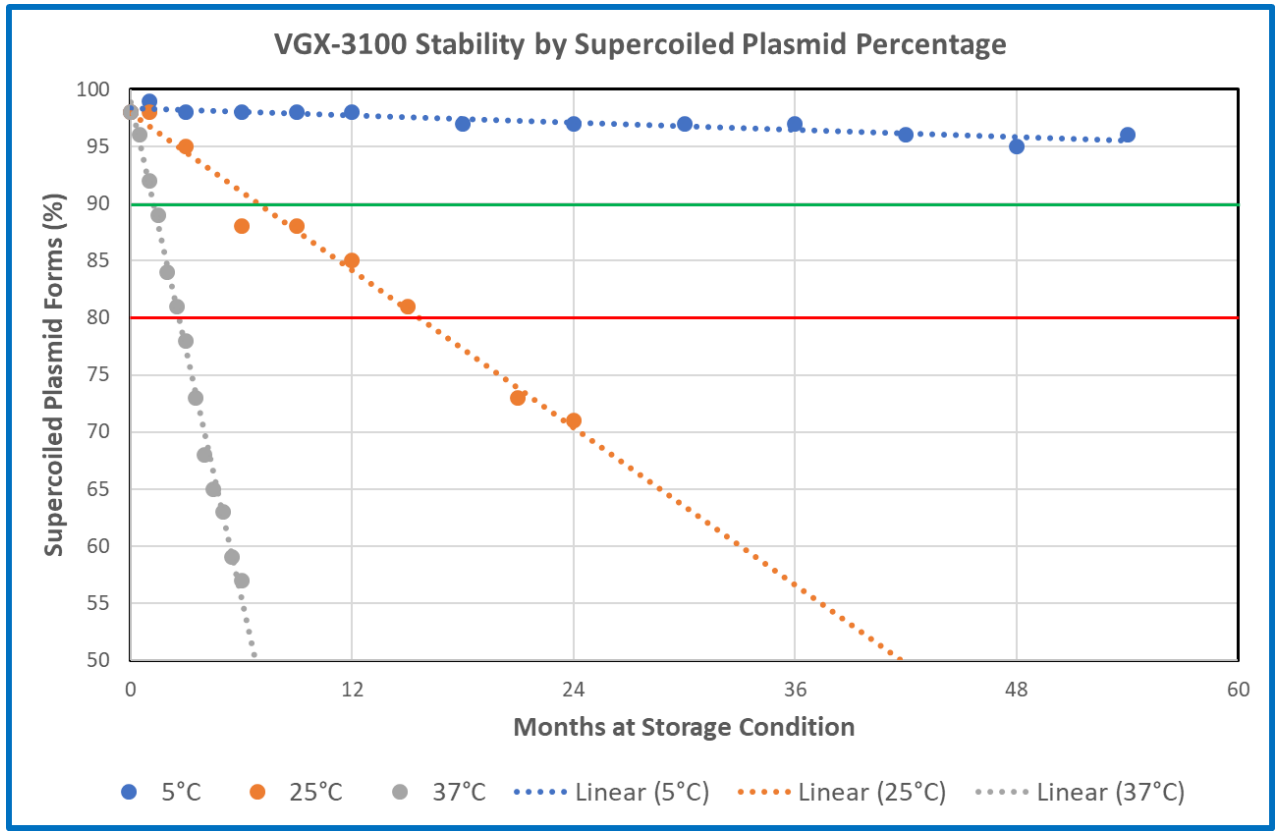
INO-4800 GMP Manufacturing – A Proven Platform

- **INO-4800 was manufactured for human clinical use using INOVIO's Platform MFG Process**
  - Process is established in a Platform Master File with FDA – 20 Drug Substances, 12 Drug Products
  - Process has received Advanced Therapy Medicinal Products (ATMP) certification for quality for manufacture of VGX-3100 (HPV 16/18 precancerous dysplasia)
  - Identical critical processing parameters (CPPs) and critical quality attributes (CQAs) for upstream and downstream drug substance manufacture and drug product fill/finish
- **Accelerated timeline from plasmid construction to release for human use**
  - 31-Jan (plasmid received by CMO) to 03-Apr (release for human use)



Stability Advantages of a DNA Plasmid Drug Product



- **VGX-3100 stability assessed at multiple storage conditions**
  - Real-time 5°C
  - Accelerated 25°C (Room Temp)
  - Stressed 37°C
- **Supercoiled % is most applicable measure of plasmid stability**
- **Only first order degradation of supercoiled to open circular form (single nicked strand)**
  - 2% loss over 54 months at 5°C
  - 85% supercoiled after 12 months at 25°C
  - Total circular forms maintained at 99-100% at all stability conditions – no formation of linearized plasmid

Clinical Safety and Success of the 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 approx. 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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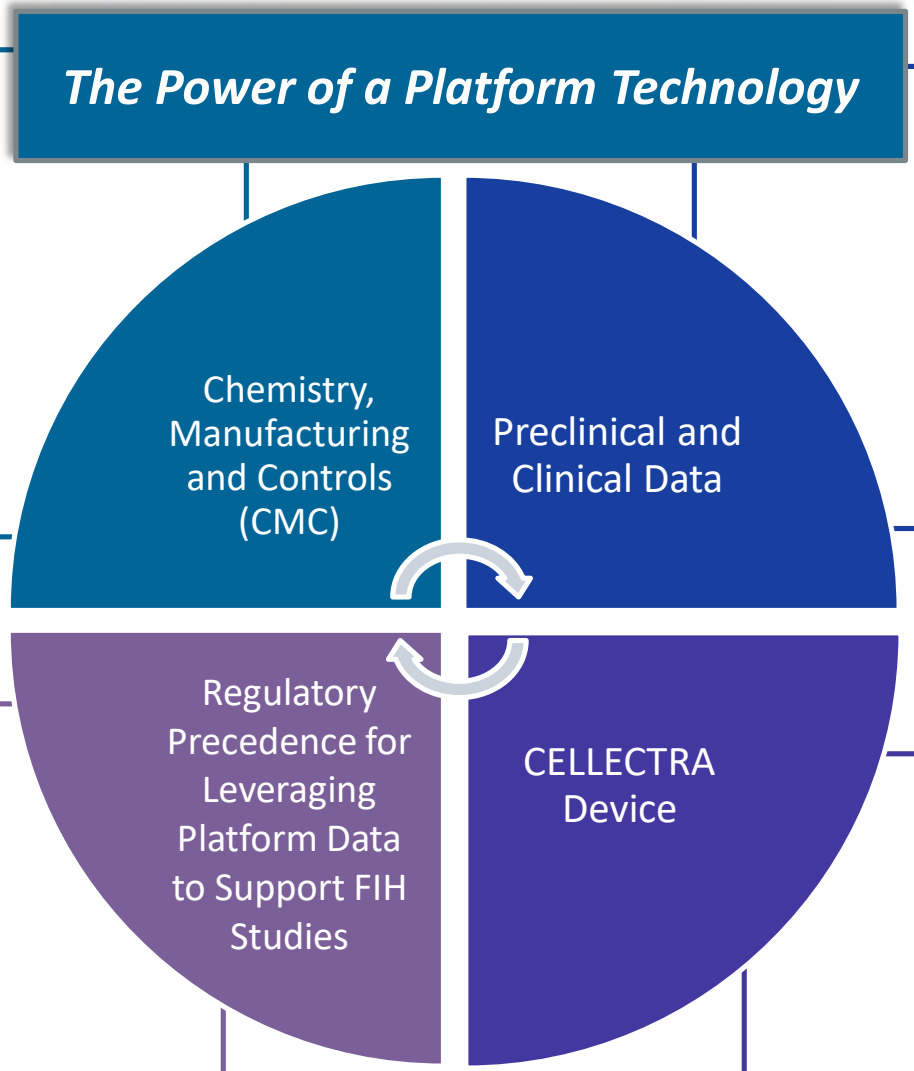
INO-4800: Regulatory Strategy - Leveraging the Power of A Platform Technology to Rapidly Advance a COVID-19 Vaccine Candidate to Phase 1 testing in the United States



- INO-4800 Release Data
- Standard plasmid construction and platform manufacturing process
- 20 drug substances and 12 drug products in a platform master file

- INO-4800 Preclinical Study Data
- Supportive preclinical and clinical data from similarly designed plasmids

US IND was given authorization to proceed on April 2nd, First subject dosed on April 6th 2020

- INO-4800 is the 16th program since 2008 to utilize this same regulatory approach for rapid advancement into Phase 1 testing

- Utilized in 34 Phase 1 and Phase 2 trials since 2008

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INO-4800: Global Regulatory Interactions (Feb/Mar 2020)

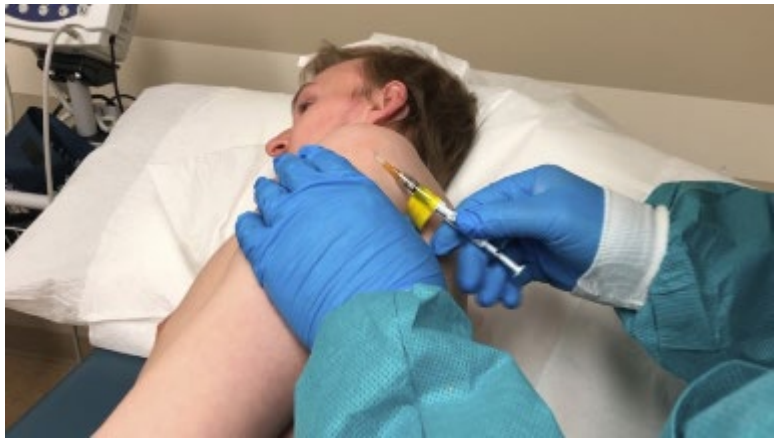
FDA	EMA	Ministry of Food & Drug Safety	NMPA China
Resounding support for platform technology approach • Facilitation of IND Review • Preliminary information on Emergency Use Authorization (EUA) for future consideration • Assess theoretical risk of vaccine-enhanced disease	Open and receptive to future discussions; specifically rapid Scientific Advice Assess theoretical risk for vaccine-enhanced disease	Highly motivated to rapidly advance to Phase 1 testing in Korea • Will consider waiver of GLP toxicology and biodistribution study requirement • Assess theoretical risk of vaccine-enhanced disease	Willing to evaluate platform data from similarly designed plasmids Facilitation of IND Review Assess theoretical risk of vaccine-enhanced disease

INO-4800 US Phase 1 Progress

- An open label **study design** in a small sample size – 40 healthy volunteers - to gain preliminary assessment on safety, tolerability and immunogenicity
- Utilize **historical experience** with clinical trial sites to quickly complete start-up activities
- **Front load preparatory** activities at the operational level for subjects to be dosed as soon as the clinical investigational product is available
- **Motivated** study sites and volunteers
- **Supportive** DSMB members to make rapid decision

Penn
University of Pennsylvania

The Center for Pharmaceutical Research
An AMR Company



Unprecedented speed in starting the study (**83** days from plasmid design to clinical testing) and completing enrollment (**17** working days)

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INO-4800 Looking Forward

JUNE – JULY 2020

- In June, U.S. Phase 1 trial and animal challenge results to be announced
- Phase 2/3 trial to evaluate vaccine efficacy in humans is expected to begin
- Human clinical trials expected to begin in China and South Korea*

ONGOING

- Scale-up INO-4800 COVID-19 vaccine production to target one million doses by the end of 2020, and 100's million doses by the end of 2021, for potential use under emergency authorization.*

**** Pending appropriate regulatory guidance and external funding***

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