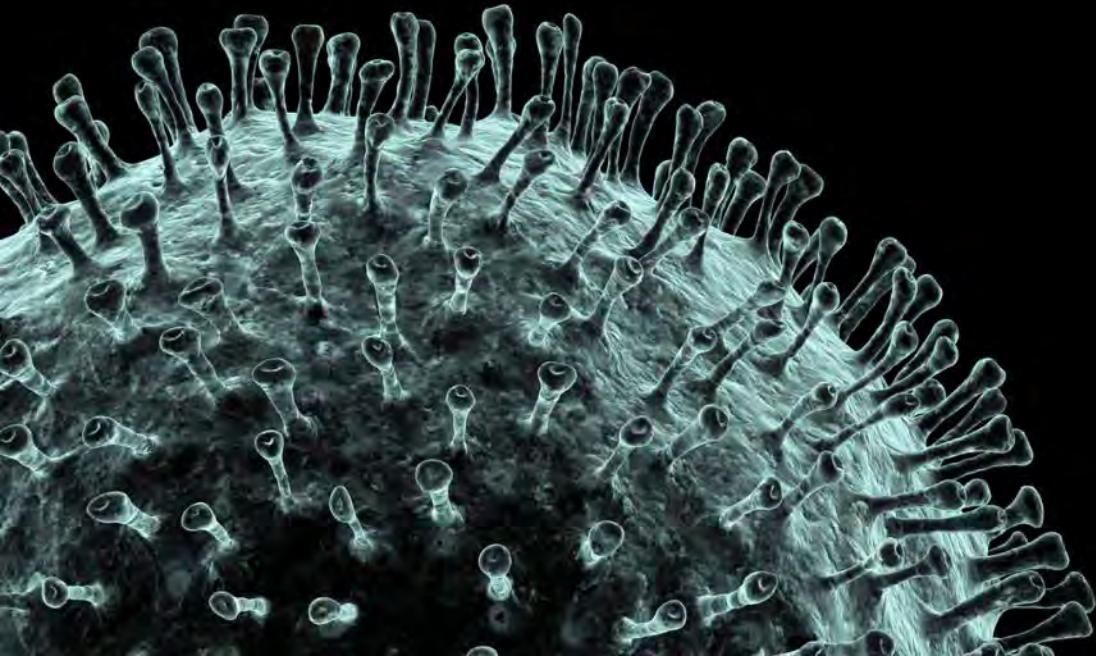


# COVID-19 Conversations



Larry Corey

Fred Hutchinson Cancer Research Center



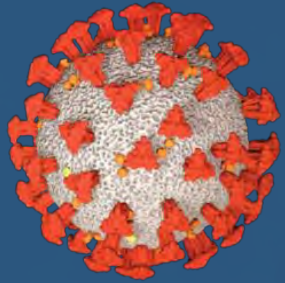
[COVID19Conversations.org](https://COVID19Conversations.org)

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





**FRED HUTCH**  
CURES START HERE



**COVID-19**  
Prevention Network

# Vaccines and the Virus Omicron

Larry Corey, MD

Professor, Vaccine and Infectious Disease Division  
PI, COVID-19 Prevention Network (CoVPN) Operations Center  
Fred Hutchinson Cancer Research Center

January 26, 2022

# State of the COVID-19 Pandemic in January 2022 (month 24)

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**We have developed highly effective biomedical interventions; COVID-19 has been an unprecedented scientific success story**

- Highly effective vaccines
- Highly effective monoclonal antibodies both for outpatient therapy and longer-term prevention
- Increasingly effective outpatient antiviral therapy to prevent hospitalization
  - PAXLOVID
  - IV Remdesivir 3-day regimen
  - Oral Molnupiravir

# State of the COVID-19 Pandemic in January 2022 (month 24)

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- Yet the Delta variant wave has become an Omicron tsunami of cases with public fatigue and discontent
- COVID-19 lifestyle restrictions are still operant for most of us in the US and globally
- It's clear the virus is firmly established in the human population
  - New variants likely to emerge
  - Even the less lethal variants, such as Omicron, can produce significant morbidity and mortality

# The Winter of Our Discontent

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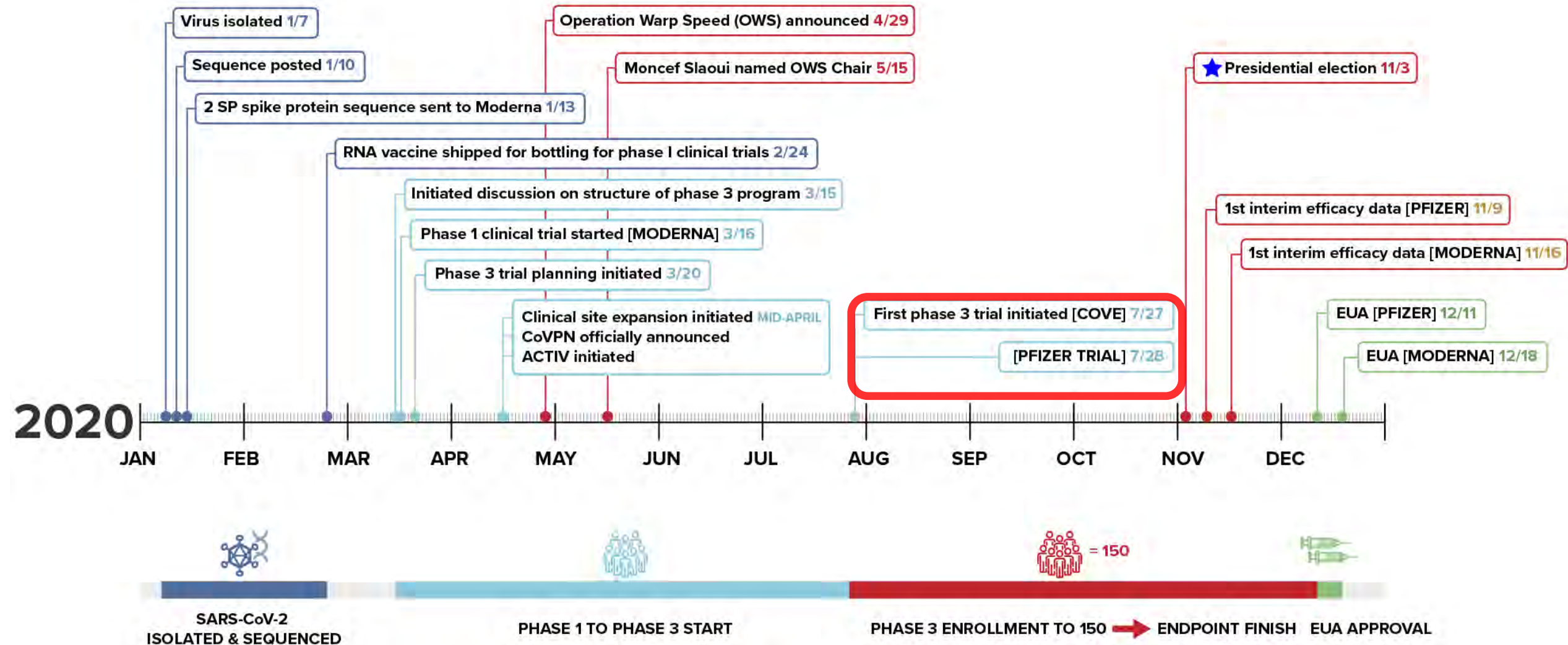
- Why are we living John Steinbeck's book or perhaps, more correctly, Shakespeare had it right; as always!
- Has science not led us out of this wilderness as well as we need ?
  - Are our tools not good enough?
- It is clear the virus is 'quite skilled' at antigenic variation, altering itself, and spreading quicker than any other human pathogen.
  - We must build and sustain an implementation science ,basic and translational research infrastructure that matches these viral alterations and continue to improve our countermeasures.

# My Role as Panelist

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- Quick review of USG vaccine program
- How has the unanticipated variant change affected vaccination efficacy and strategy?
- What's next?

# From Discovery to Public Vaccination in 11 Months: Remarkable



# Efficacy Results - starting Nov 2020

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## Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

FP Polack et al. for the C4591001 Clinical Trial Group

- 2-dose regimen of BNT162b2
- 43,548 participants randomized
- 95% Ve (95% CI 90.3; 97.6)
- EUA issued December 11, 2020
- FDA approval August 23, 2021



## Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

LR Baden et al. for the COVE Study Group

- 2-dose regimen of mRNA-1273
- 30,420 participants randomized
- 94.1% Ve (95% CI 89.3; 96.8)
- EUA issued Dec 18, 2020



## Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

J Sadoff et al. for the ENSEMBLE Study Group

- 1-dose regimen of Ad26.COV2.S
- 44,325 participants randomized
- 66.1% Ve (95% CI 55.0; 74.8) overall
- US: 72% Ve (95% CI 58.2; 81.7)
- EUA issued Feb 27, 2021



# Science's Breakthrough of the Year 2020: COVID-19 Vaccines





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

## Harmonized Efficacy Trials

RNA  
Platform 1

ChAdOx1  
Platform 2

Ad26  
Platform 3

Nanoparticle  
Platform 4

Pre-fusion Spike  
Recombinant Protein  
Platform 5

Collaborating  
clinical trial  
networks  
(CoVPN)

Harmonized  
endpoint data  
collection

- Common Labs**
1. Defining infection from disease
  2. Quantitative immune responses to spike and spike epitopes
  3. T-cell responses

Correlates of  
protection  
analyses within  
and cross  
protocols

Common DSMB

WHAT'S THE  
CHALLENGE?



Sally Bock



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





STUDIO-ONE

dream center  
THRIFT

Penny Mall

KITCHEN

STOP

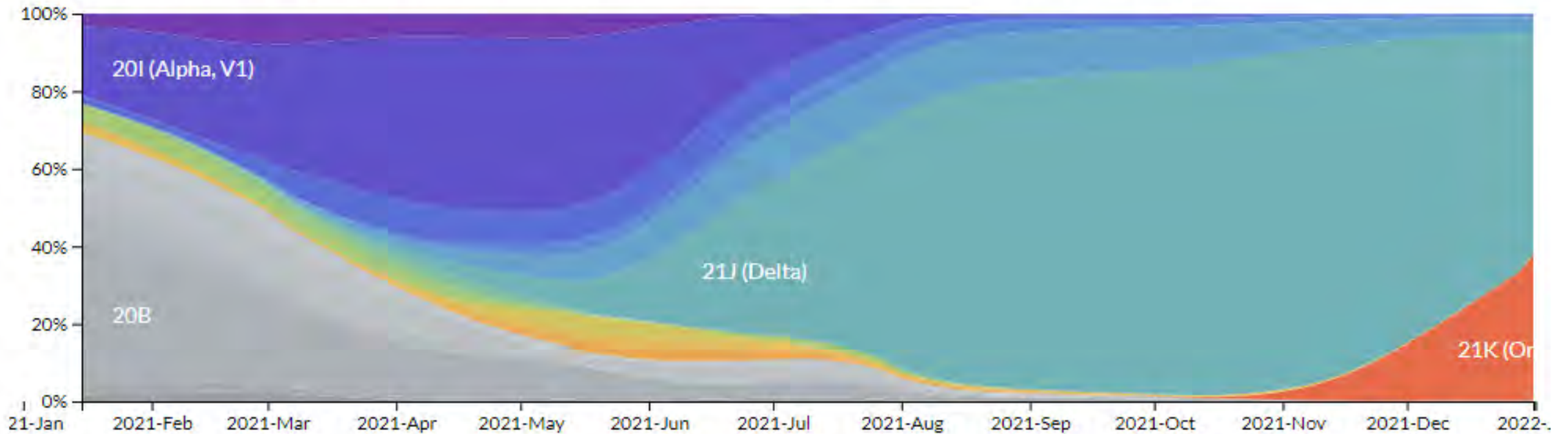
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# The COVID 19 vaccine success was not quick!

It was based upon 20-years of hard scientific effort  
from basic science to translational vaccinology

# The virus has fought back with rapid antigenic variation

Frequencies (colored by Clade and normalized to 100% at each time point for 2695 out of a total of 3272 tips)



# Projected variant proportions in the US





# Geometric mean of decrease in neutralization titers by variant

	Fold	95% CI
Alpha	1.6	1.5 - 1.7
Beta	8.8	8.0 - 9.7
Gamma	3.5	3.1 - 4.0
Delta	3.9	3.5 - 4.4
Omicron	30	20 - 38

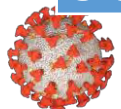
# Omicron Requires Boosting

## Variants Influence Vaccine Effectiveness

(MMWR – January 21, 2022)

<i>ER Visits</i>	Delta		Omicron	
		<u>95% CI</u>		<u>95% CI</u>
<i>mRNA vaccine</i>				
<b>2 doses</b>		<u>95% CI</u>		<u>95% CI</u>
• 14 – 179 days	86%	85 - 87	52%	46 - 58
• >180 days	76%	75 - 77	38%	32 - 43
<b>3 doses ††</b>	94%	93 - 94	<b>82%</b>	79 - 84
<i>Hospitalization</i>				
<i>mRNA vaccine</i>				
<b>2 doses</b>				
• 14 – 179 days	90%	89 - 90	81%	65 - 90
• >180 days	81%	80 - 82	57%	39 - 70
<b>3 doses</b>	94%	93 - 95	<b>90%</b>	80 - 94

†† median duration follow up post 3<sup>rd</sup> dose for Omicron period is only 44 days



# Omicron and Beyond

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- We will sweat through Omicron until we make more monoclonals and get the protease drugs into the field.
- Better treatment options will alter perception of risk.
- In the vaccine arena we have a durability issue. How to solve it? Platform versus insert or both?
- There are second generation vaccines in development; creating a research infrastructure to evaluate which ones add major benefit over current platforms is needed.

# Living with SARS-CoV-2

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- Endemicity of SARS-CoV-2 requires a sustained and thoughtful research program.
  - The structure we are working under had terrific alignment between big pharma and public health; less so now when greater innovation needed to solve the problem
- We need to fund a sustained research program for the continued development of better vaccines and therapies.
- We must take greater global responsibility than we now have. It's not effective just to donate excess vaccines. Low- and middle-income countries need the ability to make their own vaccines and have vaccines be part of their culture and economy.
- We need to merge HIV and COVID-19 policies and practices (TB also).
  - Immune suppressed persons are where the multi-mutational variants have emerged; Alpha, Beta, and Omicron

# CoVPN Leadership Team

**DAVID STEPHENS**  
Co-lead CoVPN Monoclonals



**KATHY NEUZIL**  
Co-lead CoVPN Vaccines



**LARRY COREY**  
Co-lead CoVPN Vaccines



**MIKE COHEN**  
Co-lead CoVPN Monoclonals



**BARNEY GRAHAM**  
Deputy Director, Vaccine  
Research Center



**JOHN MASCOLA**  
OWS/CAG Vaccine  
Development Team



**NELSON MICHAEL**  
CAG/OWS DoD Lead



**DAVID MONTEFIORI**  
Neut Antibody Lab, Duke



**JULIE AKE**  
Director, MHRP



**MARY MAROVICH**  
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**MONCEF SLAOU**  
CSO, OWS



**MERLIN ROBB**  
OW/CAG Clinical Trials



**DAVID KESSLER**  
CSO, CAG



**MATT HEPBURN**  
Director, COVID Vaccine  
Development - CAG



**TINA TONG**  
Assoc Dir, VRP, NIAID

