Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)

David Wholley
Senior Vice President, Research Partnerships

June 12, 2020

About the FNIH

Mission

The mission of the Foundation for the National Institutes of Health (FNIH) is to create and lead alliances and public-private partnerships that advance breakthrough biomedical discoveries and improve the quality of people's lives.

Founded by Congress

The FNIH was created by Congress in 1990 as a not-for-profit charitable organization. The Foundation began its work in 1996 to facilitate groundbreaking research at the U.S. National Institutes of Health (NIH) and worldwide.

Why Collaborate?

- Share resources
- Enable insight and innovation
- Establish standards
- Distribute expertise
- Create consensus
- Drive competitiveness in marketplace
- Disseminate knowledge

Selected Public-Private Partnerships at the FNIH

Accelerating Medicines Partnership NIH (OD), NIA, NIAMS, NIDDK, NINDS, 12 companies, 10 not-for-profit organizations	**$302 million**
Partnership for Accelerating Cancer Therapies NCI, PhRMA, 12 pharmaceutical companies	**$220 million**
Alzheimer's Disease Neuroimaging Initiative (ADNI) NIA, NIBIB, 25+ companies, 3 not-for-profit organizations	**$206 million**
Grand Challenges in Global Health (GCGH) Bill & Melinda Gates Foundation	**$201 million**
Lung-MAP: Master Lung Protocol Trial NCI (SWOG), FDA, Friends of Cancer Research, 5 companies to date	**$163 million**
Vector-Based Control of Transmission (VCTR) VRC/NIAID, Bill & Melinda Gates Foundation	**$78 million**
The Biomarkers Consortium FDA, NIH, CMS, PhRMA, BIO, pharmaceutical and nutrition companies, not-for-profit organizations	**$95 million**
Comprehensive T Cell Vaccine Immune Monitoring Consortium (CT-VIMC) Bill & Melinda Gates Foundation, NIAID	**$50 million**
MAL-ED: The Interactions of Malnutrition and Enteric Infections, Effect on Childhood Development Bill & Melinda Gates Foundation, Fogarty Institute Center (NIH)	**$46 million**

On April 17, NIH announced the launch of a public-private partnership, **Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV),** to develop a **coordinated research response to speed COVID-19 treatment and vaccine options.**

Coordinated by the Foundation for the National Institutes of Health (FNIH), **ACTIV brings together multiple partners from government, industry, and non-profits:**

7 Government Partners

BARDA
CDC
DoD
EMA
FDA
NIH
VA

18 Industry Partners

AbbVie
Amgen
AstraZeneca
Bristol Myers Squibb
Eisai
Eli Lilly and Company
Evotec
Gilead
GlaxoSmithKline
Johnson & Johnson
KSQ Therapeutics
Merck
Novartis
Pfizer
Roche-Genentech
Sanofi
Takeda
Vir Biotechnology

3 Nonprofits

Bill & Melinda Gates Foundation
Fred Hutchinson Cancer Research Center
RTI International

ACTIV is dedicated to:

- Establishing a **collaborative framework for prioritizing therapeutic candidates and accelerating vaccine evaluation**
- **Accelerating clinical trials of promising agents and leveraging existing clinical trial networks while maintaining rigorous safety standards**
- **Coordinating regulatory processes and leveraging assets among all partners**

The ACTIV partnership consists of **four fast-track focus areas,** each of which is led by a working group:

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

ACTIV Governance includes representation from all stakeholders

ACTIV Partnership Leadership Group

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

Preclinical Working Group

Sub Groups:
- Animal Models
- In Vitro Assays

Therapeutics Clinical Working Group

Sub Groups:
- Agent Prioritization
- Master Protocol

Clinical Trial Capacity Working Group

Sub Groups:
- Survey Development
- Clinical Trial Network Inventory
- Innovations

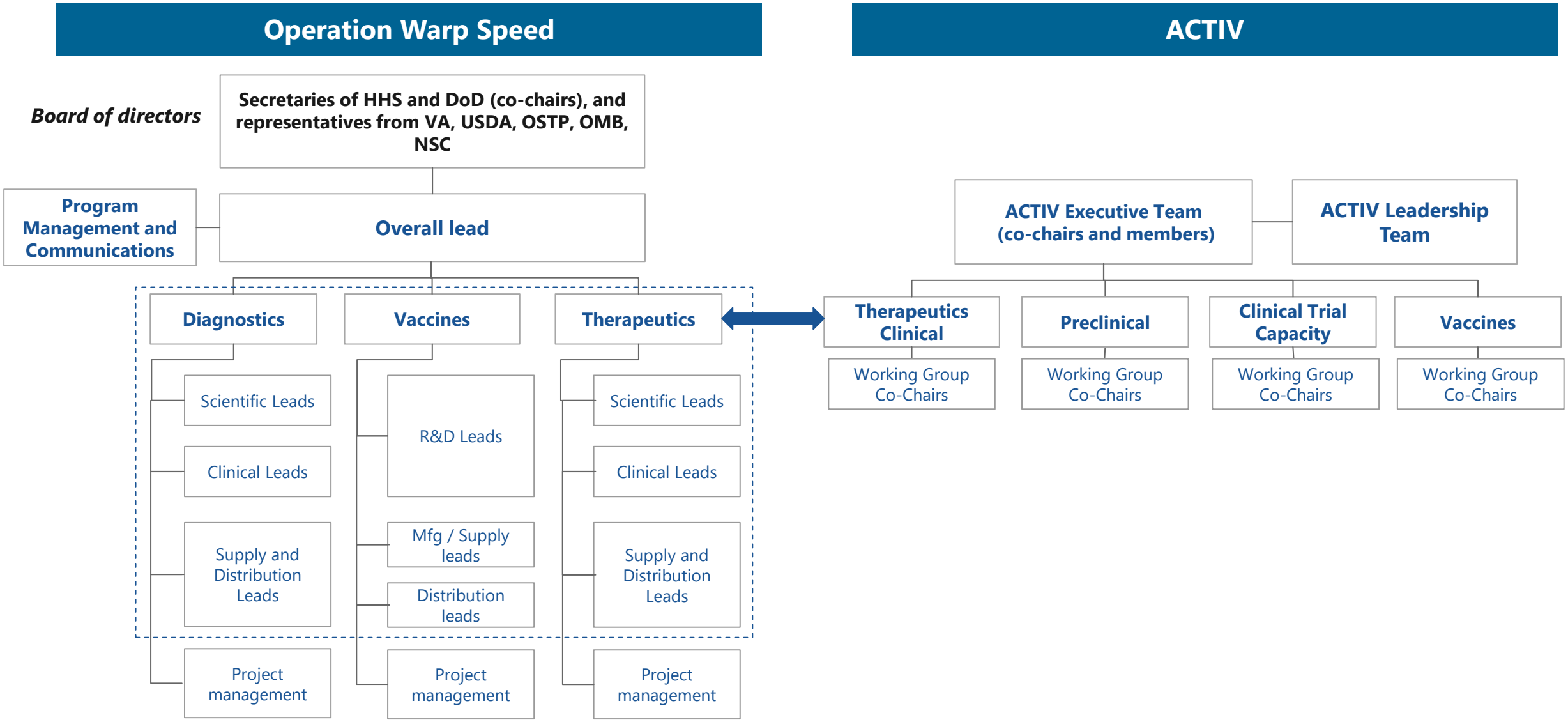
Vaccines Working Group

Sub Groups:
- Vaccines Clinical Trials
- Protective Immune Responses
- Vaccine-Associated Immune Enhancement

ACTIV Database & Inventory Effort

FNIH

Operation Warp Speed/Therapeutics and ACTIV are working together



Preclinical

The working group is standardizing and sharing preclinical evaluation methods in an open forum that allows for comparison and validation by:

Establishing a centralized process and repository for harmonizing and sharing methods and evaluating animal models

Increasing access to validated animal models

Extending access to high-throughput screening facilities, especially in biosafety level 3 (BSL-3) labs

Enhancing comparison of approaches to identify informative assays

ACTIV Preclinical Working Group Accomplishments to Date

- ✓ ***Completed***
- ○ ***In progress***

PRECLINICAL

- ✓ Developed a master **inventory of preclinical testing resources** [will be available as part of the NCATS Open Science Portal by early July 2020]
- ✓ Established **SOPs for accelerated preclinical agent development** in response to a pandemic [manuscript to be submitted by the end of June 2020]
- ✓ Developed a National Strategy for NHP Research [Coordinating Committee established by end of July 2020]
- ✓ Established a process for prioritizing in vitro assays and evaluating preclinical compounds
- ○ Establish a virtual preclinical in vitro and in vivo testing network for therapeutic sponsors to access preferred or limited resources [late summer 2020]
- ○ Create a public database for sharing preclinical data [available in late summer 2020]

Therapeutics - Clinical

The working group is dedicated to prioritizing and accelerating clinical evaluation of therapeutic candidates with near-term potential by:

Establishing a steering committee with relevant expertise and objectivity to set criteria for and rank potential candidates submitted by industry partners

Developing a complete inventory of potential candidates with different mechanisms of action and acceptable safety profiles

Designing, launching, and openly sharing master protocols with agreed-upon endpoints, sampling, and analysis for evaluating candidates

Using a single control arm to enhance trial efficiency

Agent Prioritization Overview

Source Candidates

- **Publicly Available Data**
- **Submission from Investigators**
- **Survey Responses**

Clinical Agents

Clinical Agents

- **Antivirals**
- **Host Targeted / Immunomodulators**
- **Symptomatic / Supportive**
- **Neutralizing mAbs**

Prioritization Activities

- **Score Candidates based on Pre-defined Criteria**
- **Assess Supply and Other Logistical Needs**
- **Develop Minimum Entry Criteria**

FNIH

ACTIV is Developing a Portfolio of Master Protocol Clinical Trials

OWS/ACTIV Therapeutics has been taking a portfolio approach to address the dramatic health and economic challenges posed by the pandemic, with harmonized efforts that address disease etiology and symptomology

ACTIV-1

- Inpatient, >18 years, COVID+
- Phase III - ~2000 patients
- **3 Host-targeted Immune Modulators**
- Targets - TNFα, CTLA-4, CCR2/CCR5
- CRO
- US + Global (if needed)
- Projected to Launch in late June

ACTIV-2

- Outpatient, >18 years, COVID+
- Phase II/III – 110 patients (Phase 2)/900 patients (Phase 3) per agent
- **SARS-CoV-2 Neutralizing Monoclonal Antibodies**
- NIAID ACTG + CRO
- US + Global (Targeting South America)
- Projected to Launch in early July

ACTIV-3

- Inpatient, >18 years, COVID+
- Phase III – 150 patients (Stage 1)/506 patients (Stage 2) per agent
- **SARS-CoV-2 Neutralizing Monoclonal Antibodies**
- NIAID INSIGHT + NHLBI PETAL + CRO
- US + Global (Targeting South America)
- Projected to Launch in mid-July

ACTIV-4

- Inpatient, >18 years, COVID+
- Phase II/III Master Protocol – TBD patients
- **3 Anticoagulants (leading to Anticoagulant + Immune Modulator Combos)**
- NHLBI-NINDS "Master" Network
- US
- Projected to Launch in late June

ACTIV-5 *(TBD)*

- De Novo Master Protocol
- **Promising Agents Not Evaluated Elsewhere (e.g., Antivirals)**
- Network TBD
- Projected Launch TBD

FNIH

ACTIV Therapeutics Clinical Working Group Accomplishments to Date

- ✓ ***Completed***
- ○ ***In progress***

THERAPEUTICS CLINICAL

- ✓ Developed a **process for prioritizing clinical agents** for rapid testing (April 2020)
- ✓ Evaluated hundreds of publicly available agents and **prioritized promising compounds for study**
  (1 Wave Finalized in May 2020 and designated to master protocols)
- ✓ **Assessed, designed, and harmonized multiple master protocols** for ACTIV clinical trials (April-June 2020)
- ✓ **Selected clinical trial networks** best suited for master protocols (May 2020)
- ○ Launch multiple clinical trials using candidates selected
- ○ Prioritize additional agents for study (Beginning June 2020 – performed on a rolling basis)

FNIH

Clinical Trial Capacity

The working group is maximizing clinical trial capacity and effectiveness by connecting existing networks of clinical trials and leveraging capabilities, including:

- Specializing in different populations and disease stages
- Using infrastructure and expertise from across multiple NIH and non-NIH networks and clinical research organizations
- Establishing a coordination mechanism across networks to expedite trials
- Tracking incidence across sites and projecting future capacity

Clinical Trial Capacity Working Group Accomplishments to Date

Mandate: Develop a full inventory of clinical trial capacity, including networks of NIH ICs, industry, and other organizations, that will serve as a guide for the settings in which to implement effective COVID-19 clinical trials

- **Identified 80+ novel and scalable enhancements / efficiencies** for Tx clinical protocols, MAb protocols, vaccine protocols

- Three unique clinical trial capacity surveys developed for **Networks**, **Sites**, and **Clinical Research Organizations (CROs) and Site Management Organizations (SMOs)**
- **53 Networks** have completed the survey*
- **640 total Sites** have completed the survey*
- **35 CROs/SMOs** have completed the survey*

*Additional organizations will be surveyed as identified

- A **Tableau-based dashboard** has been created to query and visualize survey data
- Clinical Trial network, site, and CRO/SMO survey data is combined **in one comprehensive view**
- **Overlay of data indicating: 1) days until peak hospitalization** from University of Pennsylvania, **2) confirmed COVID cases** (7-day moving average) from Johns Hopkins University (JHU) and **3) confirmed COVID deaths** (7-day moving average) from JHU with clinical trial capacity survey data to optimize therapeutics and vaccine site selection

FNIH

ACTIV Clinical Trial Capacity Working Group Accomplishments

- ✓ ***Completed***
- ○ ***In progress***

CLINICAL CAPACITY

- ✓ Developed and launched clinical trial capacity surveys
- ✓ Collected clinical capacity data for federal networks, industry, academic, Clinical Research Organizations (CROs) and Site Management Organizations (SMOs)
- ✓ Identified innovations to enable safe and rapid execution of clinical trials
- ✓ Establish ACTIV clinical trial capacity recommendations committees

FNIH

Vaccines

The working group is charged with accelerating evaluation of vaccine candidates to enable rapid authorization or approval.

Efficacy trials will be harmonized to enable analysis of correlates of protection across vaccines.

The group will create a collaborative framework to share insights into natural immunity and vaccine candidate–induced immune response involving:

- Evaluating protective immune response from natural history and neutralizing antibody studies
- Establishing protocols for sampling and analyses and reagents
- Understanding evidence for vaccine-associated immune enhancement of disease
- Engaging with regulators on evidence to support vaccine authorization

ACTIV Vaccine Working Group Accomplishments to Date

- ✓ ***Completed***
- ○ ***In progress***

VACCINES

- ✓ Developed harmonized vaccine protocols to enable analyses of correlates of protection across trials (to be executed by OWS/NIH/BARDA)
- ✓ Assessed protective immune response evidence to support accelerated use or approval of vaccine candidates
- ✓ Articulated scientific and operational challenges of developing controlled human infection models (manuscript submitted for publication)
- ○ Evaluate implications of evidence on immune-associated disease enhancement for COVID-19 vaccine development (manuscript expected to be submitted by June 30)

FNIH

ACTIV Accomplishments

- ✓ ***Completed***
- ○ ***In progress***

PRECLINICAL

- ✓ 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
- ✓ Established a process for prioritizing in vitro assays and evaluating preclinical compounds
- ○ Create a public database for sharing preclinical data

THERAPEUTICS CLINICAL

- ✓ Developed a process for prioritizing clinical agents for rapid testing
- ✓ Evaluated hundreds of publicly available agents and prioritized promising compounds for study
- ✓ Assessed, designed, and harmonized multiple master protocols for ACTIV clinical trials
- ✓ Selected clinical trial networks best suited for master protocols
- ○ Launch multiple clinical trials using candidates selected
- ○ Prioritize additional agents for study

CLINICAL CAPACITY

- ✓ Developed and launched clinical trial capacity surveys
- ✓ Collected clinical capacity data for federal networks, industry, academic, Clinical Research Organizations (CROs) and Site Management Organizations (SMOs)
- ✓ Identified innovations to enable safe and rapid execution of clinical trials
- ○ Establish ACTIV clinical trial capacity recommendations committees

VACCINES

- ✓ Developed harmonized vaccine protocols to enable analyses of correlates of protection across trials
- ✓ Assessed protective immune response evidence to support accelerated use or approval of vaccine candidates
- ✓ Articulated scientific and operational challenges of developing controlled human infection models
- ○ Evaluate implications of evidence on immune-associated disease enhancement for COVID-19 vaccine development

FNIH

Where do I go for more information on ACTIV?

For 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 ideas, general information on assays or agents, or candidate agents, and queries:

- ✓ NIH COVID-19 Candidate and Technologies Portal: [https://grants.nih.gov/grants/rfi/rfi.cfm?ID=107]

For 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]

FNIH