NCATS

COLLABORATE. INNOVATE. ACCELERATE.

Catalyzing Translational Innovation in the Age of COVID-19

Christopher P. Austin, M.D.

Director, NCATS

Federal Demonstration Partnership

January 11, 2021

National Center for Advancing Translational Sciences

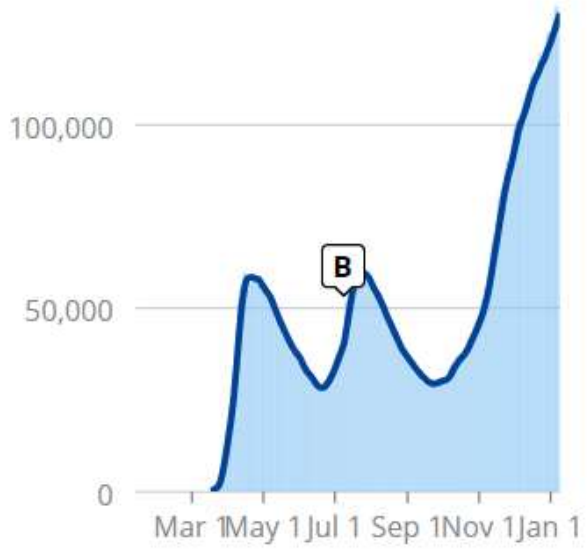
The COVID-19 Pandemic

A public health crisis unrivalled in modern times

New tests
Total test results (mixed units)

New cases (Notes)

Current hospitalizations (Notes)



New deaths (Notes)

Chart information and data ↓

The COVID Tracking Project

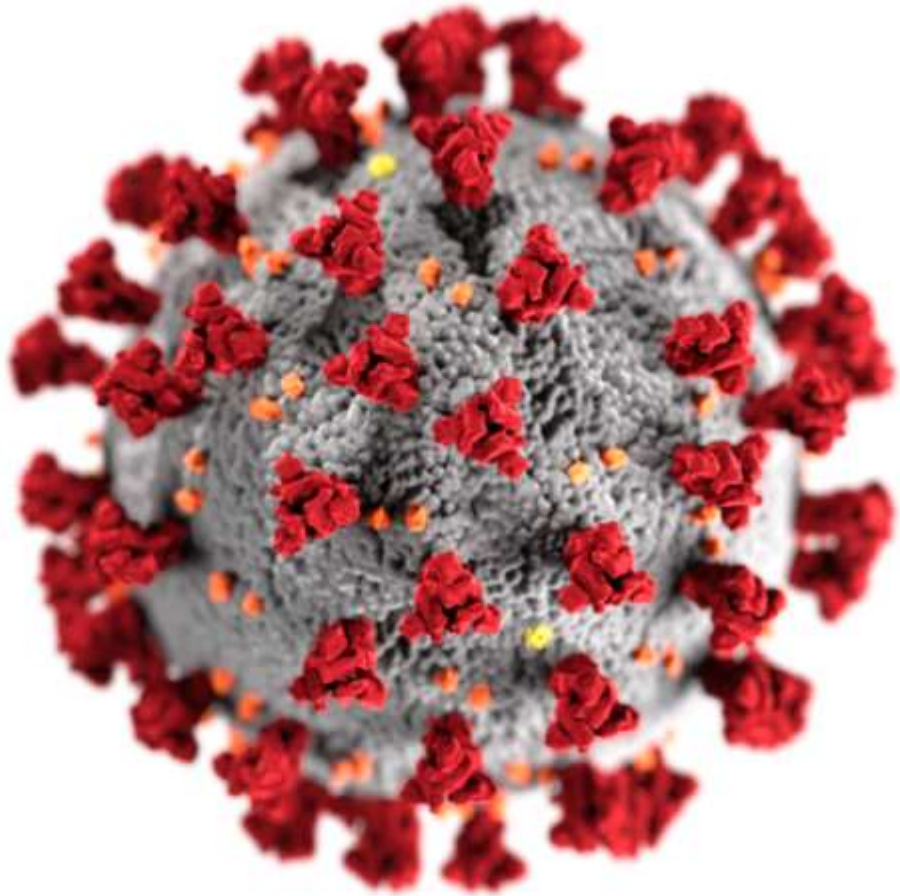
https://covidtracking.com/data

National Center for Advancing Translational Sciences

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

May 11, 2020

JAMA

The Journal of the American Medical Association

Viewpoint

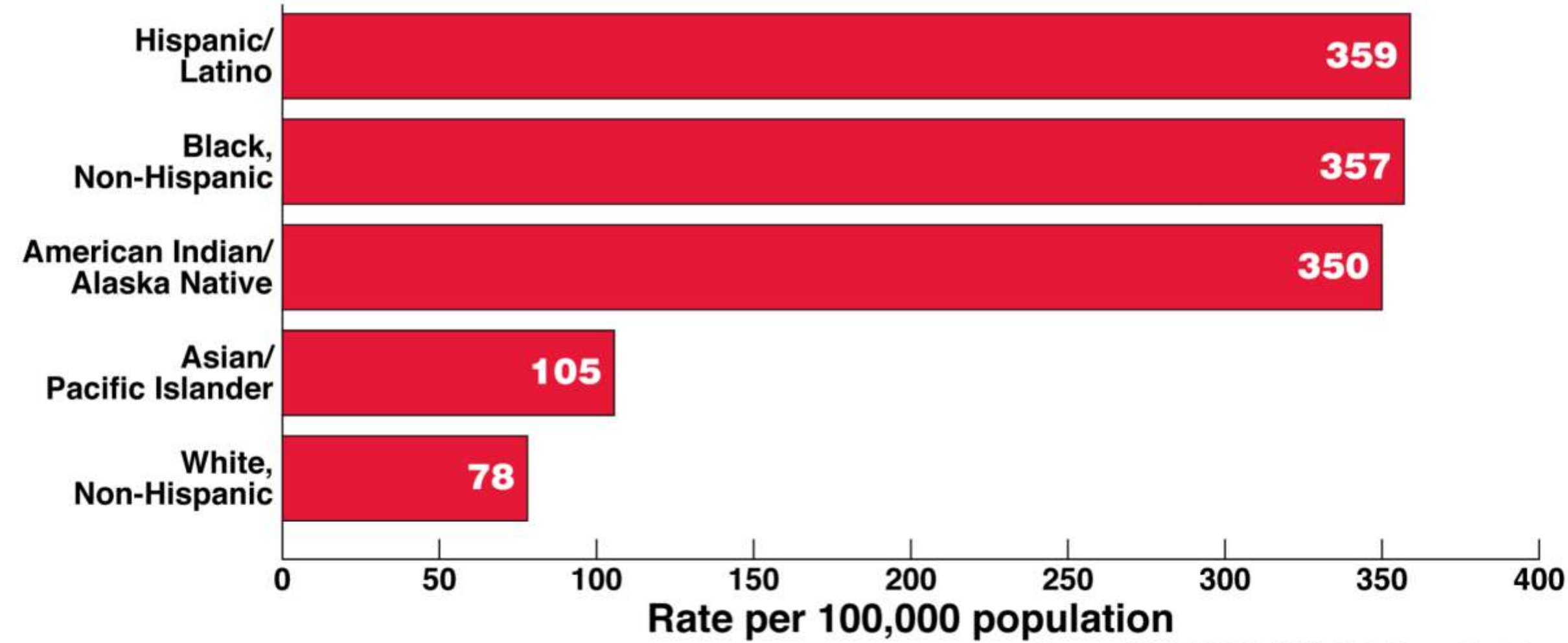
COVID-19 and Racial/Ethnic Disparities

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."

AS Fauci/NIAID

Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – September 19, 2020



AS Fauci/NIAID

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

NIH National Center for Advancing Translational Sciences

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)

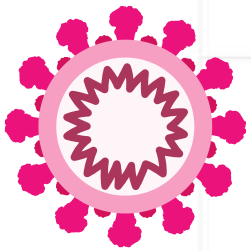
>27,000 visitors and **85,000 views** since launch

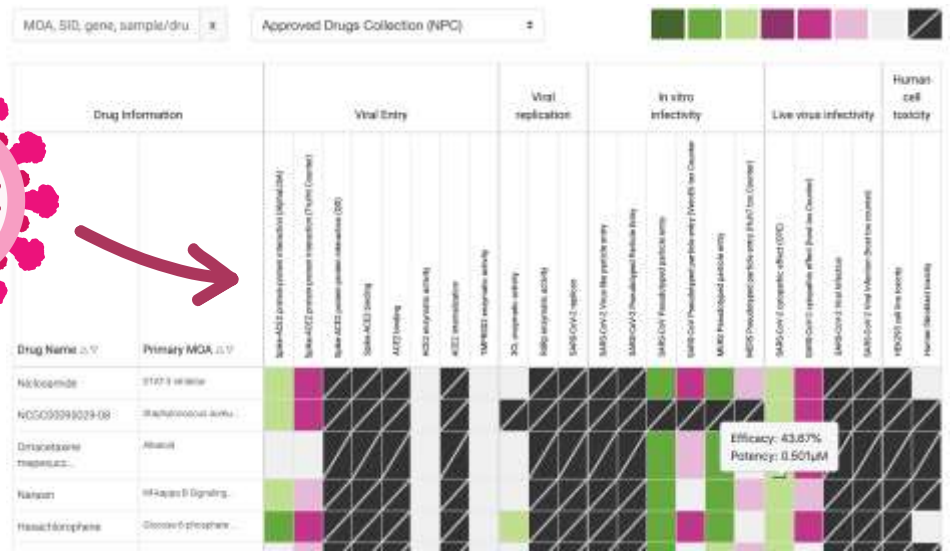
Expanding this data-sharing resource to include more complex types of data (e.g. image-based screens)

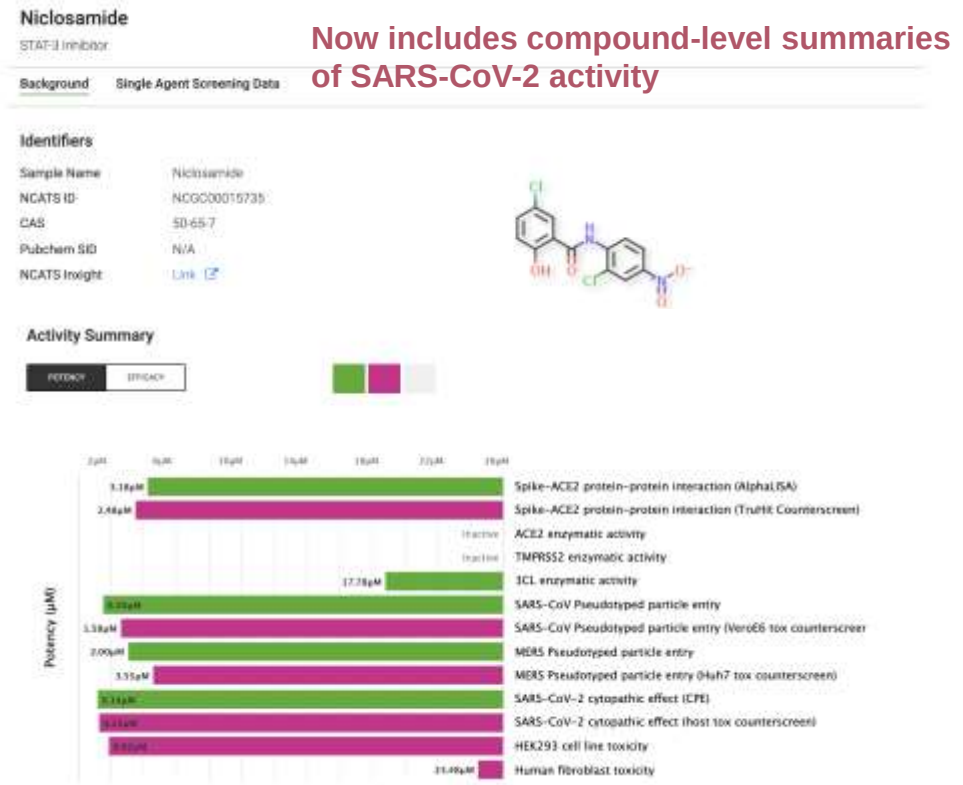
Integrating external (non-NCATS) SARS-CoV-2 data from collaborative partners across the globe, including:

- 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/
https://ncats.nih.gov/expertise/covid19-open-data-portal







Now includes compound-level summaries of SARS-CoV-2 activity

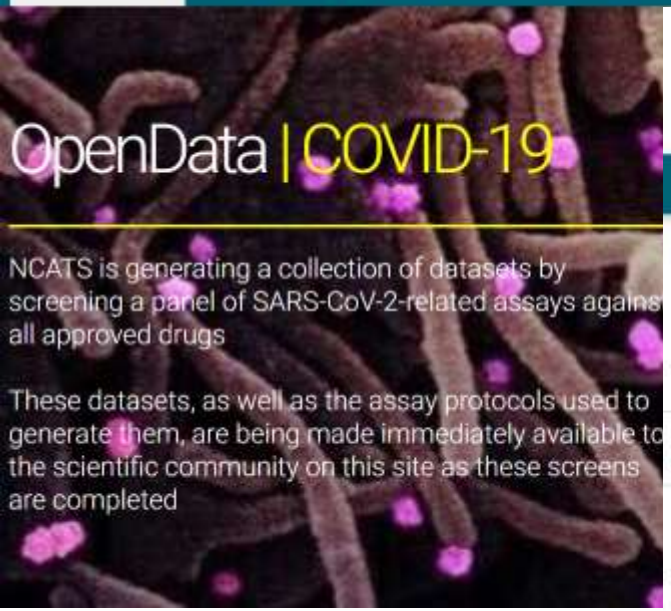
National Center for Advancing Translational Sciences

U.S. Department of Health and Human Services › National Institutes of Health › National Center for Advancing Translational Sciences

NIH National Center for Advancing Translational Sciences | OpenData Portal

https://opendata.ncats.nih.gov/covid19/

Home | OpenData Browser | Assays | Animal Models | Omics Efforts | Highlights | Resources



NIH National Center for Advancing Translational Sciences | OpenData Portal

Home | OpenData Browser | Assays | Animal Models | Omics Efforts | Highlights | Resources

Home > Animal Models

Animal Models

Summary | Small Animal Model Field Guide | ACTIV Resources

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.

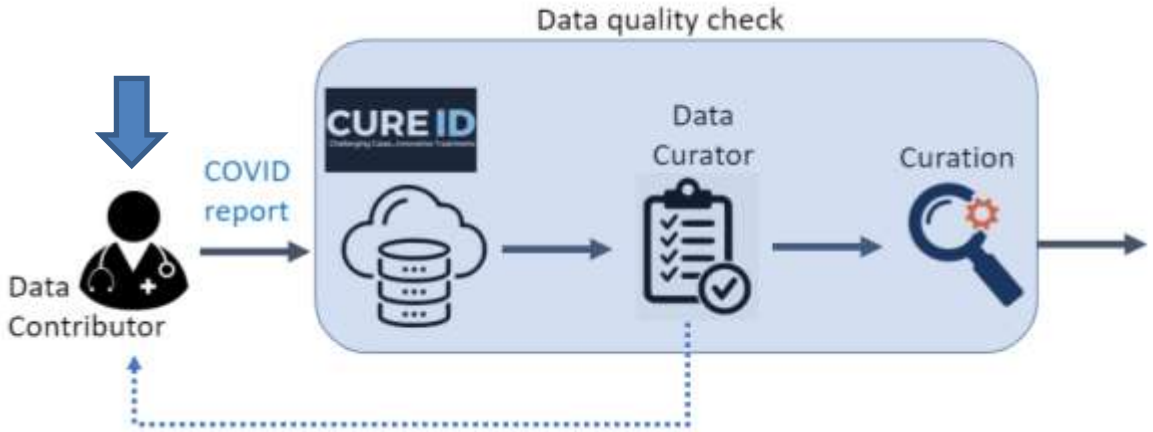
Feedback, comments, and questions are highly encouraged to further develop these pages. Please contact ACTIVpreclinical@fnih.org.

Small Animals

FNIH

Species	Modification	Model Name/Nomenclature	Vaccines	Antivirals	Neutralizing Antibodies	Other Therapies	Infectivity	Transmission	Disease Enhancement	Disease Manifestation & Pathology	Extent of disease
Ferret	Outbred Stock	Ferret	√		√		Y	Y	TBD	Viral titers in nasal washes; fever	Mild
Guinea Pig	Wild Type	Guinea Pig					N	N	N	Lung lesions	None to minimal

CURE ID: Capturing Clinicians' Experiences of Novel Uses of Existing Drugs During COVID-19



https://cure.ncats.io

Download on the App Store

GET IT ON Google Play

- **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

NIH
National Center for Advancing Translational Sciences

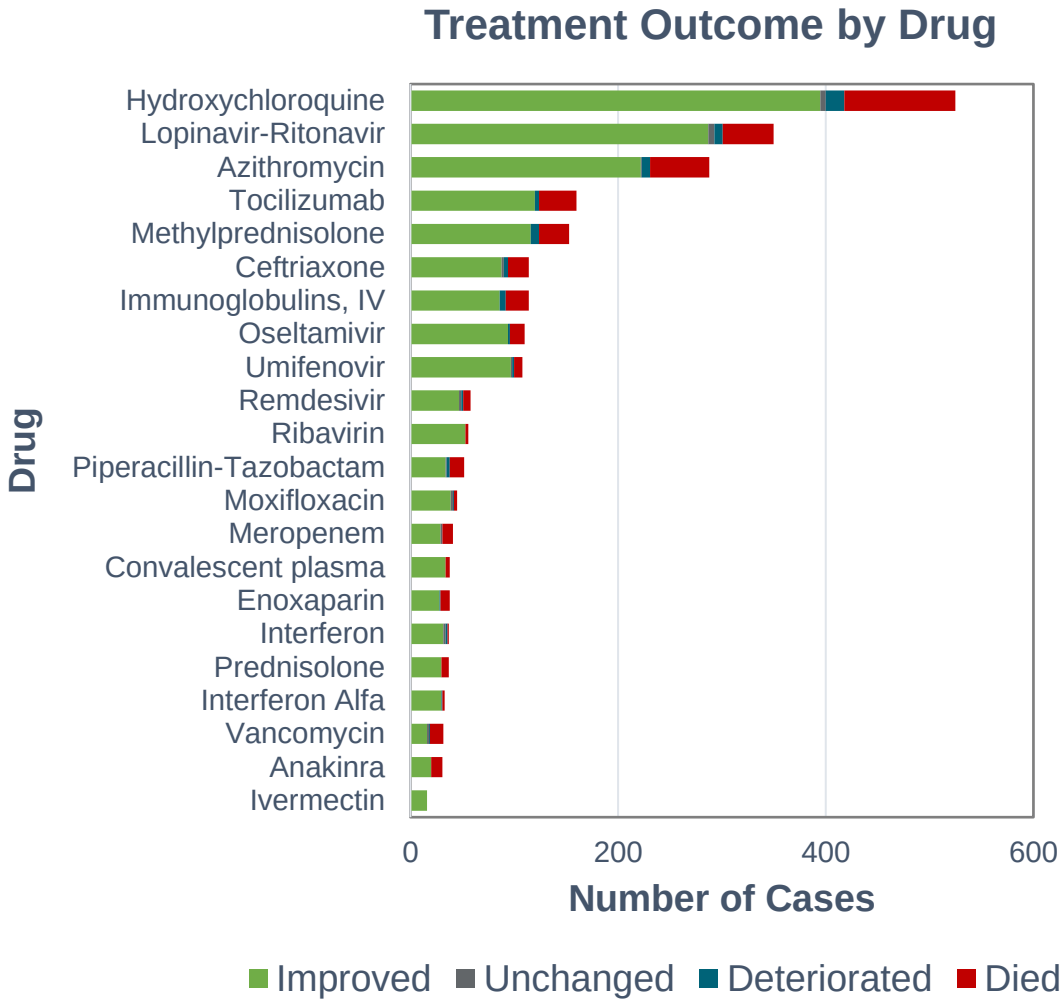
CURE ID: Capturing Clinicians' Experiences of Novel Uses of Existing Drugs During COVID-19

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



National Center for Advancing Translational Sciences

PRESS RELEASES

June 23, 2020

PRINT PDF

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.

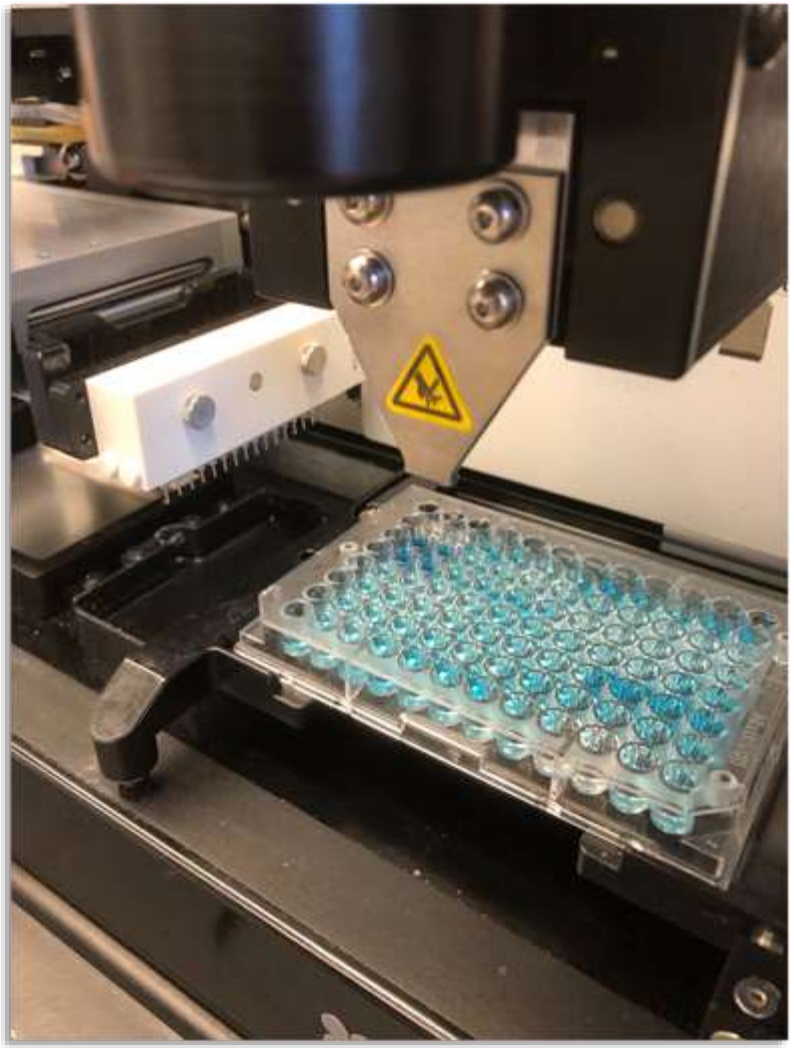
CDRC
CURE DRUG REPURPOSING COLLABORATORY
CRITICAL PATH INSTITUTE

CURE ID
Challenging Cases... Innovative Treatments

NIH
National Center for Advancing Translational Sciences

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.



https://ncats.nih.gov/covid19-translational-approach/collaboration#forming-new-collaborations

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

The N3C Data Enclave opened to researchers in September.

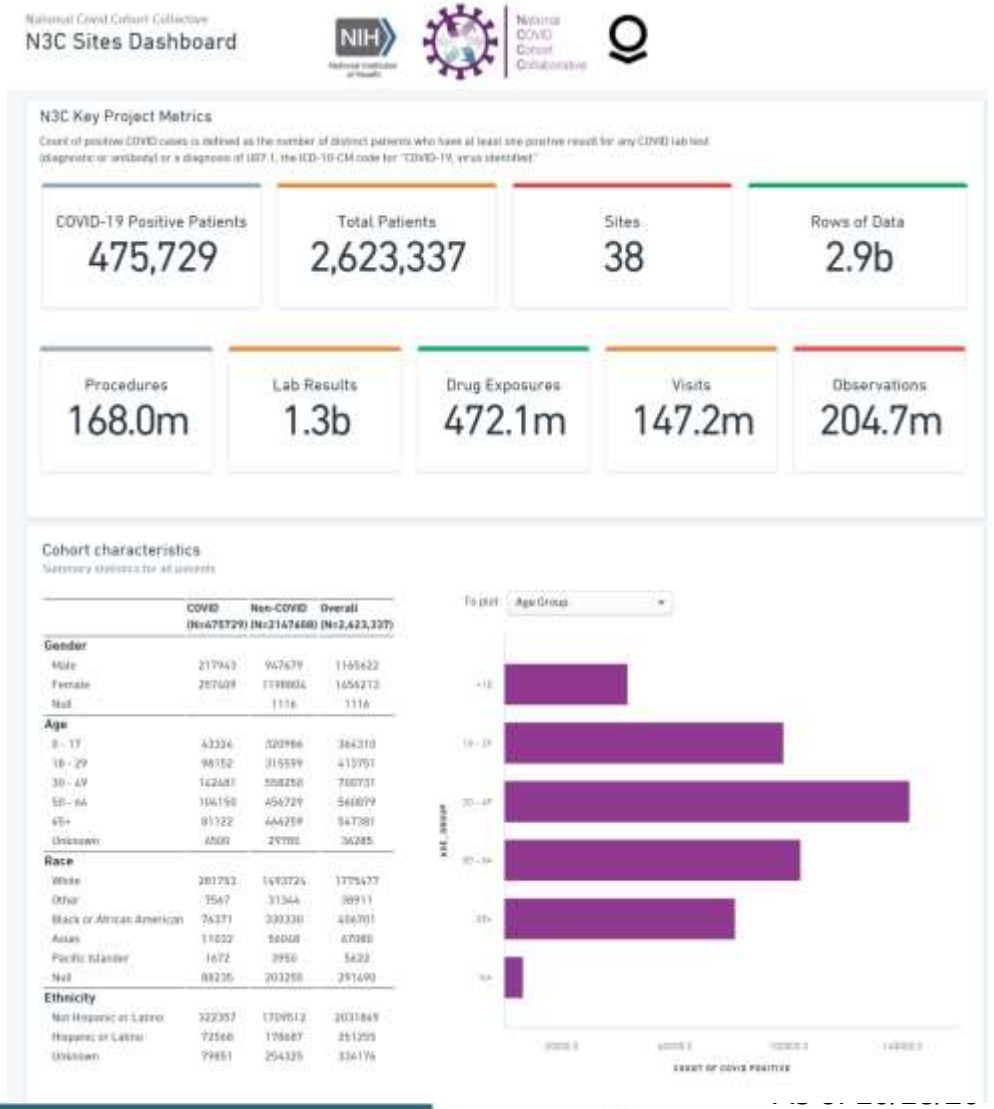
https://ncats.nih.gov/n3c

Source: Office of the Director

National COVID Cohort Collaborative

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

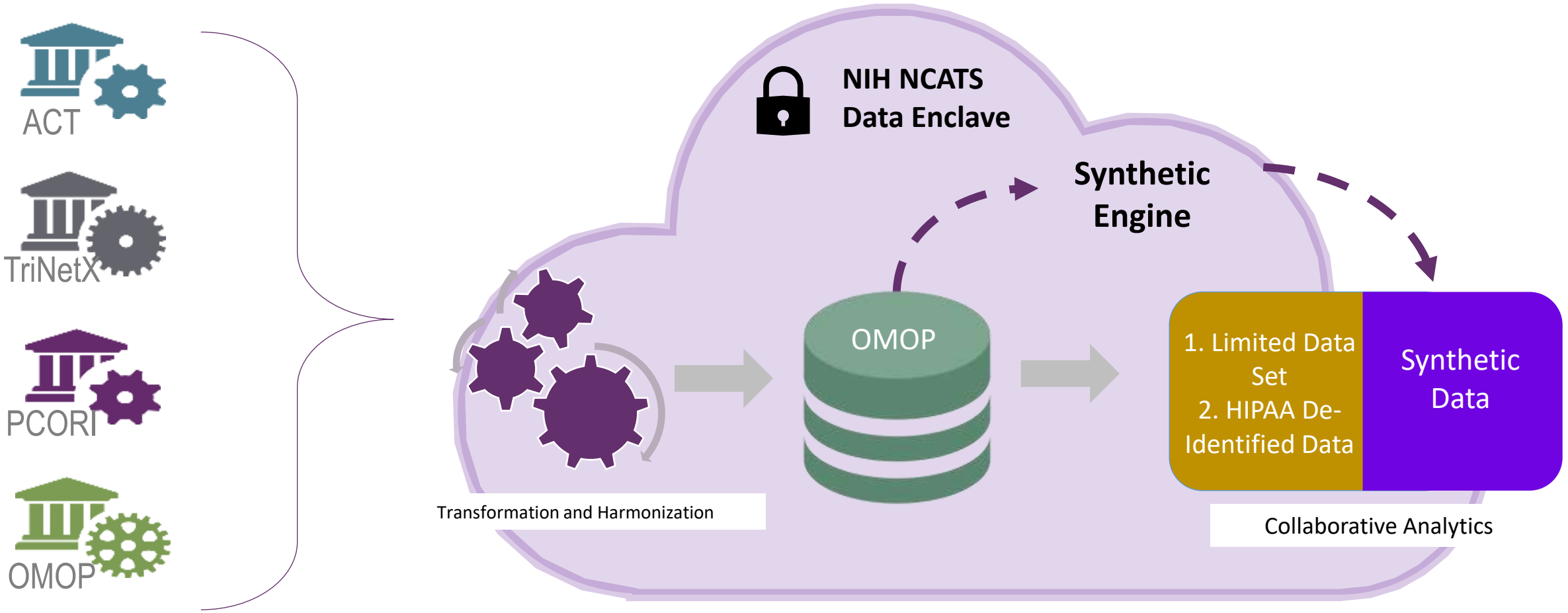


https://ncats.nih.gov/n3c

NIH National Center for Advancing Translational Sciences

National COVID Cohort Collaborative

N3C Data Pipeline

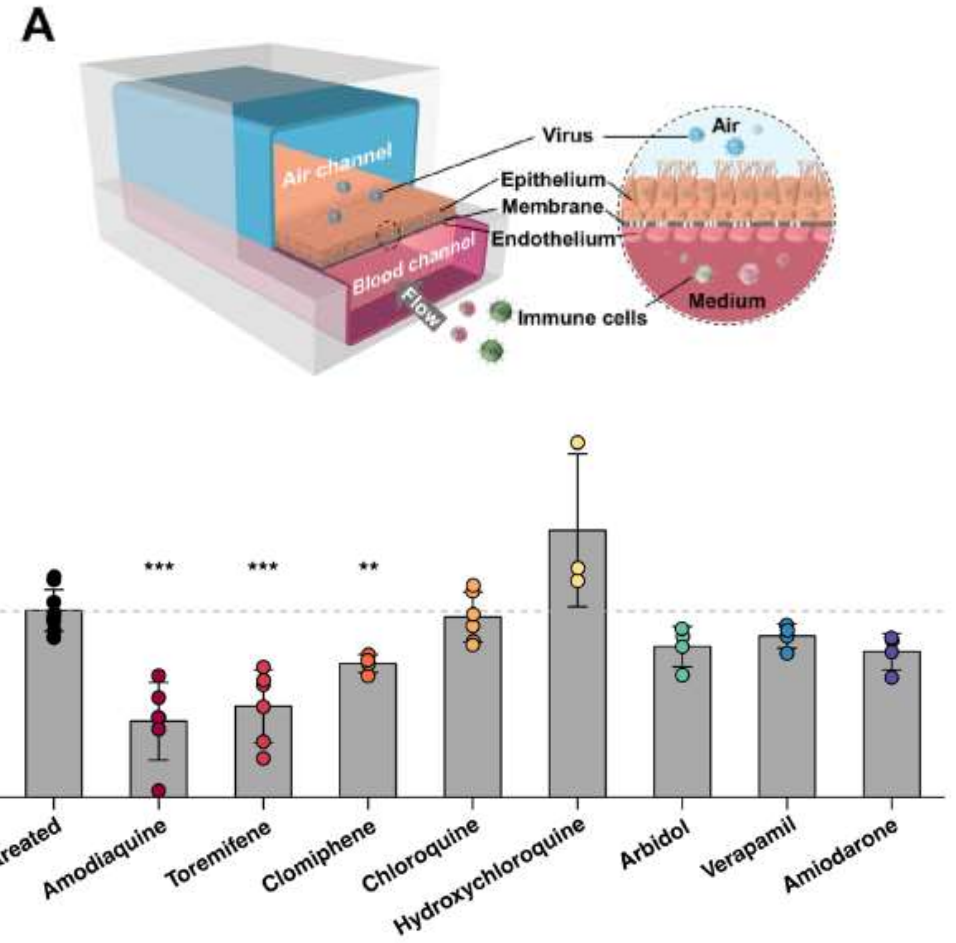


1	2	3	4
NCATS Data Transfer Agreement	**Data Acquisition**	**Data Harmonization**	**NCATS Data Use Agreement**

National Center for Advancing Translational Sciences

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.**



https://doi.org/10.1101/2020.04.13.039917 (bioRxiv)

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:

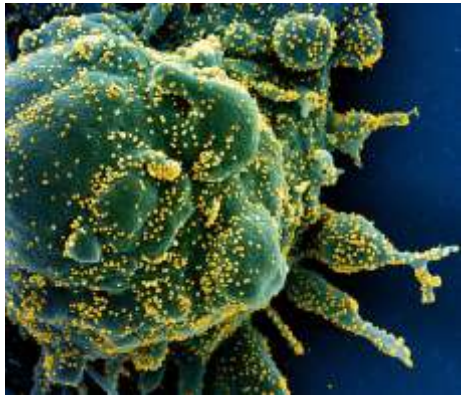
- The ACTIV-1 Immune Modulators trial is evaluating three drugs that could reduce the harmful COVID-19 cytokine storm
- Two trials led by Einstein/NYU and Vanderbilt are evaluating blood plasma donated by people who have recovered from COVID-19

The trials are currently enrolling participants.

https://ncats.nih.gov/news/releases

Source: DCI

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.

NIH
National Center for Advancing Translational Sciences

NCATS Convalescent Plasma RCTs

Multisite trials run through CTSA hubs

CONTAIN COVID-19

RANDOMIZED CONTROLLED TRIAL STUDYING THE EFFICACY AND SAFETY OF CONVALESCENT PLASMA IN LIMITING COVID-19 COMPLICATIONS

Enrollment: 725
Active Sites: 17
Anticipated Completion: February

PASS IT ON

PASSIVE IMMUNITY TRIAL FOR OUR NATION

Enrollment: 532
Active Sites: 20
Anticipated Completion: March

NCATS Accelerating Translation by:

Establishing format for direct data submission to FDA

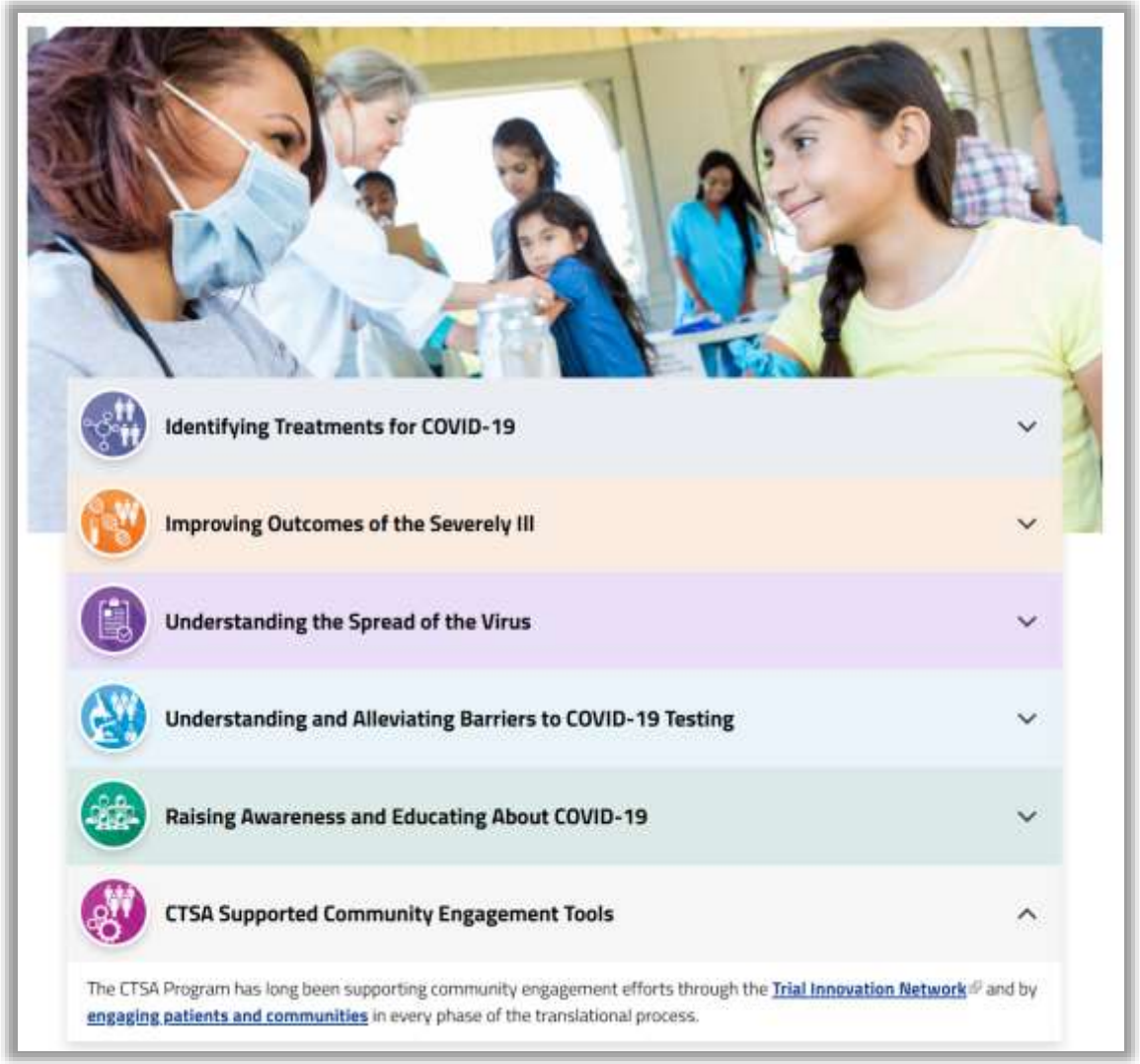
Promoting harmonization of plasma assays

NIH National Center for Advancing Translational Sciences

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.



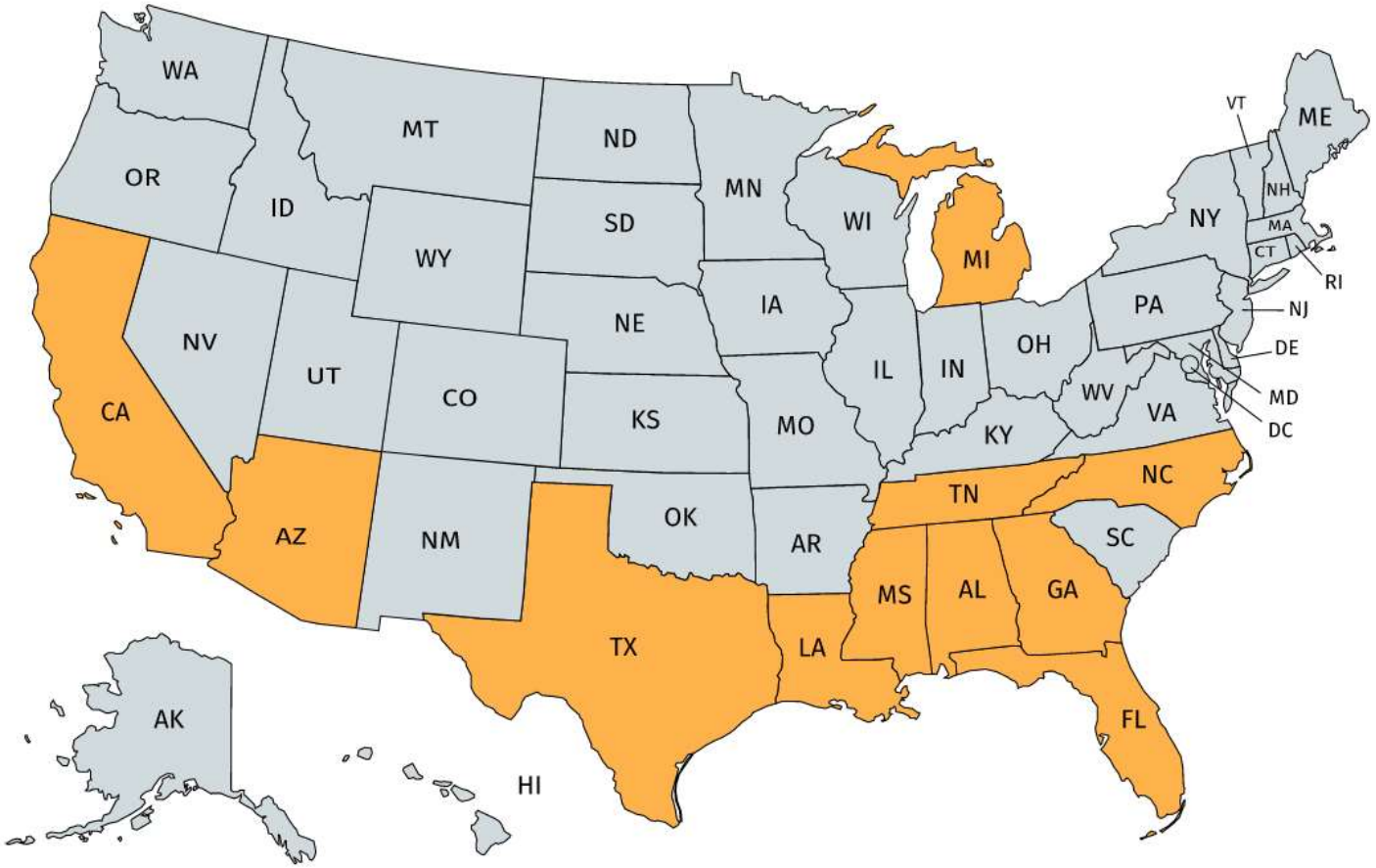
https://ncats.nih.gov/ctsa/projects/community-engagement-at-CTSA-hubs-during-the-COVID-19-pandemic

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.
6. North Carolina* - Anissa I. Vines, Ph.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 National Institutes of Health

RADx[SM] Tech

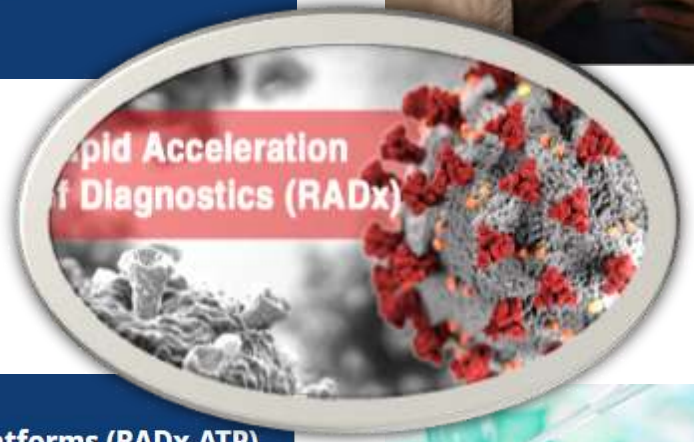
The RADx Tech initiative aims to speed the development, validation, and commercialization of innovative point-of-care and home-based tests, as well as improve clinical laboratory tests, that can directly detect the virus.

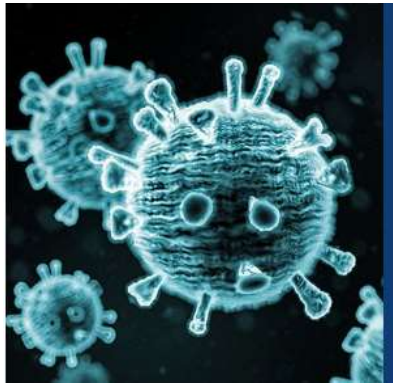
Budget: $500 Million

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: $500 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: $200 Million

NIH National Institutes of Health

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.

CTSA Clinical & Translational Science Awards Program

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/radx/funding#radx-up-funded

*Out of 32 institutions received supplements

NIH National Center for Advancing Translational Sciences

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

LAUNCH

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

MISSION

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

FNIH

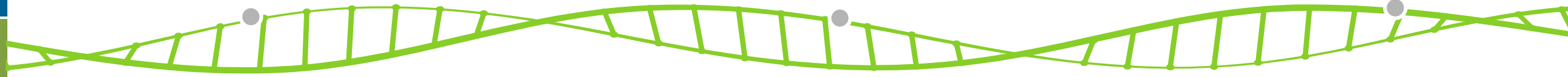
ACTIV Stakeholders

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.

8
Government Partners

20
Industry Partners

4
Non-Profits



BARDA
CDC
Department of Defense
European Medicines Agency
FDA U.S. Food & Drug Administration
Operation Warp Speed
NIH
Department of Veterans Affairs
FNIH

abbvie
AMGEN
AstraZeneca
Bristol-Myers Squibb
Eisai
Lilly
evotec
gsk
Johnson & Johnson
MERCK
moderna
NOVARTIS
RHYTHM THERAPEUTICS
Roche Genentech
Pfizer
SANOFI
Takeda
NOVAVAX
VIR

Bill & Melinda Gates foundation
Fred Hutch Cures Start Here
RTI International
FNIH

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

Members

Anthony Fauci, NIAID
Gary Gibbons, NHLBI
Janet Woodcock, OWS
William Pao, Roche
Mikael Dolsten, Pfizer
Gary Disbrow, BARDA
Peter Marks, FDA
Andrew Plump, Takeda

ACTIV Leadership Team

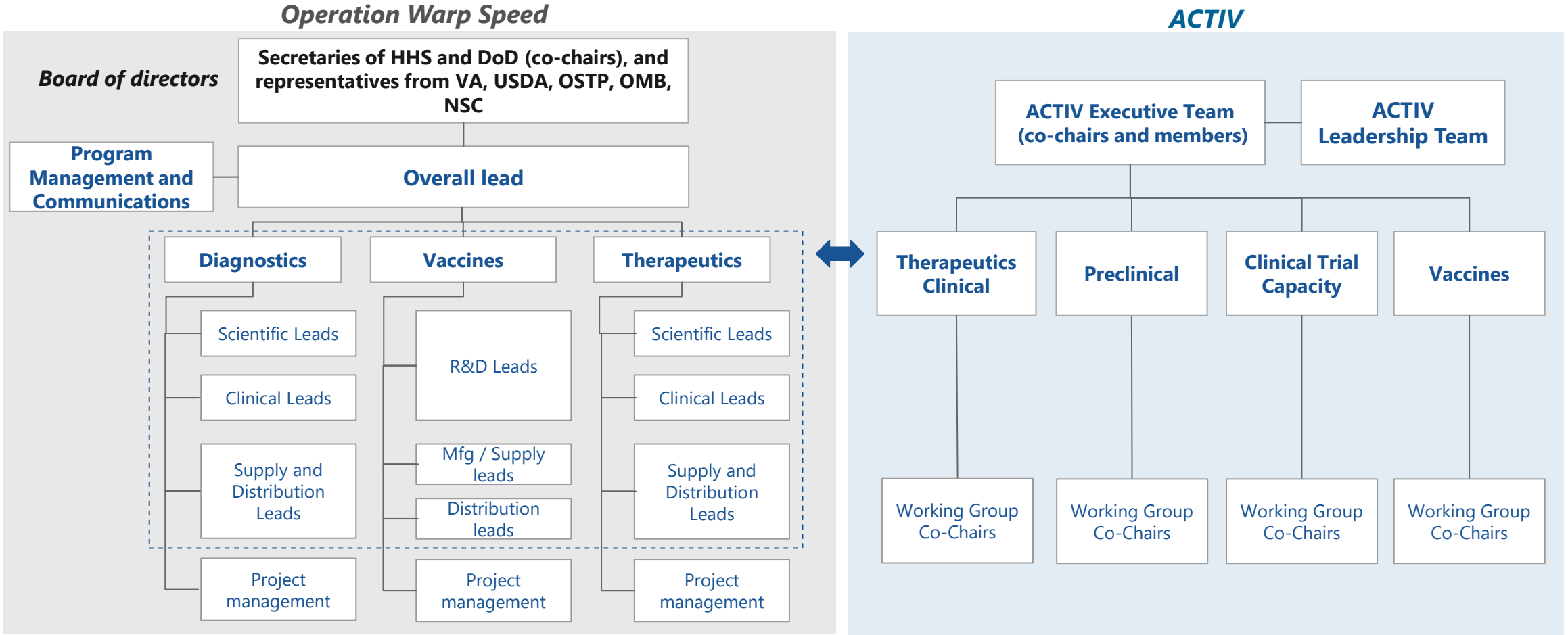
Scientific leaders from all participating organizations

- Preclinical Working Group
- Therapeutics Clinical Working Group
- Clinical Trial Capacity Working Group
- Vaccines Working Group

FNIH

ACTIV Governance & Coordination with Operation Warp Speed

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



Focus Area Objectives & Composition

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

	Preclinical	Therapeutics – Clinical	Clinical Trial Capacity	Vaccines
Objective	+ Develop a collaborative, streamlined forum to identify preclinical treatments	+ Accelerate clinical testing of the most promising vaccines and treatments	+ Improve clinical trial capacity and effectiveness	+ Accelerate the evaluation of vaccine candidates to enable rapid authorization or approval
Sub-Groups	+ Animal Models + In Vitro Assays	+ Agent Prioritization + Master Protocol	+ Survey Development + Clinical Trial Network Inventory + Innovations	+ Vaccines Clinical Trials + Protective Immune Responses + Vaccine-Associated Immune Enhancement

FNIH

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**

FNIH

✓ *Completed* ❑ *In progress*

NIH National Center for Advancing Translational Sciences

OpenData Portal

Small Animals

FNIH

Species	Modification	Model Name/Nomenclature
Ferret	Outbred Stock	Ferret
Guinea Pig	Wild Type	Guinea Pig
Hamster	Inbred Strain	Syrian Golden
Hamster	Transgenic	Tg(K18-hACE2)
Mouse	ACE2 Transduced	Adenovirus transduced hACE2
Mouse	Inbred Strain	BALB/c (adapted virus)
Mouse	Knock-In	C57BL/6-Ace2$^{em1(ACE2)Yowa}$
Mouse	Transgenic	B6.Cg-Tg(K18-ACE2)2Prlmn/J

Non-Human Primates

FNIH

Species	Geographic Origin	Route of Exposure	Vaccines	Antivirals	Neutralizing Antibodies	Other Therapies	Infectivity	Transmission	Disease Enhancement	Disease Manifestation & Pathology	Extent of disease
African Green	St. Kitts (wild-caught)	Intratracheal/intranasal, aerosol	√		√		Y	TBD	TBD	Lung lesions;interstitial pneumonia; recovery	Mild to moderate
Aged African Green	St. Kitts (wild-caught)	Intratracheal/intranasal, intratracheal, aerosol	√		√		Y	TBD	TBD	Lung lesions; interstitial pneumonia; cytokine storm; ARDS; varied death and recovery	Severe
Cynomolgus macaque	Cambodia	Intratracheal/intranasal, intratracheal	√	√	√		Y	TBD	TBD	Lung lesions; interstitial pneumonia; recovery	Mild
Rhesus macaque	China or India	Intratracheal/intranasal, intratracheal, ocular, oral, aerosol	√	√	√		Y	TBD	TBD	Lung lesions; interstitial pneumonia; recovery	Mild

https://opendata.ncats.nih.gov/covid19

Therapeutics – Clinical Working Group

OBJECTIVE

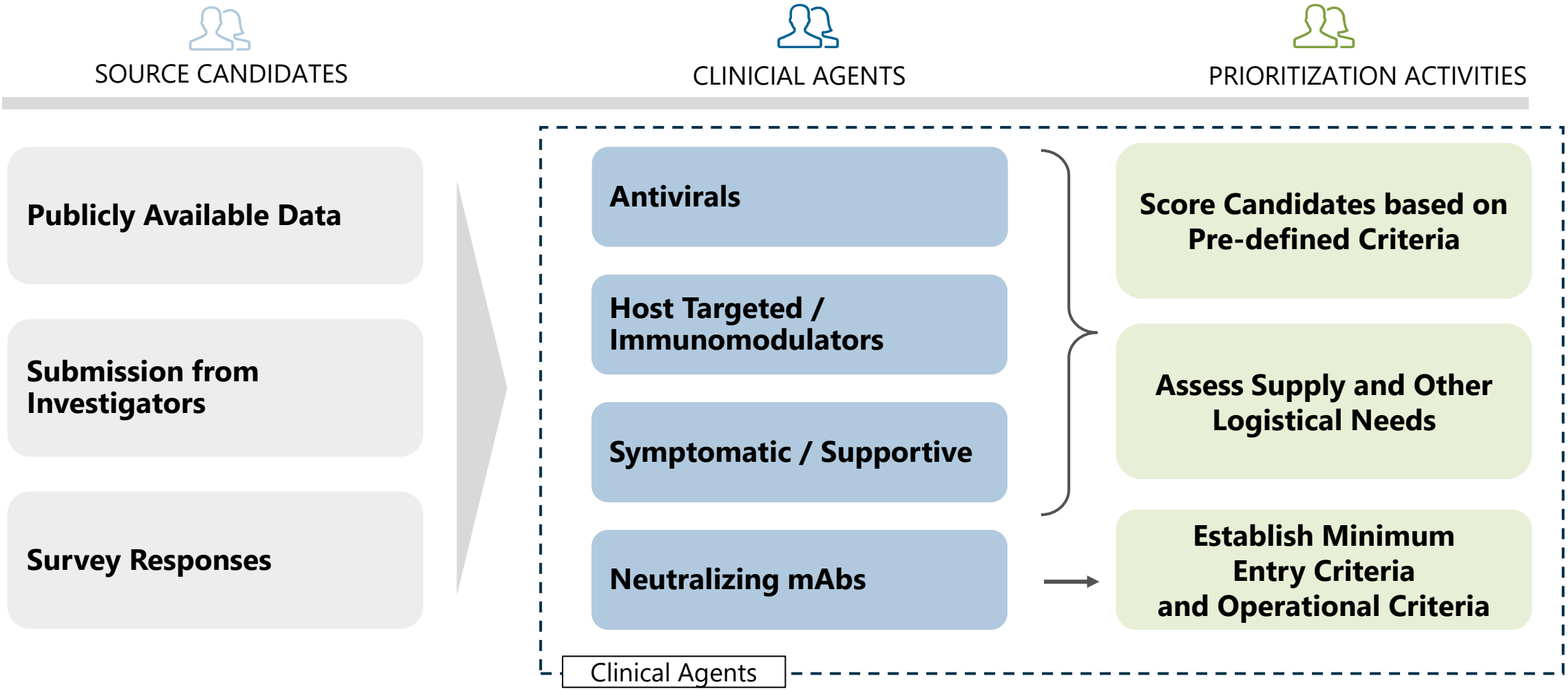
Prioritize promising therapeutic candidates and accelerate their clinical evaluation by establishing large-scale master protocol trials.

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

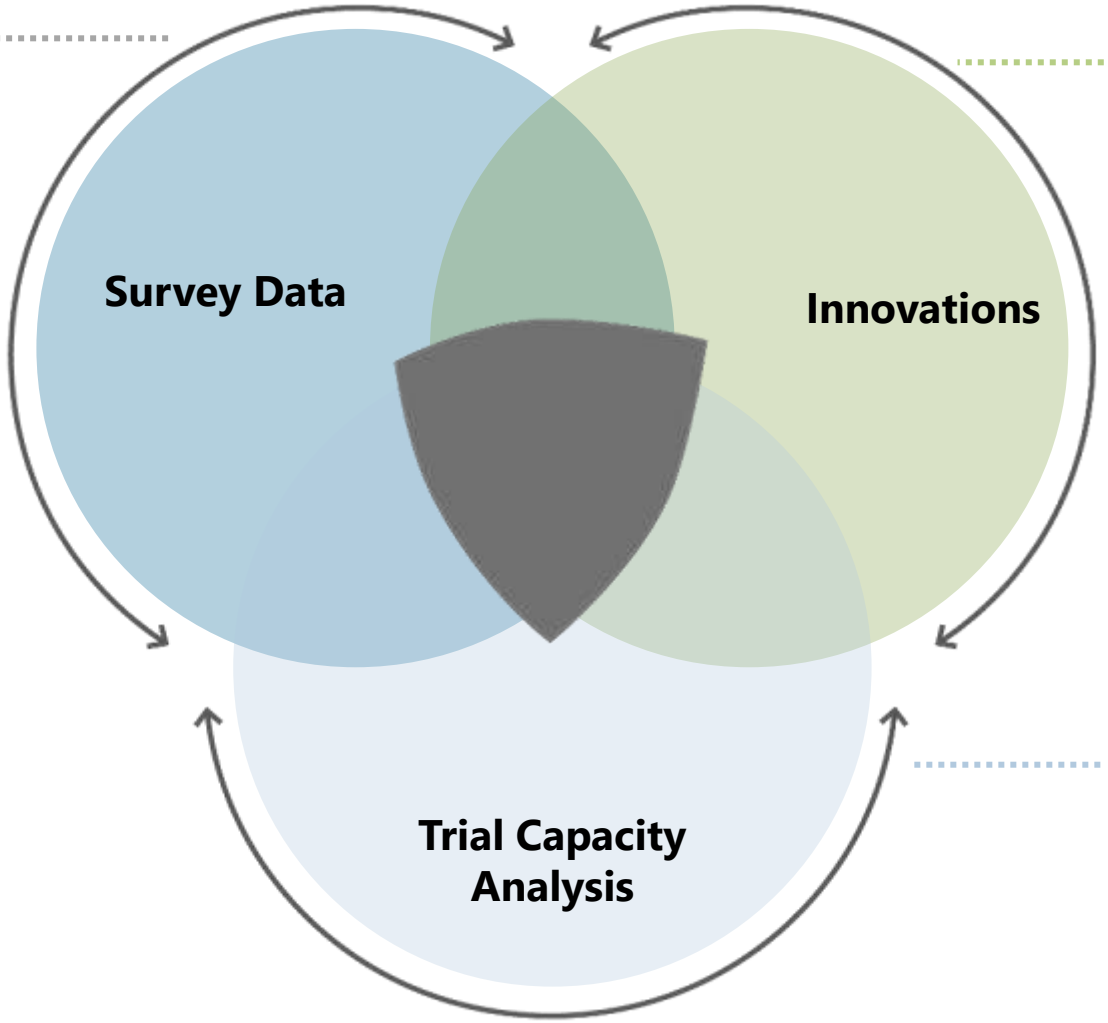
The Working Group continues to Identify agents that stop the virus or that treat its symptoms so they can be placed in a master protocol for a Phase II/II Progressive trial – so far ACTIV has reviewed more than 500 agents.



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

FNIH

*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.

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

FNIH

Where do I go for more information on ACTIV?

For:	Page / Link
General information:	✓ NIH ACTIV Website: [https://www.nih.gov/research-training/medical-research-initiatives/activ]
	✓ FNIH Website: [https://fnih.org/news/press-releases/nih-launches-partnership-to-speed-covid19-vaccines-treatments]
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]
Formal submission of agents for testing in ACTIV:	✓ ACTIV Preclinical and Clinical Asset Data Survey: [https://redcap.ncats.nih.gov/redcap/surveys/index.php?s=DAE87WPTE7]
Publications to date:	✓ Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV): An Unprecedented Partnership for Unprecedented Times [https://jamanetwork.com/journals/jama/fullarticle/2766371]
	✓ Accelerating Development of SARS-CoV-2 Vaccines — The Role for Controlled Human Infection Models [https://www.nejm.org/doi/full/10.1056/NEJMp2020076]
	✓ Bridging the Gap at Warp Speed — Delivering Options for Preventing and Treating Covid-19 [https://www.nejm.org/doi/full/10.1056/NEJMp2028535?query=TOC]
	✓ A strategic approach to COVID-19 vaccine R&D [https://science.sciencemag.org/content/368/6494/948]

FNIH

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

NCATS

COLLABORATE. INNOVATE. ACCELERATE.

ncats.nih.gov @ncats_nih_gov @ncats.nih.gov NIH-NCATS

National Center for Advancing Translational Sciences