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Learning Rapidly to Improve the Conduct of Cancer Clinical Research Beyond the COVID-19 Pandemic – What did We Learn?

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SVP, Global Medical Affairs

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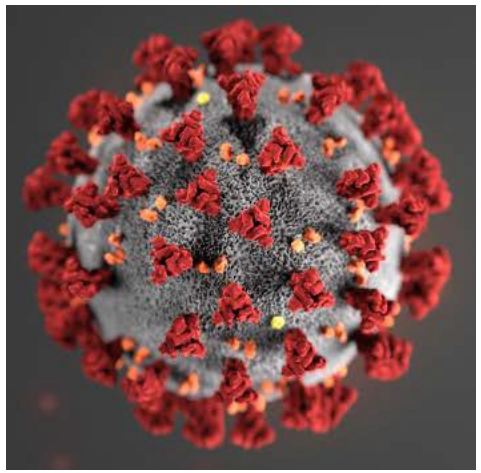
1/11/2020 Sequence

12/18/2020 FDA EUA



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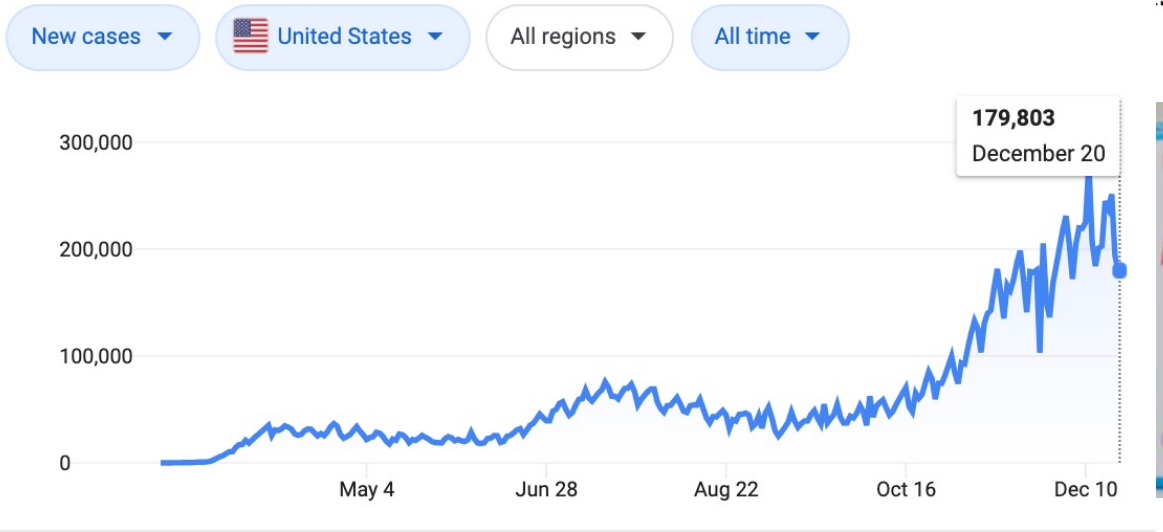

Enablers:

1. Science
2. Unmet need / shared sense of urgency
3. Collaboration with stakeholders (BARDA, NIH, PPD), Clarity from regulators (FDA)

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Criteria and Scope of the EUA

- The Moderna COVID-19 Vaccine has not been approved or licensed by the US Food and Drug Administration (FDA), but has been authorized for emergency use by FDA, under an Emergency Use Authorization (EUA), to prevent Coronavirus Disease 2019 (COVID-19) for use in individuals 18 years of age and older. There is no FDA-approved vaccine to prevent COVID-19.
- The EUA for the Moderna COVID-19 Vaccine is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of the product, unless the declaration is terminated or the authorization is revoked sooner.
- For information on the authorized use of the Moderna COVID-19 Vaccine and mandatory requirements of the EUA, please review the Fact Sheet for Healthcare Providers Administering Vaccine (Vaccination Providers) and Full EUA Prescribing Information at [https://www.modernatx.com/covid19vaccine-eua/].

COVID-19, coronavirus disease 2019.
Moderna. https://www.modernatx.com/covid19vaccine-eua/. Accessed December 21, 2020.

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Timeline From Sequence Identification to First Clinical Study

Jan 11
Chinese authorities shared the genetic sequence of the novel coronavirus

Jan 13
Sequence for Moderna COVID-19 Vaccine against the novel coronavirus finalized

Feb 7
The first clinical batch, including fill and finishing of vials, was completed

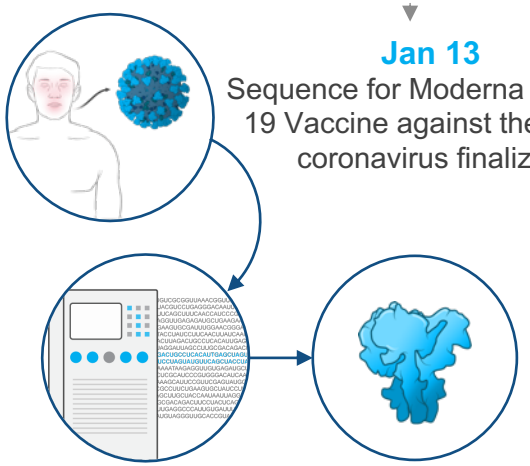
Batch proceeded to analytical testing for release

Feb 24
Clinical batch was shipped to the NIH for use in their Phase 1 clinical study

Mar 4
Investigational New Drug (IND) application filed by the NIH for Moderna COVID-19 Vaccine review completed; allowed to proceed to begin clinical trials

Mar 16
First participant in its Phase 1 study for Moderna COVID-19 Vaccine was dosed, a total of 63 days from sequence selection to first human dosing

2020



2 DAYS | **42 DAYS** | **21 DAYS**

COVID-19, coronavirus disease 2019; NIH, National Institutes of Health.

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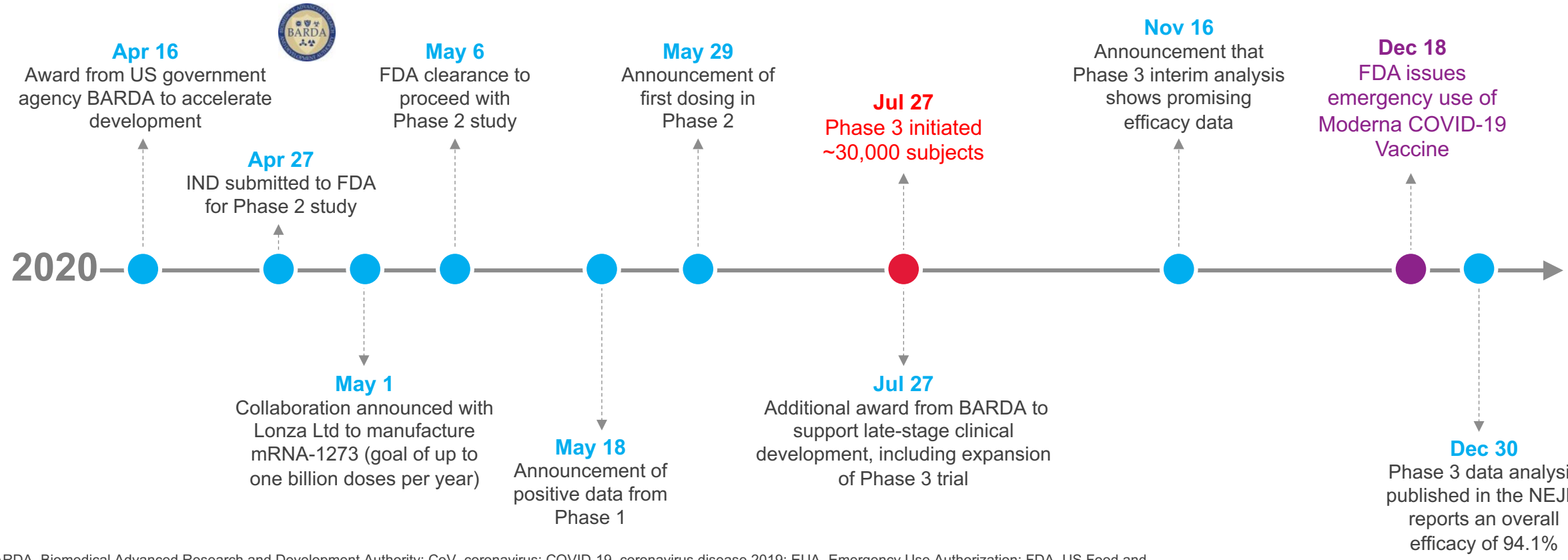
Timeline From First Clinical Study to First Authorization

Moderna COVID-19 Vaccine timeline: research and development of SARS-CoV-2 vaccine



BARDA, Biomedical Advanced Research and Development Authority; CoV, coronavirus; COVID-19, coronavirus disease 2019; EUA, Emergency Use Authorization; FDA, US Food and Drug Administration; IND, Investigational New Drug; NEJM, New England Journal of Medicine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Baden LR, et al. *N Engl J Med.* 2020. DOI: 10.1056/NEJMoa2035389.

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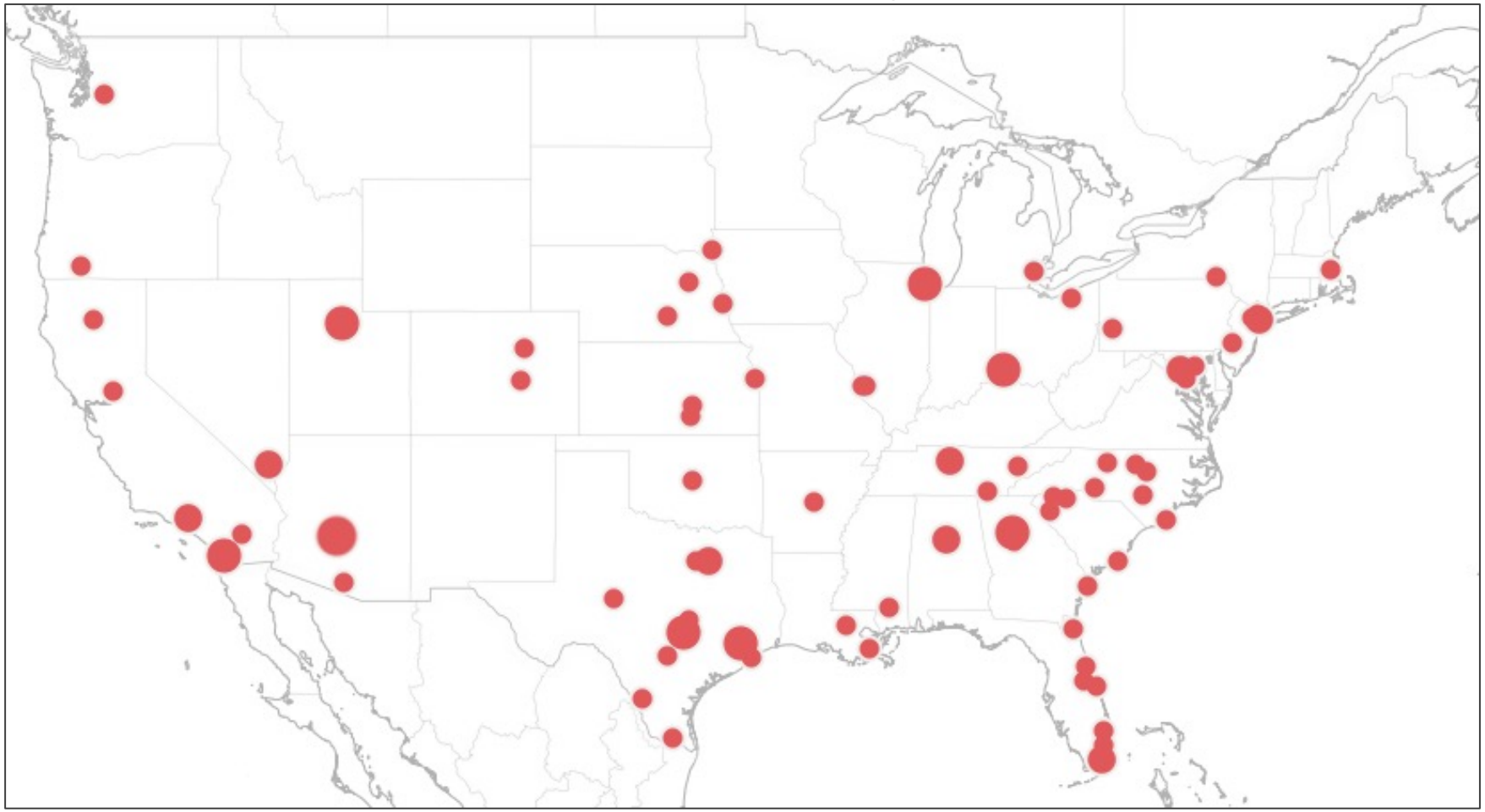
Distribution of Moderna COVE Study Sites in the US
(NCT04470427)

Size indicative of number of study sites in location



Moderna. https://www.modernatx.com/sites/default/files/mRNA-1273-P301-Protocol.pdf. Accessed February 5, 2021.

An Independent Data and Safety Monitoring Board Ensures Continuous Data Monitoring and Helps to Ensure Participant Safety (NCT04470427)

Independent review of data

Cove STUDY™ → Independent DSMB

- A **fully independent DSMB** reviews unblinded data
- Established and supported by NIAID
- Experts in infectious disease, epidemiology, and ethics
- Monitors event rates; at predefined analyses unblinds and **DSMB makes a formal recommendation**

Deliberation on best course of action

Oversight group (NIH National Institute of Allergy and Infectious Diseases; BARDA; moderna) → Moderna (sponsor)

- Oversight group receives recommendation, which **includes NIAID and BARDA for transparency**
- Sponsor (Moderna) reviews the DSMB recommendation, and discusses plans with Oversight group (NIAID, BARDA)
- Sponsor determines whether to submit the data to the FDA for review

Independent regulatory review

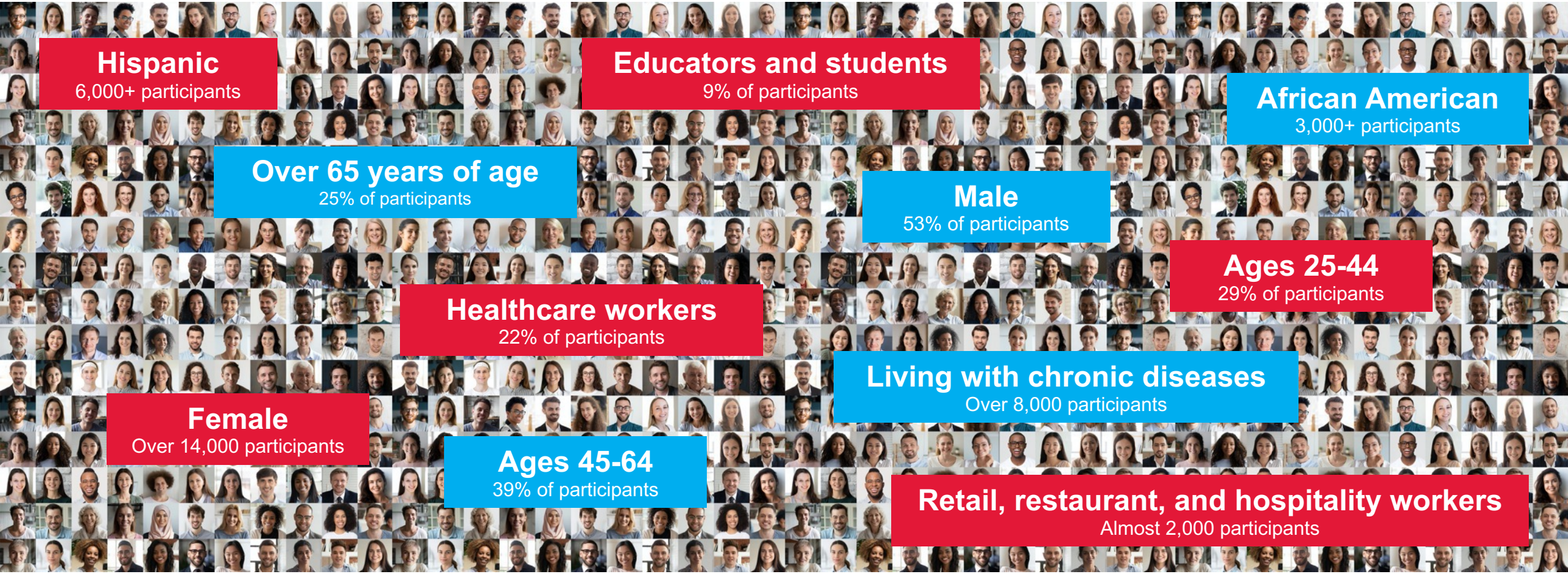
FDA

- FDA conducts independent review
- Seeks **external advisory committee** (VRBPAC) input

AE, adverse event; BARDA, Biomedical Advanced Research and Development Authority; DSMB, data safety monitoring board; FDA, Food and Drug Administration; NIAID, National Institute of Allergy and Infectious Diseases; NIH, National Institutes of Health; VRBPAC, Vaccines and Related Biological Products Advisory Committee.

The Population in the COVE Study Is Representative of the US Population at Risk for COVID-19 Disease

(NCT04470427)



COVID-19, coronavirus disease 2019.
Interim data snapshot – October 21, 2020 – subject to change.

We worked to ensure diversity in the COVE trial

Education: Ourselves & Stakeholders

Listen
We created an Advisory Committee of experts and we listened to them

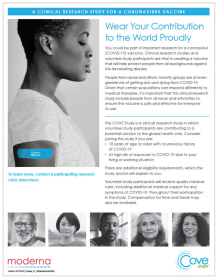
Start the Conversation
Dr Fauci and Dr Adams spoke at our PI meeting about the 'why' importance of diversity

Educate
The CoVPN CE team conducted implicit bias training & the CEAL team provided expertise

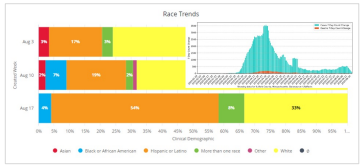
Transparency: Intent & Information

Be Transparent
Be explicit about intent; published data on progress; published protocol on our website

Create Tools
Tailored our Patient Information sheets and translated materials for different populations



Use Data
We provided each site with their ethnic enrollment trends and epi weekly, and monitored enrollment daily



Help: Partner with Experts

Partner
Seek experts and those with specific experience

National Institutes of Health

Synexus

Innovate
Be creative; new solutions are needed

TrialScope CONNECT

CVS Health

Motivate
OWS leadership motivated through visiting and listening to the sites

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Inclusion and Exclusion Criteria in the Phase 3 COVID-19 Vaccine Trial

Standard pivotal vaccine trial exclusions

- Immunosuppression: conditions, medications, bleeding disorders
- Interference with safety assessments, e.g, acute febrile illness, SARS CoV-2 infection, other febrile illness
- Interference with immunogenicity and efficacy endpoints, e.g., blood products and immunoglobulins
- Allergic reactions to vaccine or components
- History of SARS CoV-2 infection and concomitant vaccination (28 days)
- Pregnancy or inadequate contraception

Exceptions to standard exclusion/inclusions

- Inclusion of people with underlying medical comorbidities
  - Change from phase 1 and 2
    - Risk of complications from COVID-19, ex. chronic lymphocytic leukemia (CLL)
- Inclusion of people living with HIV – unique in a pivotal vaccine efficacy trial
- Administration of another investigational vaccine or ongoing trial to treat COVID-19 only at time of enrollment (perhaps excluded from per protocol analysis)

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What Did We Learn from the COVID-19 Trials?

Speed and agility
- Clear demonstration of the unmet need

Rapidly scalable study design
- Execution speed
- High unmet medical need
- Close interaction with regulators

Tight collaboration between academia and industry
- Familiarity with investigational agents

Diversity of the study
- Importance of making medicines available to those in greatest need
- Most critical take home point

COVID increased awareness of clinical trials

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Questions?

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