Laurent M. Humeau

Advantages of DNA Vaccines in Response to COVID-19

NAIIS COVID-19 Vaccine Webinar

May 12, 2020

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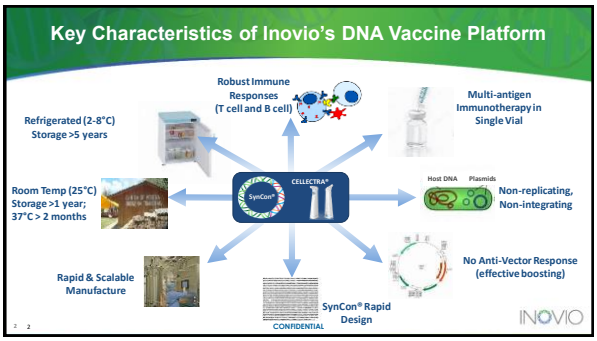
Key Characteristics of Inovio's DNA Vaccine Platform



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Applying Inovio's Platform to Emerging Infectious Disease

- Speed
  - Design of vaccine candidate
  - Rapidity of manufacture
  - Ability to harness established regulatory platform
- Safety Profile
  - Over 2000 subjects treated in the clinic with Inovio DNA + delivery technology
  - Over 6000 doses of DNA delivered
- Breadth of Immune Response
  - Ability to generate broad and robust B and T cell responses
  - Generation of neutralizing antibodies
- Duration of Response
  - Immune responses detected 3 years post immunization
  - Demonstration of protection 12 months+ following immunization
- Efficacy
  - First group to demonstrate clinical efficacy of a DNA vaccine combined with delivery technology
  - Multiple published reports of protection from challenge (MERS, Lassa, Influenza, Ebola, Zika)
- Stability of product
  - DNA product stored in optimized buffer & long term non-frozen
  - Stable at room temp for 1 year and at 37°C for 1 month

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Inovio Strategy for COVID-19 Program

Our strategy is to focus on licensure of INO-4800 by a dual strategy of emergency use authorization (EUA) and traditional approval pathway by:

- Moving rapidly into human Phase I studies to **demonstrate safety, tolerability and immunogenicity** ✓
- **Generating a preclinical** data package **that supports the clinical program** and enables potential EUA ✓
- **Aiming to be** a leader **to human proof of concept efficacy data**
- **Leveraging external funding** to conduct rapid clinical development and accelerate 3PSP development and initial scale up of manufacturing ✓
- **Expanding manufacturing capacity** for supporting delivery of 100s of millions of doses
- **Expanding our global partnerships**
  - To facilitating manufacturing scale up
  - Generate additional Phase 1 supportive data outside of the US (Korea & China)

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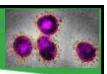
Inovio Response to Novel Coronavirus Outbreak (COVID-19) Builds Upon Prior Experience in Developing a MERS Vaccine



- To address the **urgent medical need** for a **medical countermeasure** to prevent the contined spread of COVID-19, Inovio has employed its **synthetic DNA-based vaccine technology**.
- Our DNA medicine technology is highly amenable to **accelerated candidate discovery** and **developmental timelines**, due to the ability to **rapidly design multiple product candidate constructs**, **manufacture large quantities of the drug product**, and the possibility to **leverage previous regulatory precedents to support entry to the clinic**.
- We designed our COVID-19 vaccine candidate, named INO-4800, based upon studies **targeting recent major coronavirus outbreak family members**. Our own extensive prior studies developing a countermeasure for MERS demonstrated that immunization of small and large animal models with synthetic DNA vaccines developed against MERS-CoV **spike (S) protein provided protection** against disease challenge with in multiple challenges, with out evidence of ADE.

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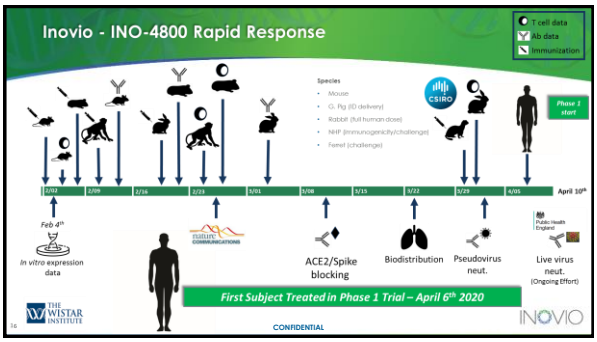
Inovio - INO-4800 Rapid Response



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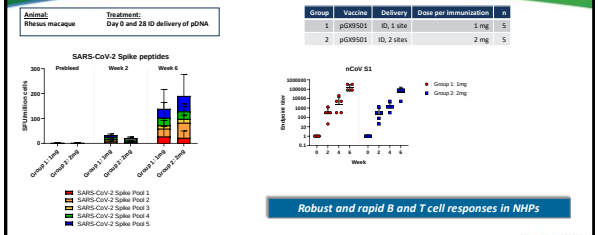
Robust Cellular and Humoral Immune Responses following Immunization of INO-4800 in Rhesus Monkeys



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

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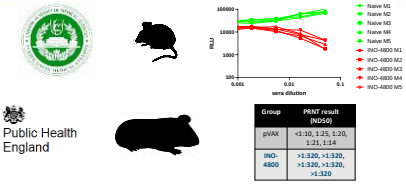
Detection of Neutralizing Antibodies



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

Neutralizing antibodies induced in mice and guinea pig in both a pseudo and live viral neut assay

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Demonstration of Preclinical Efficacy - SARS-CoV-2 Challenge Studies

ACE2 Tg Mouse Challenge at Peking Union Medical College, Beijing, China
- *18 mice – control, vs one, vs two Tx*
- *Results available May2020*

Ferret Challenge at CSIRO, Australia
- *Results from single dose challenge available June2020*

Public Health England

Primate Challenge at Porton Down, PHE, UK
- *12 NHP – two vaccine doses*
- *Includes a positive control group to address VED*
- *Results available July2020*

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INO-4800 US Phase 1 Progress

- An open label **study design** in a small sample size 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

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

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Grateful Thanks to our Financial Supporters and Partners to Date for COVID-19 Program

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BILL & MELINDA GATES foundation

International Vaccine Institute

Public Health England

THE WISTAR INSTITUTE

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