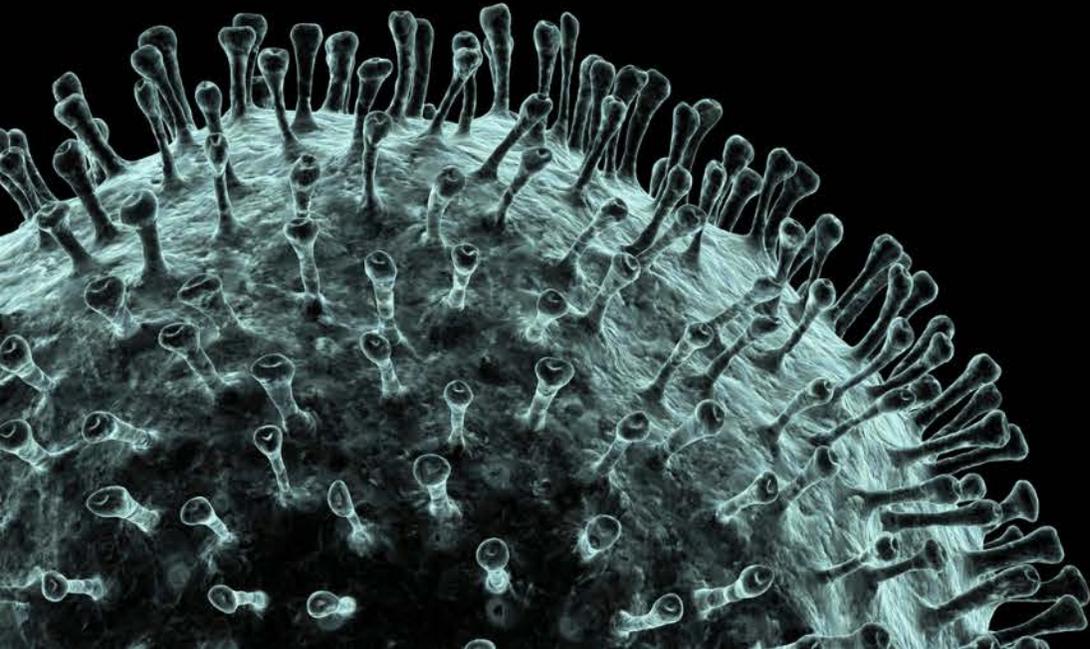


COVID-19 Conversations



Larry Corey

**Past President and Director
Fred Hutch**



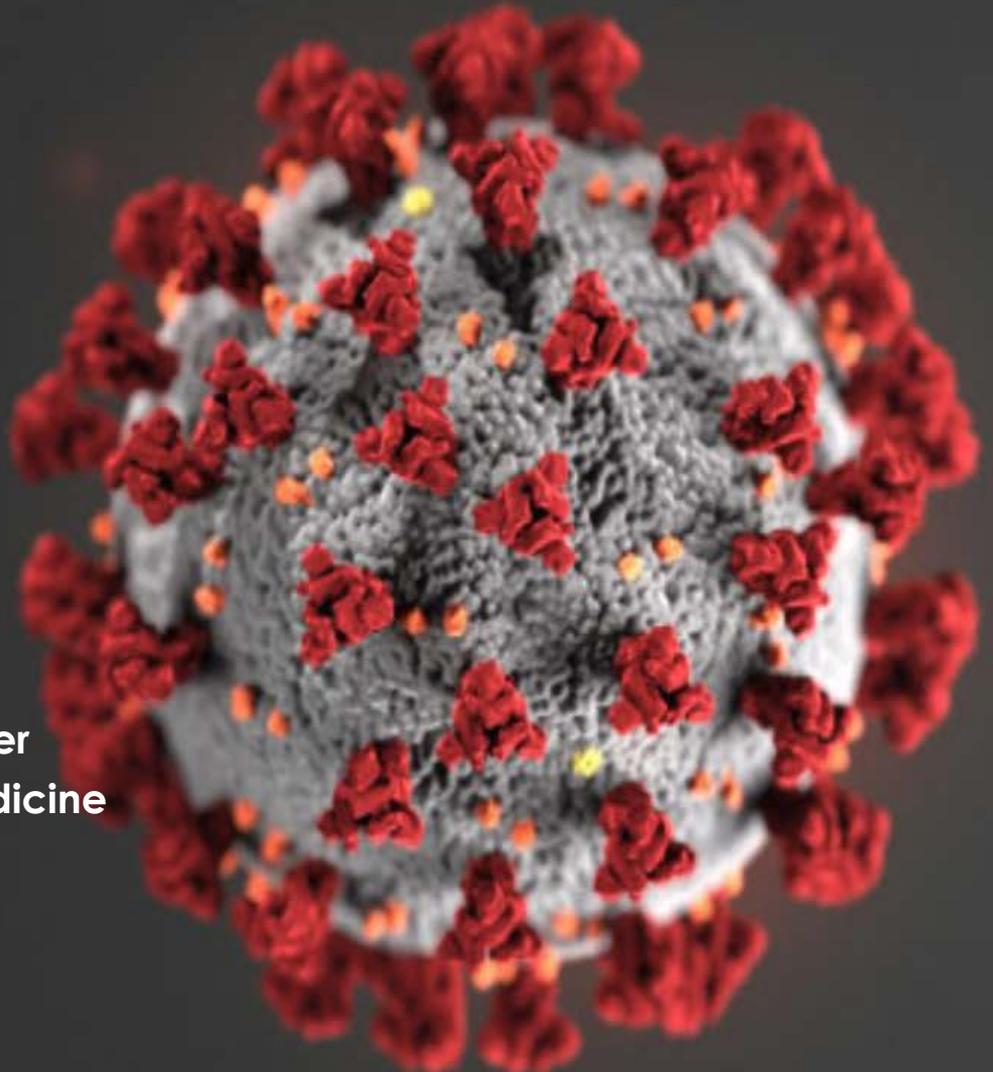
COVID19Conversations.org

[#COVID19Conversations](https://twitter.com/COVID19Conversations)



COVID-19 Vaccine Development

Larry Corey, MD
Fred Hutchinson Cancer Research Center
Professor, Medicine and Laboratory Medicine
University of Washington
Seattle, WA



Conceptual Framework for COVID-19 Vaccine Development

April 2020

We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children

- 220 million adults in US alone.

Use known platforms to cover the field scientifically.
Manufacturing scalability is a key factor.

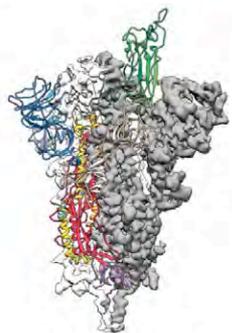
Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples' arms throughout the world.

Goal of OWS Program: To Assess Major Vaccine Platforms to COVID-19

Platform Vaccine Technologies

- Protein vaccines
 - soluble prefusion trimer (Sanofi/GSK)
 - transmembrane bound spike nanoparticle (Novavax)



- Viral vector vaccines

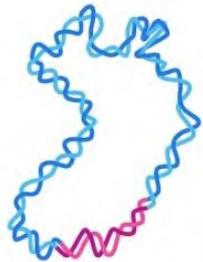
- Ad26 vector



- ChimpAdOx1



- RNA and DNA technology



Immunogenicity Data from Phase 1 Clinical Trials+

	Moderna 100 ug 2 dose	ChAdOx1 nCoV-19 2 dose	Ad26 1 dose 5x10 ¹⁰ VP	Novavax 5 ug/50 ug 2 dose
Spike GMT		1:1,000	596	
Live virus neut GMT		1:400	1:214	
Pseudovirus neut GMT				

+The data are not in the same lab.



Published online May 11, 2020

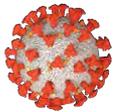
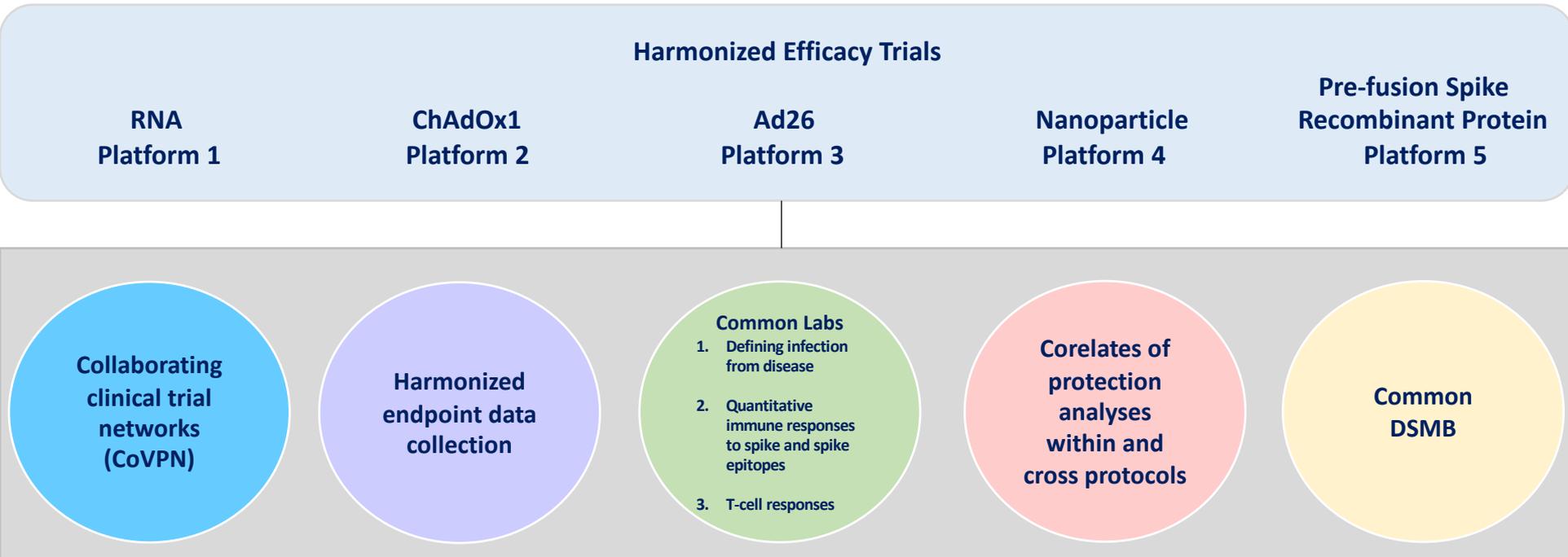
Science

A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

The full development pathway for an effective vaccine for SARS-CoV2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. . . .**We further discuss a collaborative platform for conducting harmonized, randomized controlled vaccine efficacy trials. This mechanism aims to generate essential safety and efficacy data for several candidate vaccines in parallel, so as to accelerate the licensure and distribution of multiple vaccine platforms and vaccines to protect against COVID-19**

Organizational Structure of OWS Clinical Trials Program





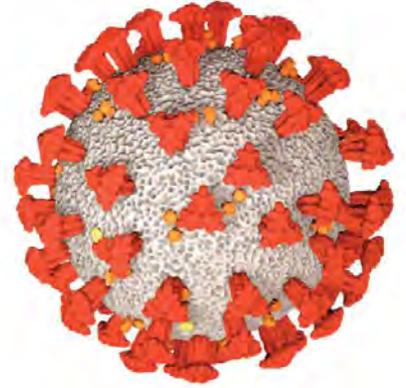
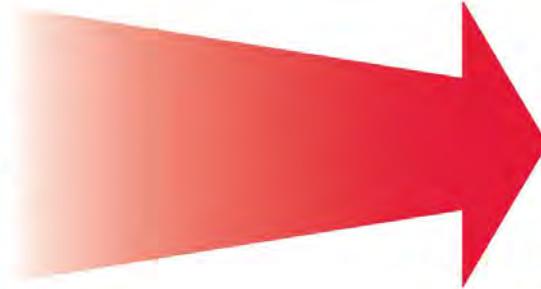
HIV VACCINE
TRIALS NETWORK



Infectious Diseases Clinical Research Consortium



HPTN
HIV Prevention
Trials Network



COVID-19
Prevention Network

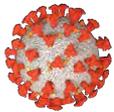
COVID-19 PREVENTION NETWORK PHASE 3 EFFICACY TRIAL TIMELINE

July	August	September	October	November
Moderna July 27	AstraZeneca August 29	Johnson & Johnson	Novavax	Sanofi
Pfizer July 28	Paused Sept 9	September 22	Early December	Late December

Balancing Harmonized Clinical Trial Design with Regulatory Realities

Main Goal: To evaluate each candidate vaccine with high veracity for safety and potential efficacy in reducing COVID-19 Disease.

- Each trial 30,000 persons; 150 disease endpoints
- Critical to enroll Black, LatinX and Tribal Communities into each trial
- Essential to evaluate vaccines in the epidemiological setting of persons at greatest risk of its complications; including comorbidities, age and race



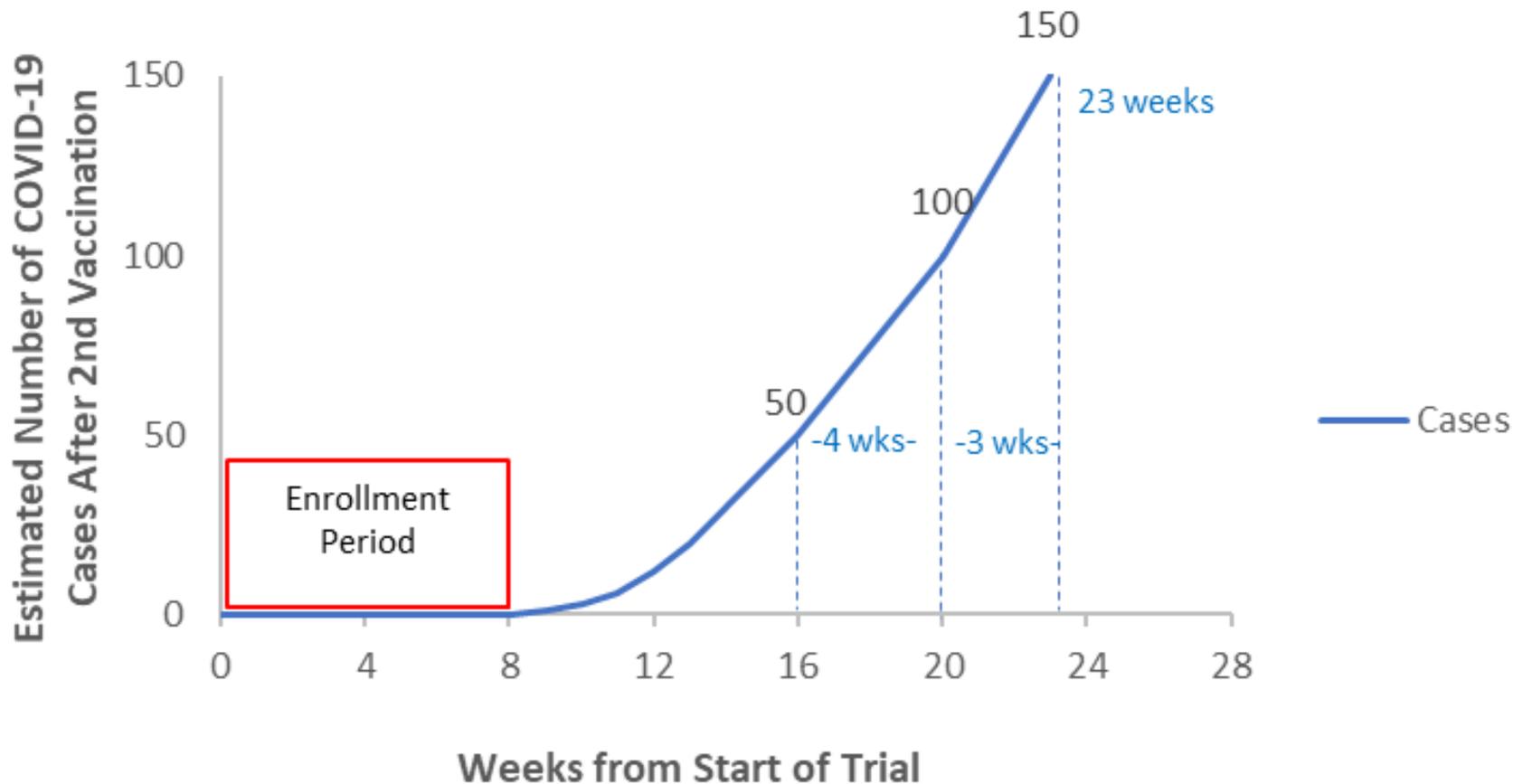
WHAT'S THE
CHALLENGE?

WE NEED OVER **125,000**
VOLUNTEERS
READY TO ROLL UP
THEIR SLEEVES BY THE
END OF 2020



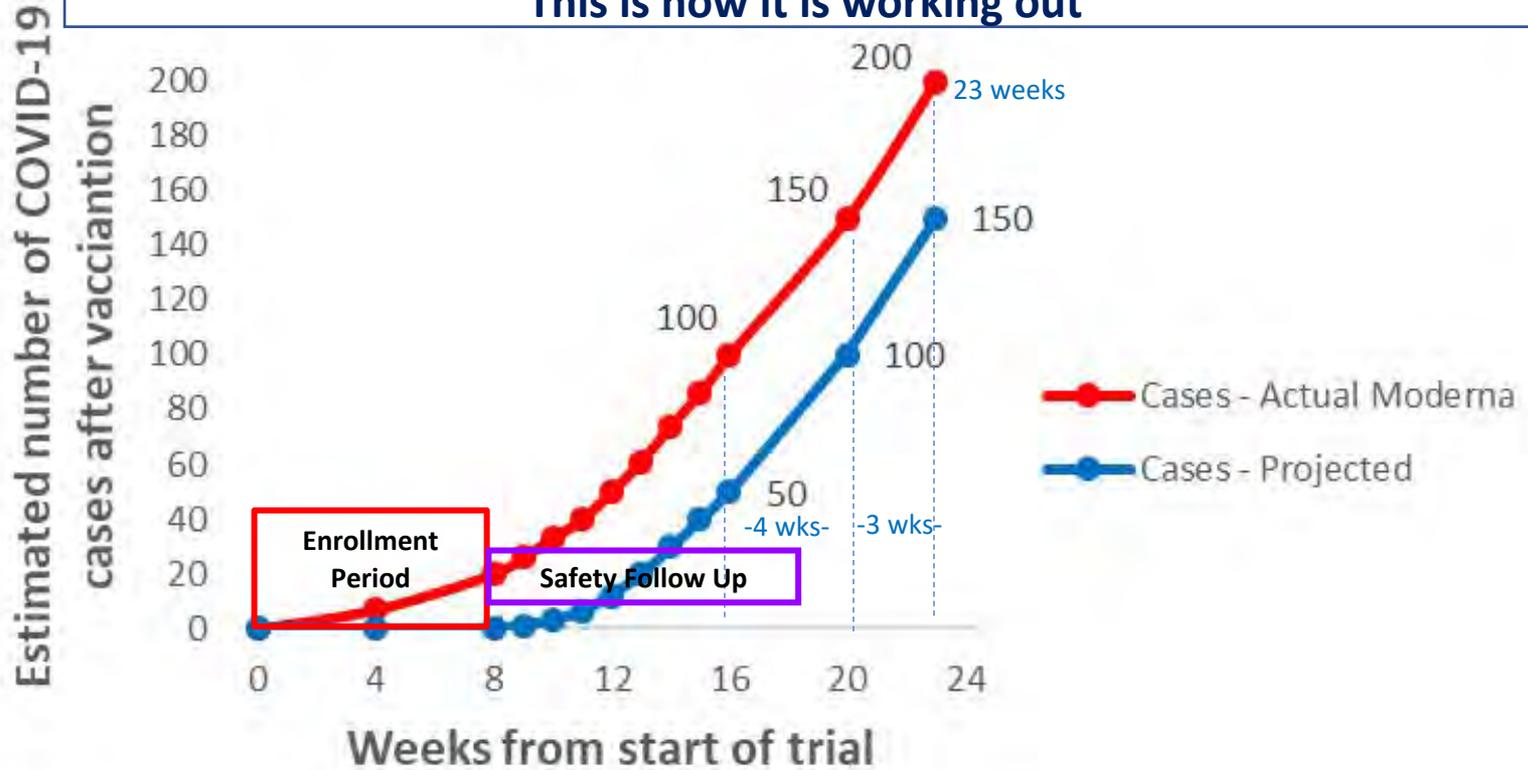
Projected # Cases of COVID-19 in 30,000-person 2 Dose SARS-CoV-2 Vaccine Trial

This is how we designed the trial



Cases of COVID-19 in 30,000-person 2 Dose SARS-CoV-2 Vaccine Trial

This is how it is working out



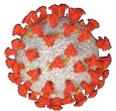
mRNA Vaccines

Pfizer Vaccine

- Prefusion spike transcript
- 2 doses 21 days apart
- VE = 95%
- 162 cases of symptomatic disease in placebo; 8 in vaccine group
- 10 cases of severe disease; 9 in placebo, 1 in vaccine
- VE 94% in those >65

Moderna Vaccine

- Prefusion spike transcript
- 2 doses 28 days apart
- VE = 94.5% efficacy
- 90 cases of symptomatic disease in placebo; 5 in vaccine group
- 11 cases of severe disease - all 11 in placebo group
- No difference in VE by age and ethnicity (20% endpoints in these groups)



Astonishing

- To have 2 large scale efficacy trials enrolled and completed independently, with such similar results, is remarkable.
- The spike part of the RNA transcript is essentially identical; allowing one to feel quite comfortable about the veracity of the efficacy data.
- The safety data from the trials needs to be made public, so one can evaluate it. Available data suggest the vaccines are well tolerated, more side effects with the second dose and somewhat lower severity of systemic side effects in older persons.
- The similarity of the data means either vaccine can do the job and should simplify that part of the distribution process.



Marvelous - but we are not done!

- Vaccines don't save lives; vaccinating people saves lives!
- USG contracts for mRNA is 100 million doses from each company.
- Timeline uncertain, but supposedly we will get these cumulative 200 million by April / May 2021.
 - 25 million doses Pfizer and 15 million Moderna in December
 - 30 million doses Pfizer and 20 million Moderna in January
 - 35 million Pfizer and 25 million Moderna in February and March
 - This is enough for first responders, medical personnel, elderly, and staff in nursing homes; and getting close to the complete NAM 1B group
- We need the other vaccines for the rest of the adult populations, as well as kids and pregnant women, where experience is much greater with Ad26 vector and the recombinant protein vaccines with adjuvants.
- Keeping the ongoing trials, as well as creating way to test the Recombinant Protein Platforms post EUA, is critical for overall vaccine strategy and getting everyone back to school and work.
- This means keeping the AZ and Janssen trials intact until end of February / mid-March.



Gap in the Phase 3 Vaccine Efficacy Trial Portfolio

- We do not know if the vaccine reduces acquisition of infection. Do persons still get infected after vaccination and if so, are they still infectious to others?
 - Shifting the disease spectrum from 75% symptomatic / 25% asymptomatic to 5% symptomatic / 95% asymptomatic
- If this is the case, community spread and population-based effects will be highly dependent on vaccine coverage; individual cases of severe disease will likely occur – especially in underserved populations.
 - In HIV terms - $U = U$
 - In COVID-19 terms - does $VE_i = U$?
- On an individual level - do I still need to wear a mask after vaccination?
 - Until we find this out – yes!
- The infectivity of this pathogen is formidable and defining the effect of these vaccines on infectivity and onward transmission is the next frontier for us to investigate.



Thank You

Network Collaboration

- HVTN Executive Management Team:
 - Glenda Gray, Scott Hammer, Georgia Tomaras, Dan Barouch, Julie McElrath, Peter Gilbert, Susan Buchbinder, Jim Kublin, Troy Martin
- Mike Cohen / HPTN
- IDCRC
- David Montefiori

DAIDS

- Emily Erbelding
- Carl Dieffenbach

VRC

- John Mascola
- Barney Graham
- Julie Ledgerwood

NIH

- Tony Fauci
- Francis Collins
- Hilary Marston
- Hugh Auchincloss

OWS

- Moncef Slaoui
- Mary Marovich
- Merlin Robb
- Tina Tong
- Julie Ake

