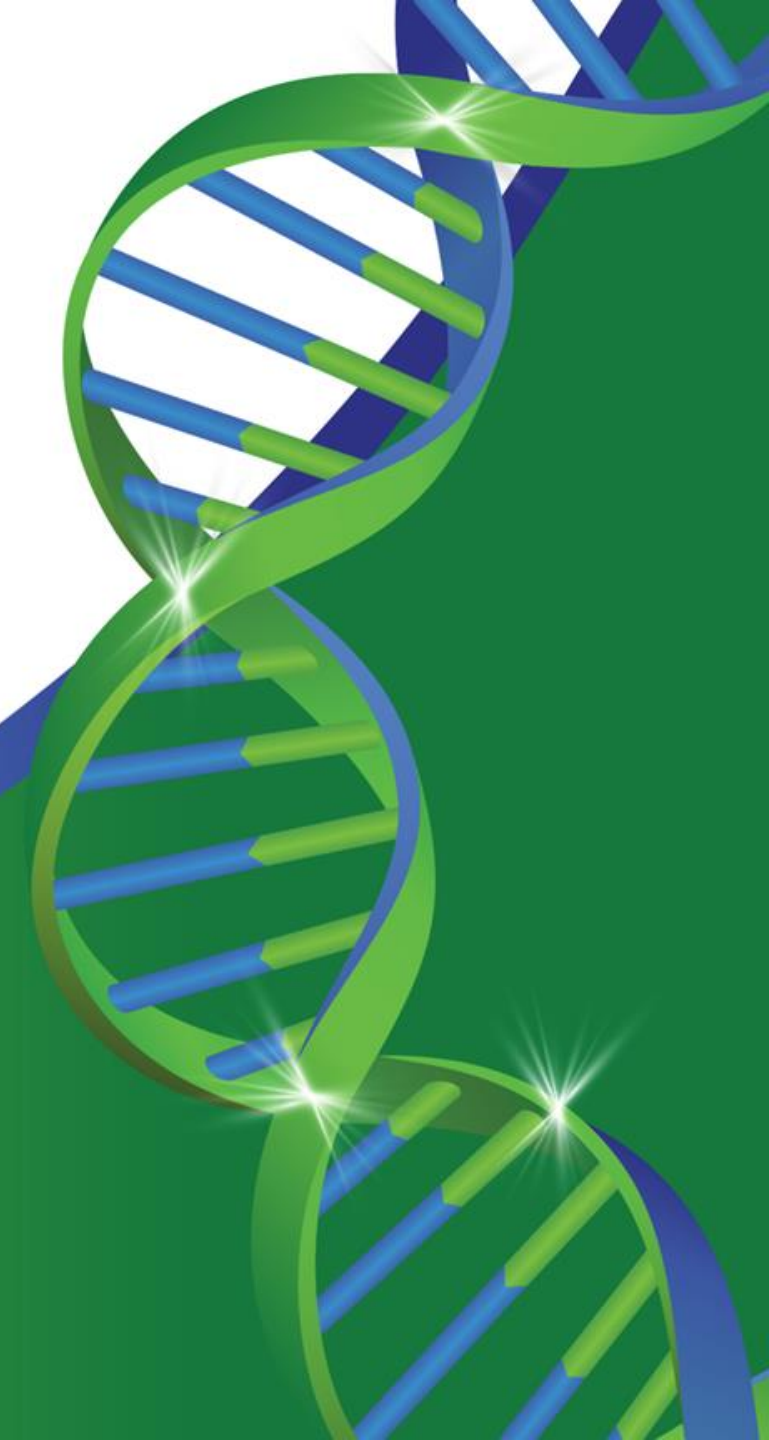


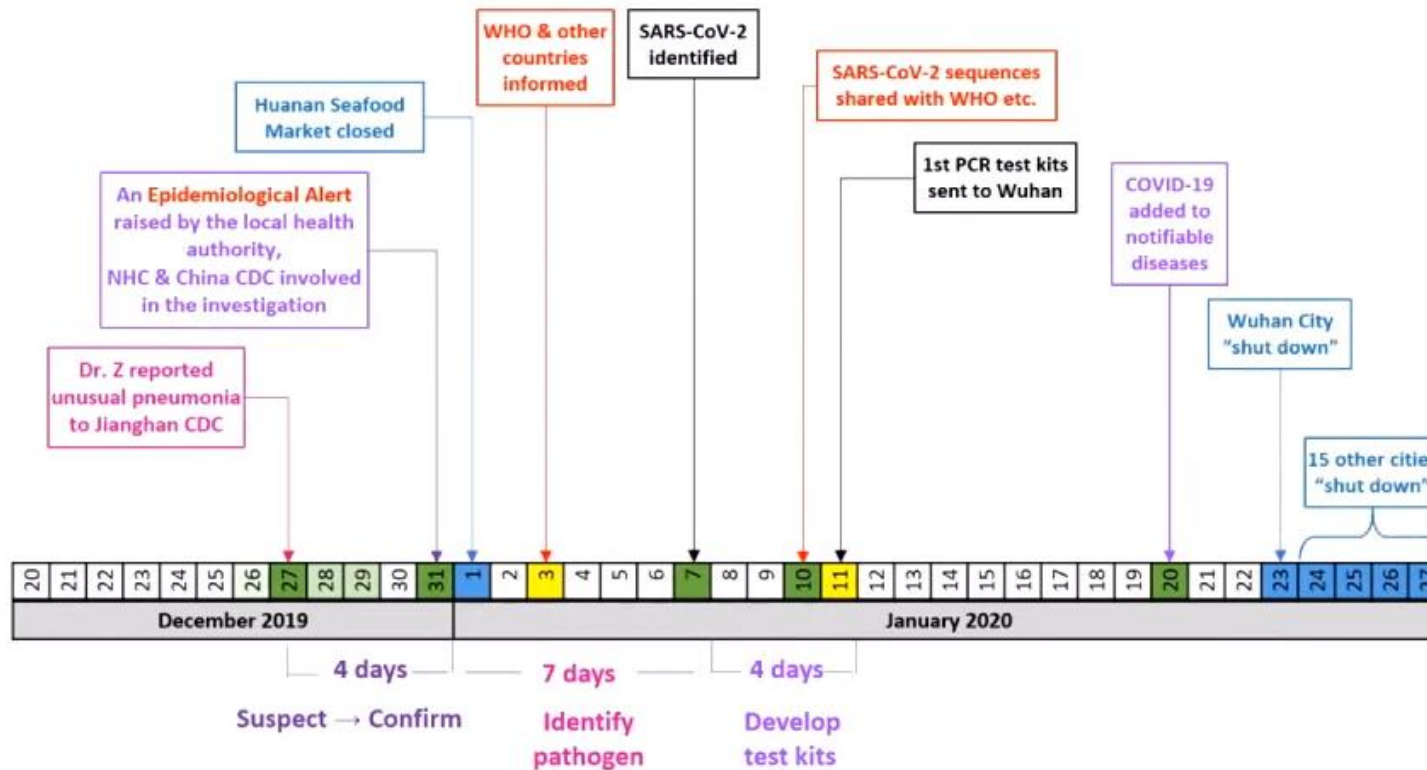
INO-4800: A vaccine against SARS-CoV-2, the infectious agent of COVID-19

**Pablo Tebas, MD
University of Pennsylvania**



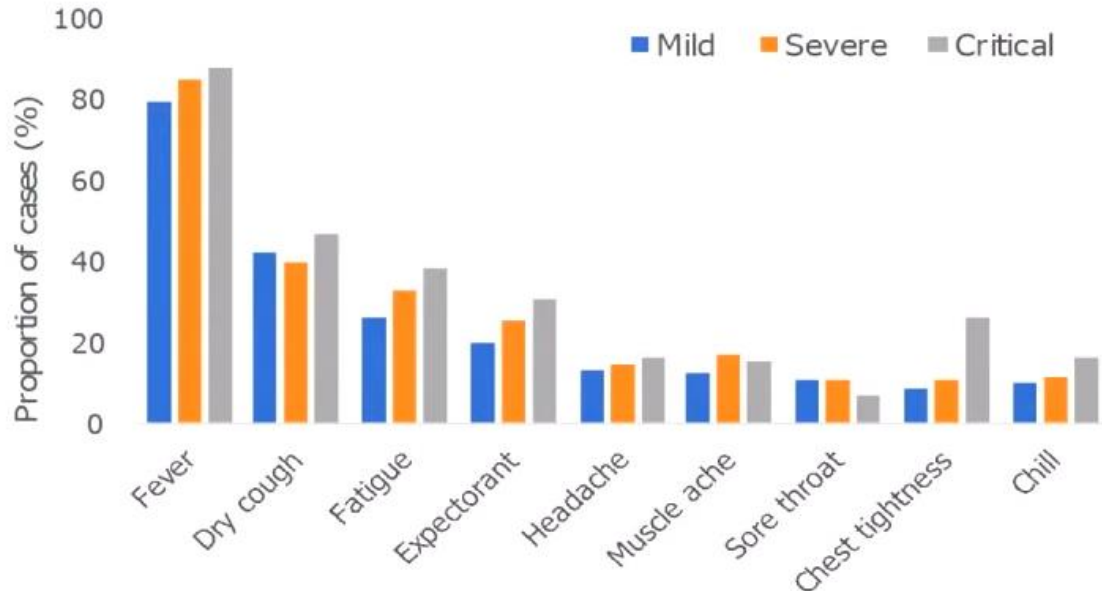
The history of COVID-19 and the remarkable Chinese response

Early Events



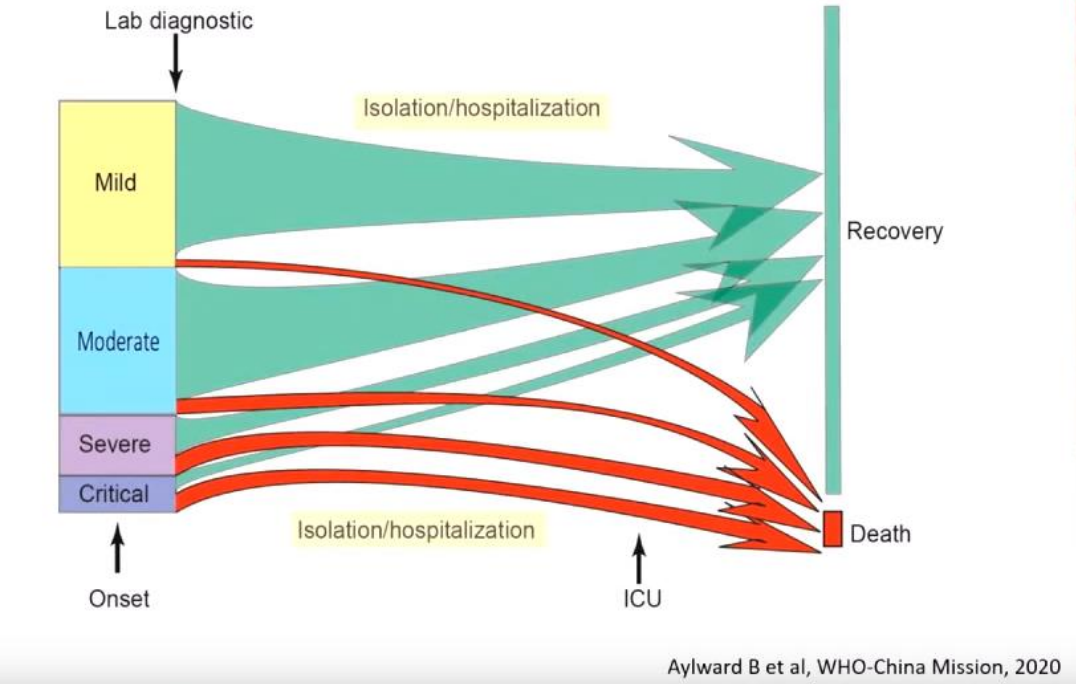
Clinical manifestations

Common Symptoms of COVID-19 in China



19230 Confirmed cases with detailed epidemiological investigation information
China CDC/NHC 2020

Clinical prognosis and recovery



Aylward B et al, WHO-China Mission, 2020

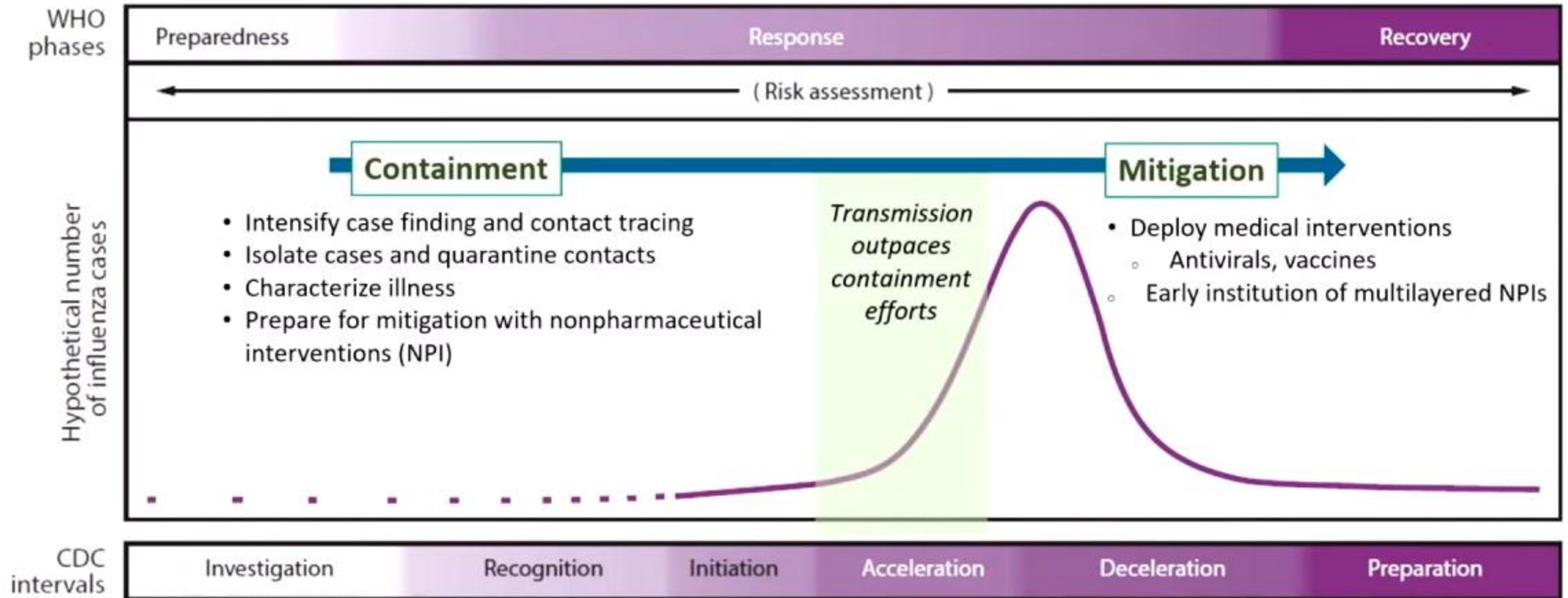
Key clinical facts about the epidemic

Key epi/technical insights from China (2 of 3)

2-Natural history:

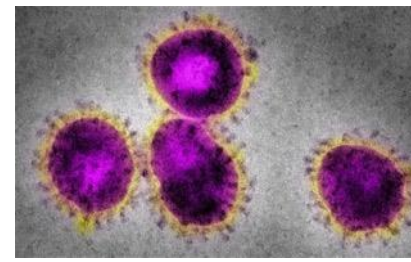
- At **diagnosis**: approx. **80%** are mild/moderate; **15%** severe; **5%** critical
- **Progression**: approx. **10-15%** of mild/moderate cases become severe, and approximately **15-20%** of severe become critical
- **Average times**:
 - from exposure to symptom onset is **5-6** days;
 - from symptom onset to recovery for mild cases is **2 weeks** and for severe cases is **3-6 weeks**;
 - from symptom onset to death is **2-8 weeks**
- Truly **asymptomatic** infection is unknown without serology, but appears to be rare using molecular testing (**<1%**)
 - an estimated **75%** of 'asymptomatic' cases at time of diagnosis soon progress to disease
- **Children** tend to have milder disease than adults

Preparedness and Response Framework for Pandemics



Adapted from: Holloway 2014, [MMWR Recomm Rep;63\(No. RR-6\)](#). Qualls 2017, [MMWR Recomm Rep; 66\(No. RR-1\)](#). Jernigan 2020, [MMWR Early Release: February 25, 2020](#).

Inovio Response to Novel Coronavirus Disease (COVID-19) Outbreak



- To address the **urgent medical need** for a **medical countermeasure** to prevent the further spread of COVID-19, Inovio has employed their **synthetic DNA-based vaccine technology** to address this critical need.
- Furthermore, this technology has **demonstrated proof of concept efficacy and safety in humans** in a phase IIb randomized, double-blind, placebo-controlled study, for human papillomavirus (HPV) associated cervical pre-cancer and is currently in two multinational phase 3 trials for that indication [NCT03185013; NCT03721978] and several phase 2 trials for related and other indications.

Inovio Response to Novel Coronavirus Outbreak (COVID-19)

- For the development of a COVID-19 vaccine candidate Inovio have **built upon their prior experience in developing a MERS coronavirus (MERS-CoV) vaccine (INO-4700)** (whose development has been partnered with CEPI) and our rapid vaccine design and manufacturing pathway previously utilized for the Zika vaccine candidate GLS-5700.
- Inovio designed the COVID-19 vaccine candidate, named INO-4800, based upon studies **targeting the SARS and MERS coronavirus family members**. Inovio's rapid vaccine design, manufacturing and development have been previously demonstrated for the Zika vaccine candidate (GLS-5700).
- INO-4800 is currently in preclinical testing and is being GMP manufactured for first in human testing in early summer (US and China sites)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Immunogenicity of an Anti-Zika Virus DNA Vaccine — Preliminary Report

Pablo Tebas, M.D., Christine C. Roberts, Ph.D., Kar Muthumani, Ph.D., Emma L. Reuschel, Ph.D., Sagar B. Kudchodkar, Ph.D., Faraz I. Zaidi, M.S., Scott White, M.D., Amir S. Khan, Ph.D., Trina Racine, Ph.D., Hyeree Choi, B.S., Jean Boyer, Ph.D., Young K. Park, J.D., Sylvie Trottier, M.D., Celine Remigio, D.P.T., R.N., Diane Krieger, M.D., Susan E. Spruill, M.S., Mark Bagarazzi, M.D., Gary P. Kobinger, Ph.D., David B. Weiner, Ph.D., and Joel N. Maslow, M.D., Ph.D.

Inovio CEPI Consortium

- Inovio Awarded up to \$56 Million from CEPI to Advance DNA Vaccines Against Lassa Fever and MERS on April 11, 2018
 - Major investment by CEPI to advance vaccine development and manufacturing on two of CEPI's highest priority infectious diseases
 - Translational portfolio program encompassing cGMP manufacturing and clinical development of DNA vaccine candidate against Lassa and MERS virus
- CEPI awarded Inovio a grant of up to \$9 million to develop a vaccine against the recently emerged strain of coronavirus (COVID-19) in January 2020



PRESS RELEASE DETAILS

[View all news](#)

Inovio Selected by CEPI to Develop Vaccine Against New Coronavirus

January 23, 2020

PLYMOUTH MEETING, Pa., Jan. 23, 2020 /PRNewswire/ -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) today announced the Coalition for Epidemic Preparedness Innovations (CEPI) has awarded Inovio a grant of up to \$9 million to develop a vaccine against the recently emerged strain of coronavirus (2019-nCoV) that has killed numerous people and infected hundreds more in China to date. This initial CEPI funding will support Inovio's preclinical and clinical development through Phase I human testing of INO-4800, its new coronavirus vaccine matched to the outbreak strain. CEPI previously awarded Inovio a grant of up to \$56 million for the development of vaccines against Lassa fever and Middle East Respiratory Syndrome (MERS), also caused by a coronavirus.

Inovio's participation in this developing effort is based on the ideal suitability of its DNA medicine platform to rapidly develop a vaccine against an emerging virus with pandemic potential, proven vaccine development capabilities and a strong track record of rapidly generating promising countermeasures against previous pandemic threats. Inovio was the first to advance its vaccine (INO-4700) against MERS-CoV, a related coronavirus, into evaluation in humans. Inovio is currently preparing to initiate a Phase 2 vaccine trial for INO-4700 in the Middle East where most MERS viral outbreaks have occurred.

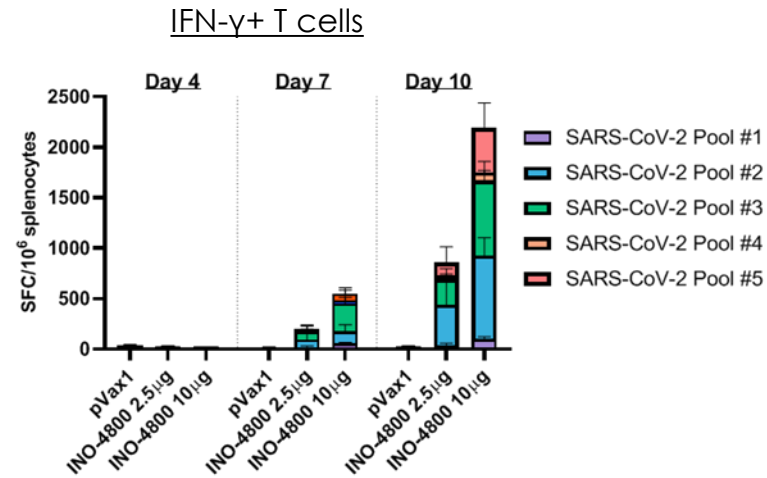
In a recently published paper in *Lancet Infectious Diseases*, Inovio's Phase 1 study of its MERS-CoV vaccine demonstrated it was well tolerated and furthermore induced high levels of antibody responses in roughly 95% of subjects, while also generating broad-based T cell responses in nearly 90% of study participants. Durable antibody responses to INO-4700 were also maintained through 60 weeks following dosing.

Richard Hatchett, CEPI's CEO, said, "Given the rapid global spread of the 2019-nCoV virus the world needs to act quickly and in unity to tackle this disease. Our intention with this work is to leverage our work with Inovio on the MERS coronavirus and rapid response platform to speed up vaccine development."

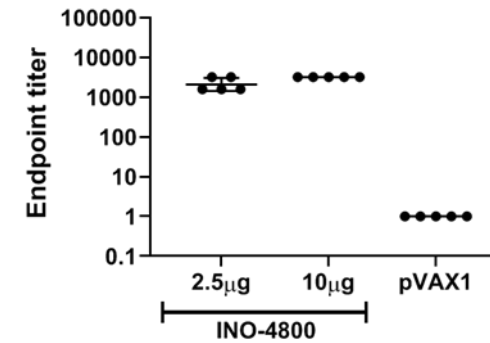
INO-4800 Vaccine Preclinical Development

INO-4800: Immunogenicity in *in vivo* models

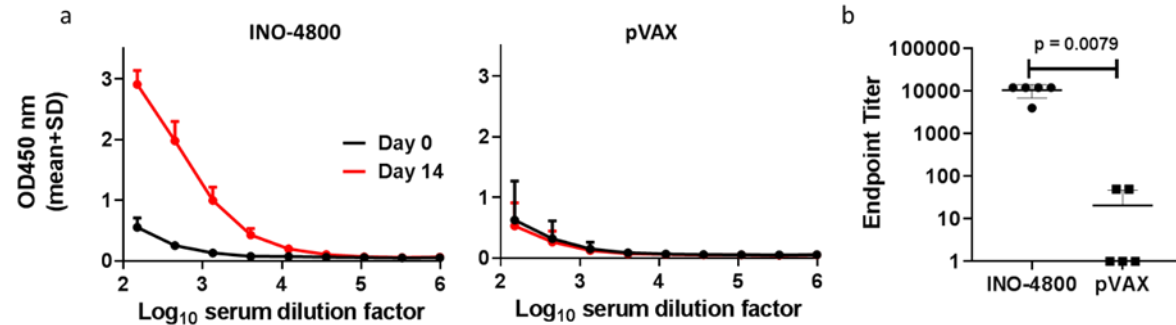
Single dose



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



SARS-CoV-2 S protein serum IgG binding



Robust cellular and humoral immune responses measured after a single dose of INO-4800 in mice and guinea pigs

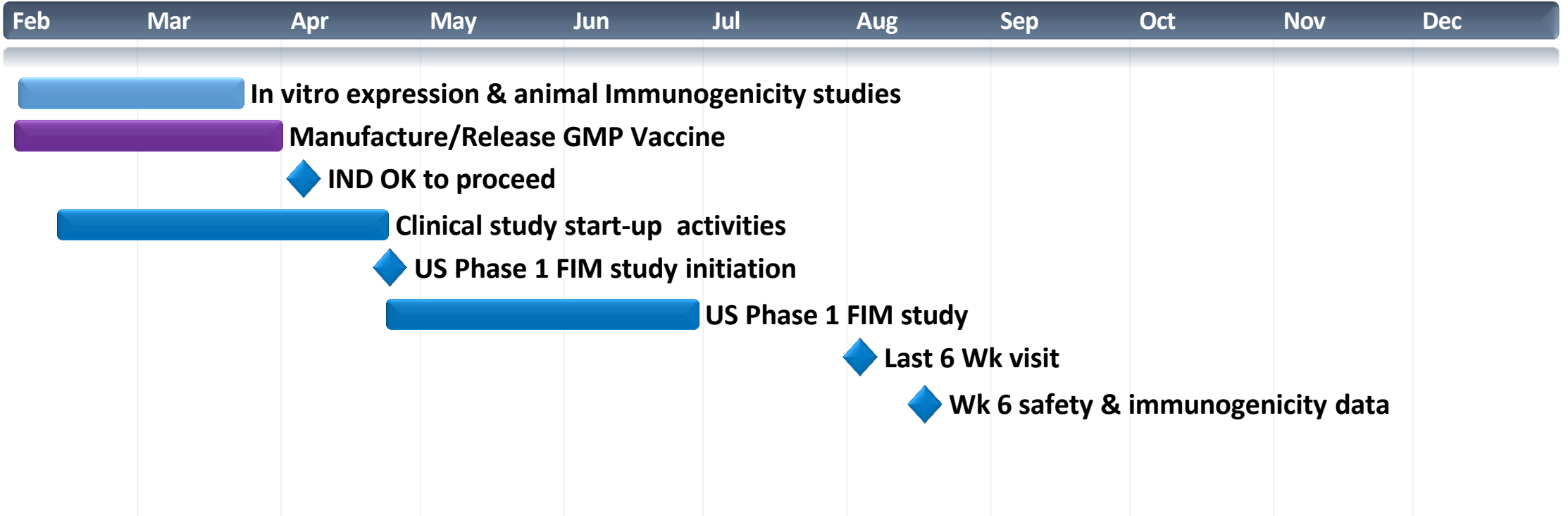
INO-4800: Clinical Development Strategy



Clinical Development Strategy for INO-4800

- **US – Phase I FIH study of INO-4800 under US IND**
- **Objective:** Rapid conduct of a Phase 1 first in human study of INO-4800 delivered by ID administration followed by electroporation in the US under an US IND.
- **Status:** Initial funding of up to \$9M awarded by CEPI and initial agreement executed. IND-enabling activities ongoing including animal immunogenicity studies and manufacture of GMP clinical investigational product.

2020

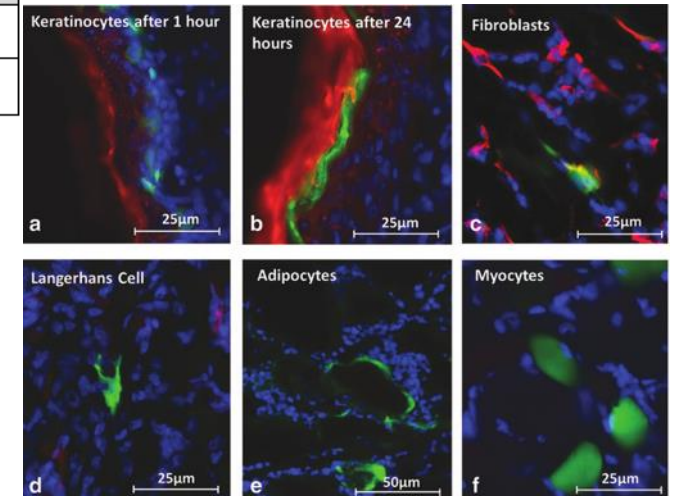


Study design

Table 1: COVID19-001 Dose Groups

Study Group	Number of Subjects	Dosing Weeks	Number of Injections + EP per Dosing Visit	INO-4800 (mg) per injection	INO-4800 (mg) per Dosing Visit	Total Dose of INO-4800 (mg)
1	20	0, 4	1	1.0	1.0	2.0
2	20	0, 4	2 ^a	1.0	2.0	4.0
Total	40					

^aINO-4800 will be injected ID followed by EP in an acceptable location on two different limbs at each dosing visit



GFP expression appearing in multiple skin-resident cell types following **ID delivery with EP**

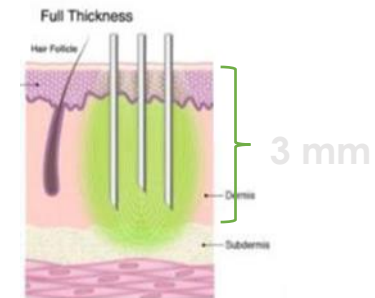


TABLE 2 - CLINICAL TRIAL SCHEDULE OF EVENTS

Tests and assessments	Screen ^a	Day 0		Day 1 (+1d)	Week 1 (± 3d)	Week 4 (± 5d)		Week 6 (± 5d)	Week 8 (± 5d)	Week 12 (± 5d)	Week 28 (± 5d)
		Pre	Post			Pre	Post				
Informed Consent	X										
Inclusion/Exclusion Criteria	X										
Medical History	X	X									
Demographics	X										
Concomitant Medications	X	X			X	X		X	X	X	X
Physical Exam ^b	X	X			X	X		X	X	X	X
Vital Signs	X	X			X	X		X	X	X	X
Height and Weight	X										
CBC with Differential	X				X			X	X	X	X
Chemistry ^c	X				X			X	X	X	X
Serology ^d	X										
12-lead ECG	X										
Urinalysis Routine ^e	X				X			X	X	X	X
Pregnancy Test ^f	X	X				X					
INO-4800 + EP ^g		X ^h				X ^h					
Download EP Data ⁱ			X				X				
Adverse Events ^j	X	X	X	X ^k	X	X	X	X	X	X	X
Immunology (Whole blood) ^l	X	X				X		X	X	X	X
Immunology (Serum) ^m	X	X				X		X	X	X	X