Catalyzing Translational Innovation in the Age of COVID-19

Christopher P. Austin, M.D.
Director, NCATS

Federal Demonstration Partnership
January 11, 2021
The COVID-19 Pandemic
A public health crisis unrivalled in modern times

https://covidtracking.com/data

Chart information and data

https://covidtracking.com/data
People at Increased Risk for Severe COVID-19 Illness

- Older adults
- People of any age with certain underlying medical conditions

Source: CDC, 6/25/2020
Underlying Medical Conditions Strongly Associated with Increased Risk for Severe COVID-19 Illness

- Serious heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)
- Chronic kidney disease
- Chronic obstructive pulmonary disease (COPD)
- Diabetes, type 2
- Obesity (BMI ≥ 30)
- Cancer
- Sickle cell disease
- Immunocompromised state from solid organ transplant

Source: CDC, 7/28/2020
Viewpoint

COVID-19 and Racial/Ethnic Disparities

MW Hooper, AM Nápoles and EJ Pérez-Stable

“The most pervasive disparities are observed among African American and Latino individuals, and where data exist, American Indian, Alaska Native, and Pacific Islander populations.”
Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – September 19, 2020

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Rate per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic/Latino</td>
<td>359</td>
</tr>
<tr>
<td>Black, Non-Hispanic</td>
<td>357</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>350</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>105</td>
</tr>
<tr>
<td>White, Non-Hispanic</td>
<td>78</td>
</tr>
</tbody>
</table>

Source: CDC COVID-NET. Data from 14 states.
NCATS took an unprecedentedly open, collaboration-based approach to COVID-19

https://ncats.nih.gov/covid19-translational-approach
COVID-19 OpenData Portal

This online data resource launched in May to openly and quickly share COVID-19-related drug discovery data and experiments for all approved drugs.

NCATS is sharing complete data from 13 SARS-CoV-2-related experiments screened against ~10,000 approved drugs/candidates (>500,000 data points)

>27,000 visitors and 85,000 views since launch

Expanding this data-sharing resource to include more complex types of data (e.g. image-based screens)

Integrating external (non-NCATS) SARS-CoV-2 data from collaborative partners across the globe, including:

- Recursion Pharmaceuticals (UT, USA)
- University of Michigan (MI, USA)
- Fraunhofer Institute for Molecular Biology (Aachen, Germany)
- Beijing University of Chemical Technology (Beijing, China)
- Karolinska Institutet/SciLifeLab (Sweden)

https://opendata.ncats.nih.gov/covid19/
NCATS is generating a collection of datasets by screening a panel of SARS-CoV-2 related assays against all approved drugs. These datasets, as well as the assay protocols used to generate them, are being made immediately available to the scientific community on this site as these screens are completed.

**Animal Model Summary Overview**

The animal model summaries and descriptions have been curated by the National Institutes of Health (NIH) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Preclinical Working Group with support from the Foundation for the National Institutes of Health (FNIH). New and updated information, including detailed individual animal model pages, will be provided as more scientific studies are shared. Please continue to check back for more information. Feedback, comments, and questions are highly encouraged to further develop these pages. Please contact ACTIVpreclinical@fnih.org.

## Small Animals

<table>
<thead>
<tr>
<th>Species</th>
<th>Modification</th>
<th>Model Name/Nomenclature</th>
<th>Vaccines</th>
<th>Antibody</th>
<th>Neutralizing Antibodies</th>
<th>Open Therapeutics</th>
<th>Translational</th>
<th>Disease Manifestation &amp; Pathology</th>
<th>Extent of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferret</td>
<td>Outbred Stock</td>
<td>Ferret</td>
<td>✓</td>
<td>✓</td>
<td>Y</td>
<td>Y</td>
<td>TBD</td>
<td>Viral titers in nasal washes; fever</td>
<td>Mild</td>
</tr>
<tr>
<td>Guinea Pig</td>
<td>Wild Type</td>
<td>Guinea Pig</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Lung lesions</td>
<td>None to minimal</td>
</tr>
</tbody>
</table>
CURE ID: Capturing Clinicians’ Experiences of Novel Uses of Existing Drugs During COVID-19

- **CURE ID** – A mobile application and website
- Data captures clinical experience with *novel uses of existing drugs* - **Repurposing**
- Data used for hypothesis generation – confirming hypothesis via clinical trials – integration into clinical practice
- Released Dec 2019; COVID-19 update May 2020
- Developed collaboratively by FDA and NCATS/NIH, with the support of WHO and IDSA

[link](https://cure.ncats.io)
CURE ID: Capturing Clinicians’ Experiences of Novel Uses of Existing Drugs During COVID-19

CURE ID and COVID-19
- 1109 clinical case reports
- 250 repurposed drugs
- 1327 clinical trials
- 113 discussion threads

Ongoing Initiative Expansion
- Special interest collaborations to capture repurposing efforts for neonates, pregnant and lactating women
- PCOR-TF Grant – Collaboration between VIRUS registry, JHU and Mayo to expand COVID-19 surveillance using EMRs
- Bridge to randomized trial platform initiative for COVID-19 with mild to moderate disease
C-Path Launches CURE Drug Repurposing Collaboratory to Accelerate Identification of New Uses of Existing Drugs to Treat Infectious Diseases, Including COVID-19

Clinicians to report novel uses of existing drugs through FDA-NCATS CURE ID Mobile App.

TUCSON, Ariz., June 23, 2020 — As millions of patients struggle with diseases that lack adequate treatments, there is a critical need to understand how existing drugs can be used in new ways to improve clinical outcomes. Health care professionals use drugs in novel ways as a potential life-saving intervention when no specific approved therapies are available. However, without the ability to share these experiences in a systematic manner, the clinical and research communities cannot benefit from lessons learned.

To address the challenge, the Critical Path Institute (C-Path) today announced the launch of the CURE Drug Repurposing Collaboratory (CDRC) funded by the U.S. Food and Drug Administration (FDA), in collaboration with the National Center for Advancing Translational Sciences (NCATS), part of the National Institutes of Health (NIH). A public-private partnership, CDRC will provide a forum for the exchange of clinical practice data to inform potential new uses of existing drugs for areas of high unmet medical need, advancing research in these areas. The Collaboratory will also create a network connecting major treatment centers, academic institutions and researchers, private practitioners, government facilities and health care professionals around the world.
COVID-19 Serosurvey

❖ NCATS with NIAID, NIBIB, and NCI quickly enrolled 10,000 participants and analyzed their samples to give NIH and other health organizations more information on the current spread of COVID-19. Results will be reported shortly.

❖ Two longitudinal follow-ups at 4 and 8 months are planned. Follow-up already has started.

❖ CTSAs: University of Alabama, University of Pittsburgh

❖ A rare disease patient serosurvey with RDCRN will be shortly underway.

Source: DPI/ETB
National COVID Cohort Collaborative (N3C)

❖ A collaboration among the CTSA Program hubs and CD2H to share electronic health records in a centralized, secure location housed at NCATS.
❖ More than 82 projects are now approved to access the N3C Data Enclave to look at real-world clinical data to help speed COVID research and improve clinical care.
❖ Rapid development and execution of data agreements, assessment of Federal policy implications, and implementation of operational policies
❖ Created and launched a federal Data Access Committee (DAC) with accompanying policies and procedures

https://ncats.nih.gov/n3c
Source: Office of the Director
What makes the N3C unique?

- **Robust Scale and Scope:** Includes demographics, symptoms, laboratory test results, procedures, medications, medical conditions, physical measurements
- **Harmonized Data:** Makes data from different types of medical records comparable
- **Collaborative Analytics:** Enables team-based research, machine-learning and rigorous statistical analyses
- **Centralized and Secure:** Data remain in NCATS’ secure FedRAMP-certified cloud, provides standardized assessment, authorization and continuous monitoring

https://ncats.nih.gov/n3c
1. Limited Data Set
2. HIPAA De-Identified Data

NIH NCATS Data Enclave

Synthetic Engine

Transformation and Harmonization

NCATS Data Transfer Agreement

Data Acquisition

Data Harmonization

NCATS Data Use Agreement

Synthetic Data

Collaborative Analytics
COVID-19 Tissue Chips

- Don Ingber and team (Wyss Institute) previously funded by NCATS to model human lung-on-chip and response to influenza
- Chip used to model viral entry of SARS-CoV2 and test repurposed drugs
- Amodiaquine, toremifene, and clomiphene inhibit viral infection under physiological conditions
- Hydroxychloroquine, chloroquine and arbidol did not inhibit viral entry, consistent with clinical data
- Proof-of-concept that tissue chips can help identify existing drugs that may be repurposed for pandemic viral applications.

MPSCoRe: Microphysiological Systems for COVID-19 Research Working Group

- Joint working group to support and help coordinate global MPS efforts to study COVID-19 and future infectious disease applications.
- Partnership between NC3Rs, NICEATM, NCATS, NIAID/DMID, US Army DEVCOM CBC
- ~60 members have accepted targeted invitations so far, including stakeholders from pharma, MPS developers, academia, regulatory agencies, etc.
- Informational webinar planned for 29 January 9:00-11:00 am EST
- Workshop planned as satellite to NCATS Tissue Chip Consortium spring meeting

MPSCoRe WG Objectives include:
- Raise awareness of COVID-19 MPS research
- Facilitate connections between MPS developers and end-users
- Engage global regulatory authorities
- Characterize model performance and readiness criteria
- Support the assessment of MPS against in vivo/clinical data
- Ensure the 3Rs opportunities are recognized.
COVID-19 Clinical Trials

NCATS and its CTSA Program are playing lead roles in rigorous clinical trials to test potential treatments in hospitalized adults with COVID-19:

• The ACTIV-1 Immune Modulators trial is evaluating three drugs that could reduce the harmful COVID-19 cytokine storm
• Two trials led by Einstein/NYU and Vanderbilt are evaluating blood plasma donated by people who have recovered from COVID-19

Source: DCI

The trials are currently enrolling participants.
Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

ACTIV-1 IM: Randomized Master Protocol for Immune Modulators for Treating COVID-19

Study Snapshot

Evaluating treatment of three therapeutic agents in moderately or severely ill hospitalized patients (adults) infected with SARS-CoV-2.

- Therapeutic agents:
  - **Infliximab (Remicade)** - TNF-alpha blocker
  - **Abatacept (Orencia)** - CTLA-4
  - **Cenicriviroc (CVC)** - CCR2/CCR5 antagonist

- Target enrollment: 2,160 participants

Infrastructure and Support:

- Leveraging existing NCATS CTSA Program Trial Innovation Network
- Supported by Operation Warp Speed (OWS) via a Biomedical Advanced Research and Development Authority (BARDA) Task Order awarded to Technical Resources International (TRI, Inc.)
- Coordination and oversight by NCATS

Major Milestones and Progress

- Launched on October 16, 2020
- 25 active sites in the U.S.
NCATS Convalescent Plasma RCTs
*Multisite trials run through CTSA hubs*

**CONTAIN COVID-19**
- Enrollment: 725
- Active Sites: 17
- Anticipated Completion: February

**PASS IT ON**
- Enrollment: 532
- Active Sites: 20
- Anticipated Completion: March

NCATS Accelerating Translation by:
*Establishing format for direct data submission to FDA*
*Promoting harmonization of plasma assays*
Community Engagement to Address COVID-19

NCATS’ CTSA Program hubs are trusted community partners, which allowed them to rapidly pivot to address COVID-19 health disparities.

They are working closely with community partners on initiatives to speed the discovery and delivery of COVID-19 treatments and vaccines to those in greatest need.


Source: DCI
Community Engagement to Reduce COVID-19 Health Disparities

- **Community Engagement Alliance (CEAL) Against COVID-19 Disparities**
  - To provide trustworthy information through active community engagement with, investment in, and outreach to underserved communities, building long-lasting partnerships to improve diversity and inclusion in our scientific response to the COVID-19 pandemic

- **Rapid Acceleration of Diagnostics (RADX) Initiative**
  - To speed innovation in the development, commercialization, and implementation of technologies for COVID-19 testing
  - **RADx-UP**: Rapid Acceleration of Diagnostics for Underserved Populations
NIH-Funded Community Engagement Alliance (CEAL) Against COVID-19 Disparities Research Teams

CEAL Awardee States / PIs

1. Alabama* - Mona Fouad, M.D., M.P.H.
2. California* - Arleen F. Brown, M.D., Ph.D.
3. Florida* - Olveen Carrasquillo, M.D., M.P.H.
4. Georgia* - Tabia Henry Akintobi, Ph.D., M.P.H.
5. Michigan* - Erica Marsh, M.D.
7. Tennessee* - Paul Juarez, Ph.D.
8. Texas* - Jamboor Vishwanatha, Ph.D.
9. Mississippi – Caroline Compretta, Ph.D.
10. Arizona – Sairam Parthasarathy, M.D.
11. Louisiana – Marie A. Krousel-Wood, M.D.

*CTSA affiliation

NIH. CEAL. https://covid19community.nih.gov/
RADx™ Tech
The RADx Tech initiative aims to speed the development, validation, and commercialization of innovative point-of-care and home-based tests, as well as improve clinical laboratory tests, that can directly detect the virus.
Budget: $500 Million

RADx Underserved Populations (RADx-UP)
The overarching goal of the RADx-UP initiative is to understand the factors associated with disparities in COVID-19 morbidity and mortality and to lay the foundation to reduce disparities for those underserved and vulnerable populations who are disproportionately affected by, have the highest infection rates of, and/or are most at risk for complications or poor outcomes from the COVID-19 pandemic.
Budget: $200 Million

RADx Advanced Technology Platforms (RADx-ATP)
The RADx ATP program seeks to increase testing capacity and throughput by identifying existing and late stage testing platforms for COVID-19 that are far enough advanced to achieve rapid scale-up or expanded geographical placement in a short amount of time. These efforts will focus on scaling up technologies, including improving existing high-throughput platforms, to increase performance.
Budget: $230 Million

RADx Radical (RADx-rad)
RADx-rad will support new, non-traditional approaches, including rapid detection devices and home-based testing technologies, that address current gaps in COVID-19 testing. The program will also support new or non-traditional applications of existing approaches to make them more usable, accessible, or accurate. These may lead to new ways to identify the current SARS-CoV-2 virus as well as potential future viruses.
Budget: $1.0 Million
RADx-UP

➢ A collaborative clinical research network of existing large-scale programs that have adequate capacity, infrastructure and relationships with underserved communities.

➢ Research on the social, ethical and behavioral implications of these health disparities to inform the development and evaluation of testing programs.

➢ A coordination and data collection center, providing overarching support and guidance on administrative operations and logistics, facilitating effective use of COVID-19 testing technologies, supporting community and health system engagement and providing overall infrastructure for data collection, integration and sharing.
RADx-UP CTSA Supplement Sites

- Medical College of Wisconsin
- The Ohio State University
- The University of Utah
- Rutgers Biomedical and Health Sciences
- The University of Texas Health Science Center at Houston
- University of Kansas Medical Center

https://www.nih.gov/research-training/medical-research-initiatives/радx/funding#радx-up-funded

*Out of 32 institutions received supplements
On April 17, NIH announced the launch of a public-private partnership, Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Develop a coordinated research response to speed COVID-19 treatment and vaccine options.
**ACTIV Stakeholders**

ACTIV is being coordinated by the Foundation for the National Institutes of Health (FNIH), and has brought together multiple partners from government, industry and non-profits.

<table>
<thead>
<tr>
<th>Government Partners</th>
<th>Industry Partners</th>
<th>Non-Profits</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>20</td>
<td>4</td>
</tr>
</tbody>
</table>
ACTIV Governance

ACTIV Governance includes representation from key stakeholders in both the private and public sector.

### ACTIV Executive Committee

**Co-Chairs**
- Francis Collins, NIH
- Paul Stoffels, J&J
- Anthony Fauci, NIAID
- Gary Gibbons, NHLBI
- Janet Woodcock, OWS
- William Pao, Roche
- Mikael Dolsten, Pfizer
- Gary Disbrow, BARDA
- Peter Marks, FDA
- Andrew Plump, Takeda

**Members**

### ACTIV Leadership Team

Scientific leaders from all participating organizations

### Departments

- Preclinical Working Group
- Therapeutics Clinical Working Group
- Clinical Trial Capacity Working Group
- Vaccines Working Group
ACTIV Governance & Coordination with Operation Warp Speed

OWS and ACTIV working groups have been closely collaborating to ensure alignment across both efforts.

**Operation Warp Speed**

- **Board of directors**
  - Secretaries of HHS and DoD (co-chairs), and representatives from VA, USDA, OSTP, OMB, NSC

- **Overall lead**
  - Secretaries of HHS and DoD (co-chairs), and representatives from VA, USDA, OSTP, OMB, NSC

**ACTIV**

- **ACTIV Executive Team**
  - (co-chairs and members)
  - **ACTIV Leadership Team**

**Therapeutics**
- **Clinical**
- **Preclinical**
- **Clinical Trial Capacity**
- **Vaccines**

**Scientific Leads**

**Clinical Leads**

**Supply and Distribution Leads**

**Project management**

**Distribution leads**

**Mfg / Supply leads**

**R&D Leads**

**Supply and Distribution Leads**

**Clinical Leads**

**Project management**

**Working Group Co-Chairs**

<table>
<thead>
<tr>
<th>Therapeutics</th>
<th>Preclinical</th>
<th>Clinical Trial Capacity</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working Group Co-Chairs</td>
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<td>Working Group Co-Chairs</td>
</tr>
</tbody>
</table>
Focus Area Objectives & Composition

Each focus area is a Working Group that contains several sub groups to oversee tactical operations:

**Preclinical**
- Develop a collaborative, streamlined forum to identify preclinical treatments

**Therapeutics – Clinical**
- Accelerate clinical testing of the most promising vaccines and treatments

**Clinical Trial Capacity**
- Improve clinical trial capacity and effectiveness

**Vaccines**
- Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval

### Objective

- **Preclinical**
  - Develop a collaborative, streamlined forum to identify preclinical treatments
- **Therapeutics – Clinical**
  - Accelerate clinical testing of the most promising vaccines and treatments
- **Clinical Trial Capacity**
  - Improve clinical trial capacity and effectiveness
- **Vaccines**
  - Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval

### Sub-Groups

- **Preclinical**
  - Animal Models
  - In Vitro Assays
- **Therapeutics – Clinical**
  - Agent Prioritization
  - Master Protocol
- **Clinical Trial Capacity**
  - Survey Development
  - Clinical Trial Network Inventory
  - Innovations
- **Vaccines**
  - Vaccines Clinical Trials
  - Protective Immune Responses
  - Vaccine-Associated Immune Enhancement
Preclinical Working Group

OBJECTIVE
Standardize and share preclinical evaluation methods and sharing testing resources in an open forum that allows for effective validation and comparison of therapeutic candidates.

ACCOMPLISHMENTS TO DATE

✓ Developed a master inventory of preclinical testing resources
✓ Established SOPs for accelerated preclinical agent development in response to a pandemic
✓ Developed a National Strategy for NHP Research and a process to coordinate NHP studies centrally through NIH, and “field guides” for the use of small animal testing models
✓ Created and published online 9 “field guide” videos for use of small animal models in COVID-19 preclinical development
✓ Established a process for prioritizing in vitro assays and evaluating preclinical compounds
✓ Created a public database for sharing preclinical data (NCATS Open Science Portal)

☐ Conducting a “matchmaking” process to pair promising compounds with available preclinical resources and funding, on an ongoing basis

☐ Assess the impact of emerging viral mutations on efficacy of vaccines and therapeutics
**Small Animals**

<table>
<thead>
<tr>
<th>Species</th>
<th>Modification</th>
<th>Model Name/Nomenclature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferret</td>
<td>Outbred Stock</td>
<td>Ferret</td>
</tr>
<tr>
<td>Guinea Pig</td>
<td>Wild Type</td>
<td>Guinea Pig</td>
</tr>
<tr>
<td>Hamster</td>
<td>Inbred Strain</td>
<td>Syrian Golden</td>
</tr>
<tr>
<td>Hamster</td>
<td>Transgenic</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>ACE2 Transduced</td>
<td></td>
</tr>
<tr>
<td>Mouse</td>
<td>Inbred Strain</td>
<td></td>
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<tr>
<td>Mouse</td>
<td>Knock-In</td>
<td></td>
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<tr>
<td>Mouse</td>
<td>Transgenic</td>
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</tr>
</tbody>
</table>

**Non-Human Primates**

<table>
<thead>
<tr>
<th>Species</th>
<th>Geographic Origin</th>
<th>Route of Exposure</th>
<th>Vaccine</th>
<th>Antigen</th>
<th>Neutralizing Antibodies</th>
<th>Other Therapies</th>
<th>Transgenic</th>
<th>Disease Manifestation &amp; Pathology</th>
<th>Extent of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Green</td>
<td>St. Kitts (wild-caught)</td>
<td>Intratracheal/intranasal, aerosol</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>Lung lesions, interstitial pneumonia; recovery</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>Aged African Green</td>
<td>St. Kitts (wild-caught)</td>
<td>Intratracheal/intranasal, aerosol</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>Lung lesions, interstitial pneumonia; cytokine storm, ARDS, varied death and recovery</td>
<td>Severe</td>
</tr>
<tr>
<td>Cynomolgus macaque</td>
<td>Cambodia</td>
<td>Intratracheal/intranasal, aerosol</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>Lung lesions, interstitial pneumonia; recovery</td>
<td>Mild</td>
</tr>
<tr>
<td>Rhesus macaque</td>
<td>China or India</td>
<td>Intratracheal/intranasal, ocular, oral, aerosol</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
<td></td>
<td>Lung lesions, interstitial pneumonia; recovery</td>
<td>Mild</td>
</tr>
</tbody>
</table>

https://opendata.ncats.nih.gov/covid19
Therapeutics – Clinical Working Group

OBJECTIVE
Prioritize promising therapeutic candidates and accelerate their clinical evaluation by establishing large-scale master protocol trials.

ACCOMPLISHMENTS TO DATE

✓ Developed and continuously enhanced a world-class process for prioritizing clinical agents for rapid testing.

✓ Evaluated ~500 available agents with potential relevance for COVID-19 therapies and prioritized the most promising agents for further study (agent prioritization continues on a rolling basis).

✓ Assessed, designed, and harmonized seven master protocols for ACTIV clinical trials, focusing on candidates selected through the agent prioritization process.

✓ Selected clinical trial networks best suited to execute these master protocols and supported NIH efforts to launch them; six protocols have been launched to date.

☐ Actively working with NIH and OWS across all protocols to ensure they are effectively coordinated, efficiently managed, and meet recruitment targets.
Prioritizing the most promising therapeutic agents for COVID-19

The Working Group continues to identify agents that stop the virus or that treat its symptoms so they can be placed in a master protocol for a Phase II/II Progressive trial – so far ACTIV has reviewed more than 500 agents.

Publicly Available Data
Submission from Investigators
Survey Responses

Antivirals
Host Targeted / Immunomodulators
Symptomatic / Supportive
Neutralizing mAbs

Score Candidates based on Pre-defined Criteria
Assess Supply and Other Logistical Needs
Establish Minimum Entry Criteria and Operational Criteria
Clinical Trial Capacity Working Group

The Working Group developed an inventory of clinical trial capacity, including networks of NIH ICs, industry, and other organizations, that will serve as a guide for how and where to implement effective COVID-19 clinical trials.

- 3 unique clinical trial capacity surveys developed for Networks, Sites, and Clinical Research Organizations (CROs) and Site Management Organizations (SMOs)
- 63 Networks completed the survey*
- 725 total Sites completed the survey*
- 39 CROs/SMOs completed the survey*

- Identified 52 novel and scalable enhancements / efficiencies for therapeutic clinical protocols and vaccine protocols
- A Tableau-based dashboard was created to query and visualize survey data
- Clinical Trial network, site, and CRO/SMO survey data is combined in one comprehensive view
- Dashboard includes overlay of COVID-19 infection data with collected survey data to inform decisions around optimizing site selection for therapeutic and vaccine trials

*Additional organizations will be surveyed as identified
**Current Portfolio of ACTIV Master Protocols**

ACTIV Therapeutics has been taking a portfolio approach to address the dramatic health and economic challenges posed by the pandemic, with harmonized “master protocol” trials.

<table>
<thead>
<tr>
<th>ACTIV-1</th>
<th>DESIRED OUTCOMES</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Phase III trial of 3 host-targeted immune modulators</td>
<td>Trial launched October 16</td>
<td></td>
</tr>
<tr>
<td>• Inpatient (hospitalized) patient population</td>
<td>First 3 agents selected – Abatacept,Infliximab, and Cenicriviroc</td>
<td></td>
</tr>
<tr>
<td>• NCATS Trial Innovation Network + CRO</td>
<td></td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>ACTIV-2</th>
<th>DESIRED OUTCOMES</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Phase II/III trial of up to 5-7 Neutralizing Antibodies and Oral Antivirals</td>
<td>Trial launched August 3</td>
<td></td>
</tr>
<tr>
<td>• Outpatient population</td>
<td>Initial agent: nAb from Lilly; onboarding other agents</td>
<td></td>
</tr>
<tr>
<td>• NIAID ACTG network + CRO</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>ACTIV-3</th>
<th>DESIRED OUTCOMES</th>
<th>STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Phase III trial of 5-7 Neutralizing Antibodies and Oral Antivirals</td>
<td>Trial launched August 4</td>
<td></td>
</tr>
<tr>
<td>• Inpatient population</td>
<td>Initial agent: nAb from Lilly (halted for futility Oct. 26); onboarding other agents</td>
<td></td>
</tr>
<tr>
<td>• NIAID INSIGHT + NHLBI PETAL + NHLBI CSTN + VA networks + CRO</td>
<td></td>
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<thead>
<tr>
<th>ACTIV-4</th>
<th>DESIRED OUTCOMES</th>
<th>STATUS</th>
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<tbody>
<tr>
<td>• Phase III trial of anticoagulants (heparin, aspirin) and antiplatelet drug</td>
<td>Hospitalized and Pre-Hospitalized cohorts launched Sept 17, Post-hospitalized cohort launched early December</td>
<td></td>
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<tr>
<td>• Three different populations: pre-hospitalized, hospitalized, &amp; post-hospitalized</td>
<td>First agents – LMWH and UFH (hospitalized) and low dose aspirin, high dose aspirin, and apixaban (pre-hospitalized)</td>
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<tr>
<td>• NHLBI-NINDS CONNECTS network</td>
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<tr>
<th>ACTIV-5 (Big Effect Trial)</th>
<th>DESIRED OUTCOMES</th>
<th>STATUS</th>
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<tbody>
<tr>
<td>• Phase II “proof of concept” study to identify multiple promising treatments</td>
<td>Trial launched October 12</td>
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<tr>
<td>• Inpatient population</td>
<td>Two initial agents selected – Risankizumab + Lenzilumab</td>
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<tr>
<td>• NIAID networks + CRO</td>
<td>Prioritizing additional agents</td>
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## Where do I go for more information on ACTIV?

<table>
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<tr>
<th>For:</th>
<th>Page / Link</th>
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| **General information:** | ✓ NIH ACTIV Website: [https://www.nih.gov/research-training/medical-research-initiatives/activ](https://www.nih.gov/research-training/medical-research-initiatives/activ)  
| **To submit information for a diagnostic, vaccine, technology, or other information for the awareness of NIH:** | ✓ NIH COVID-19 Candidate and Technologies Portal: [https://grants.nih.gov/grants/rfi/rfi.cfm?ID=107](https://grants.nih.gov/grants/rfi/rfi.cfm?ID=107) |
| **Publications to date:** | ✓ Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): An Unprecedented Partnership for Unprecedented Times [https://jamanetwork.com/journals/jama/fullarticle/2766371](https://jamanetwork.com/journals/jama/fullarticle/2766371)  
✓ A strategic approach to COVID-19 vaccine R&D [https://science.sciencemag.org/content/368/6494/948](https://science.sciencemag.org/content/368/6494/948) |
What have we learned?

• It is possible to go from fundamental discovery to therapeutics and vaccines much more quickly than has historically occurred

• Ingredients for this are
  • Feeling of urgency in all participants in the research ecosystem
  • Recalculation of benefit:risk based on urgency
  • Willingness to share based on recalculation of benefit:risk
  • Proactive collaboration among public sector, private sector, and public-private orgs that derives from desire to share

• This is a potentially positively self-reinforcing cycle since increased efficiencies lead to increased productivity which has potential to increase return on investment despite sharing of credit/profits

• But many of the conditions, regulatory/policy exemptions, and additional funding will likely not continue without proactive steps by all participants in the university, industry, and government sectors