

COVID-19 Therapeutics Emergency Use Authorizations

Center for Drug Evaluation and
Research

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Panel 1: Use of the Emergency Use Authorization During the COVID Pandemic

Opening Remarks

Communication is a Pillar of CDER's Pandemic Response



- Since the beginning of the COVID-19 public health emergency, we have maintained constant coordination with other U.S. Government agencies, our international counterparts and the research community.
- Extensive coordination has been and remains essential to our ability to obtain and maintain the most up-to-date understanding of
 - the pathogen, including viral variants of SARS-CoV-2
 - the clinical course of disease in patients
 - the development of potential medicines for prevention or treatment of COVID-19, and
 - the trajectory of the virus and the impact of interventions at the regional, national and global scales.
- Efficient and rapid exchange of information on a dynamic and changing pandemic allows our scientific and regulatory teams to quickly provide guidance to sponsors and other stakeholders to expedite the development of drugs.

Coronavirus Treatment Acceleration Program (CTAP)



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CTAP will use every available method to move new treatments to patients as quickly as possible, balancing patient needs for medicine while supporting trials to gather evidence and weighing the risks and benefits

- Emergency program for potential coronavirus therapies created April 2020.
- Enabled FDA to leverage cross-agency scientific resources and expertise to facilitate COVID-19 therapeutic development and review.
- Facilitated fast, early, and frequent discussions between FDA and drug sponsors -- an essential element in expediting efficient development of therapies.
- Includes significant emphasis on providing timely FDA feedback to industry on clinical trial development – reinforcing the gold standard for assessing whether a particular therapeutic is safe and effective for its investigational use.

Surge in Workload

CTAP Snapshot, as of August 31, 2021:

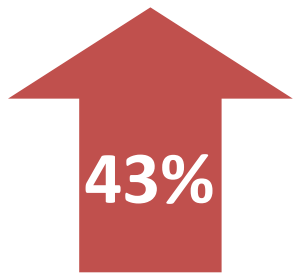


640+ drug development programs in planning stages

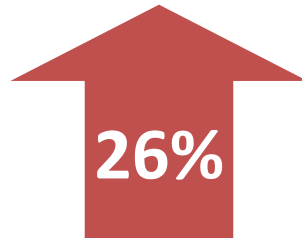


470+ trials reviewed by FDA

Pre-Pandemic (FY19) vs Pandemic (FY20) Workload Increase



New INDs received



Formal meeting requests



Avg time between request and meeting

No Corresponding Increase in Staff



Applying the EUA Standard in a Dynamic Environment

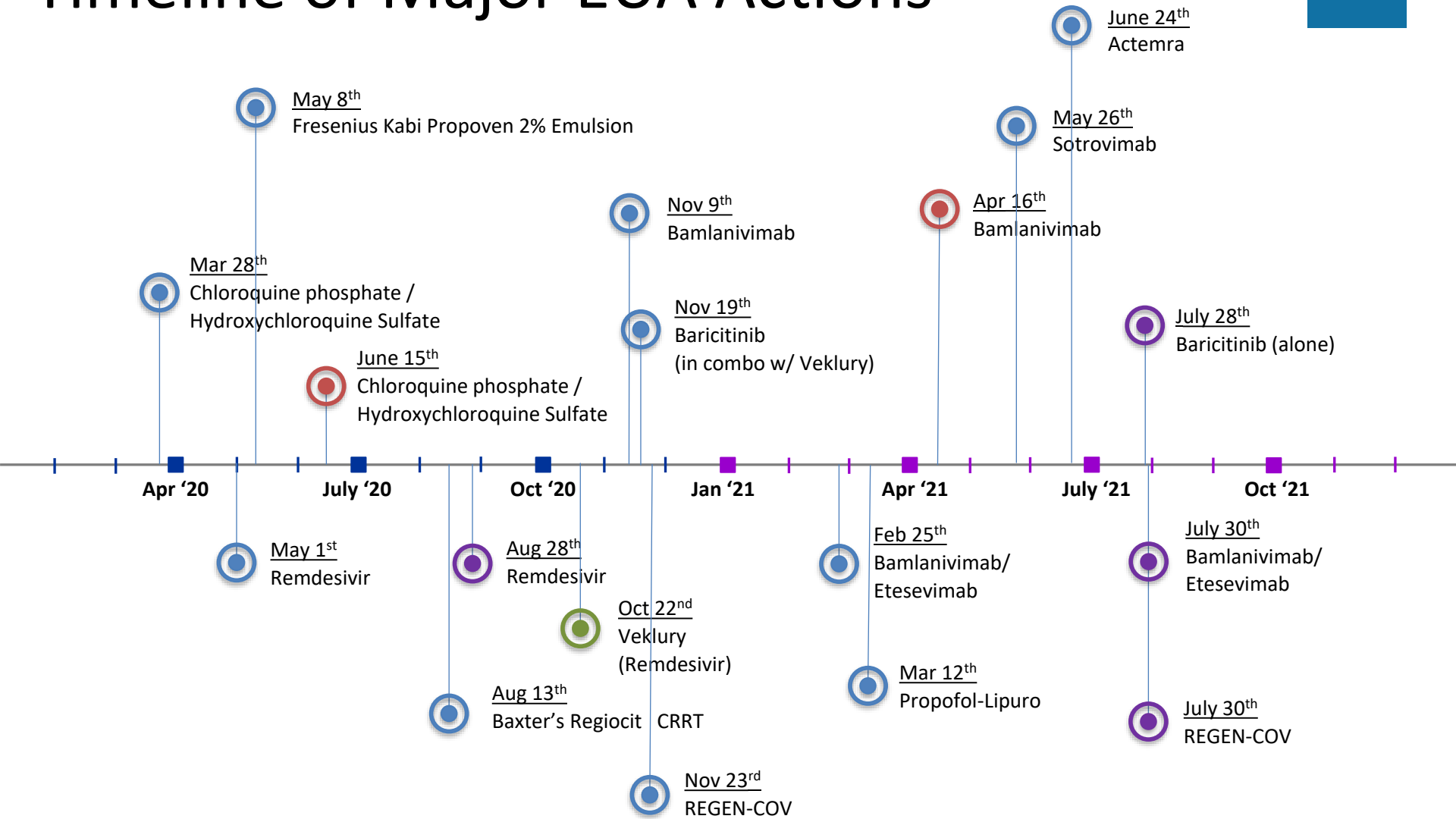
- EUA is a mechanism to provide rapid access to potential new therapies during a public health emergency when there is *no adequate, approved and available alternative* and the expected potential benefit outweighs the risk
 - EUAs are appropriate where it is reasonable to believe that the product *may be effective* for its proposed use, and when used for such purposes, the known and potential benefits outweigh the known and potential risks
 - The Agency must consider the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available
- Involves balancing early access against uncertainty
- The calculus to make that determination may change over the course of the emergency as more therapeutic options emerge
- EUAs are a temporary measure; sponsors of products authorized under EUA are expected to continue development of an authorized product toward licensure or approval.

Applying the EUA Standard in a Dynamic Environment (2)



- The EUA authority is sufficiently robust and flexible to enable the Agency to:
 - Act, when scientifically supportable, to rapidly make available potentially effective therapeutics to meet the public health need, taking into consideration adequate, approved and available alternative therapies; and
 - Adapt to an evolving and increasingly dynamic epidemiological and clinical landscape; or
 - Revoke when the scientific data no longer support that the product is appropriate for its authorized uses (e.g., new clinical trial data, circulating variants)
- Generally, CDER has issued EUAs when top-line, scientifically robust and interpretable data available from at least one adequate and well-controlled clinical trial supports the Agency's determination that the criteria for issuance of an EUA are met.
- CDER has required, as conditions to the EUA, not only enhanced adverse event reporting but also expedited reporting on product quality defects for authorized biologics, and, in the case of monoclonal therapies potential loss of efficacy against circulating viral variants of SARS-CoV-2

Timeline of Major EUA Actions



Key

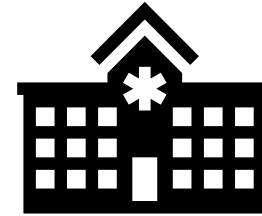
- Initial Authorization
- Revision
- Approved
- Revoked

CRRT - Continuous Renal Replacement Therapy

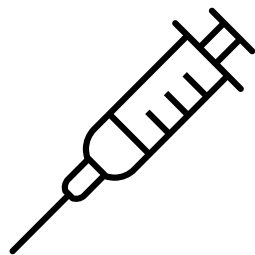
COVID-19 Monoclonal Antibodies: Public Health Impact



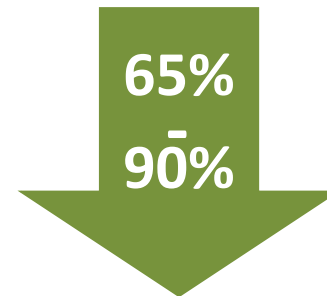
2.52 million treatment courses distributed



8098 sites receiving product



Reported Usage:
1.2 million treatment courses



Reduction in risk of COVID-19 related hospitalization or death in high-risk patients was observed in clinical trials

While our work to respond to the pandemic isn't over, we are taking stock of our experience and capturing lessons learned

Lessons Learned – Evidence Generation

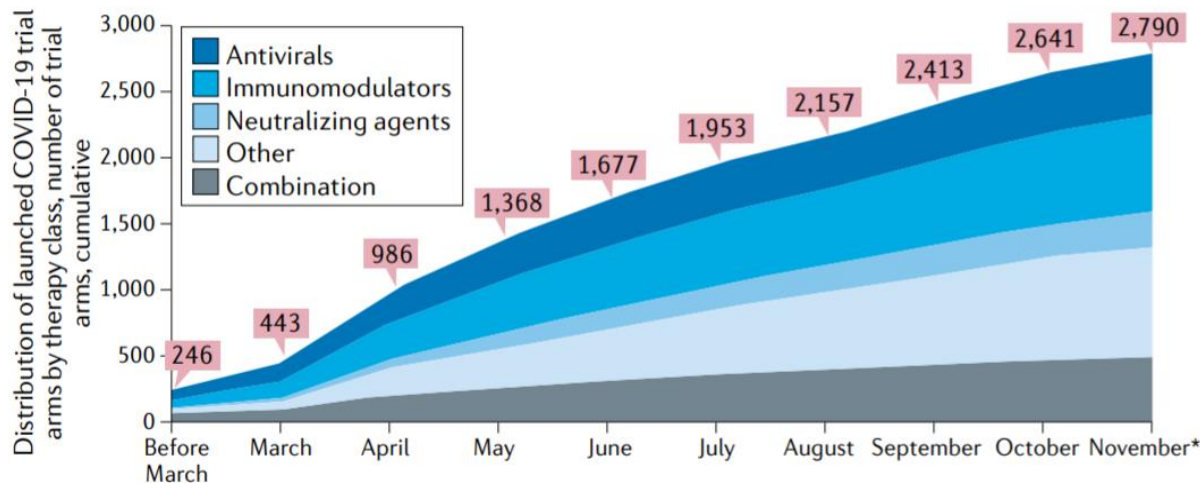
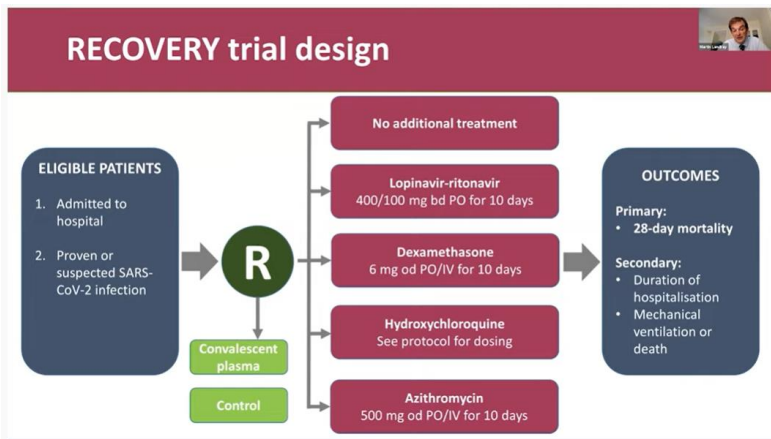


Fig. 1 | **Expansion of the clinical trial landscape for COVID-19 therapeutics in 2020.** Source: ClinicalTrials.gov and WHO clinical trial registry. *As of 20 Nov 2020. See Supplementary information for details.

- Investigators launched clinical trials rapidly
- But few were sufficiently powered to provide actionable data
- Collective resources were not used efficiently to generate data that could lead to authorization or approval of products
- The use of different endpoints across trials made it difficult to compare therapies
- Despite CTAP – not all sponsors engaged with FDA on the design of their trials

Lessons Learned – Evidence Generation

The value of master protocols:



ACTIV-1

Immune Modulators



The ACTIV-1 master protocol will test promising immune modulator compounds, a class of drugs that help minimize the

ACTIV-2

Outpatient Monoclonal Antibodies and Other Therapies



ACTIV-3

Inpatient Monoclonal Antibodies and Other Therapies



ACTIV-3 protocols are Phase 3 randomized, placebo-controlled trials testing multiple therapies, beginning with monoclonal

ACTIV-4

Antithrombotics



ACTIV-5

Big Effect Trial



Lessons Learned – Evidence Generation



- Rapid implementation of master protocols and other large randomized trials requires a research ready network
 - Research Staff
 - Contracts
 - Central IRBs



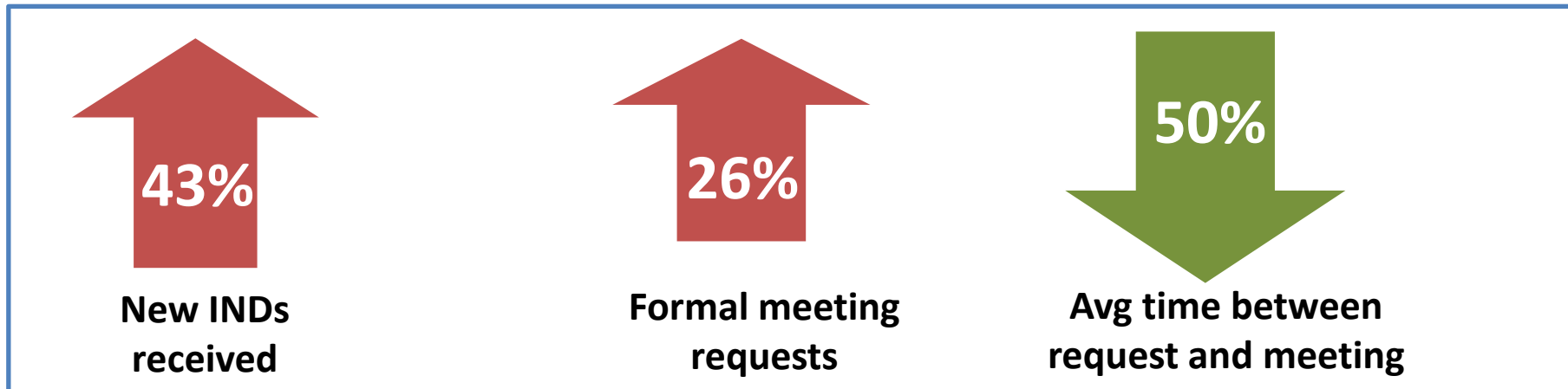
Public Transparency



- Transparency is critical to public confidence in the Agency's scientific review process
- Scientific reviews that underpin our decisions to issue, revise or revoke an EUA are made public on our website*
- However, there may be delays in such release as we engage with the sponsor on what must be protected from disclosure
 - this delays health care provider and patient access to the evidence underlying EUA
- We need broader authority to disclose safety and effectiveness information that underpin our EUA decisions

* <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/cder-scientific-review-documents-supporting-emergency-use-authorizations-drug-and-biological>

FDA's Strength Is Its People



To be ready to respond to pandemics, FDA needs to be able to build enduring surge capacity in the core scientific disciplines and supporting operations.

