Foundation for the National Institutes of Health (FNIH)

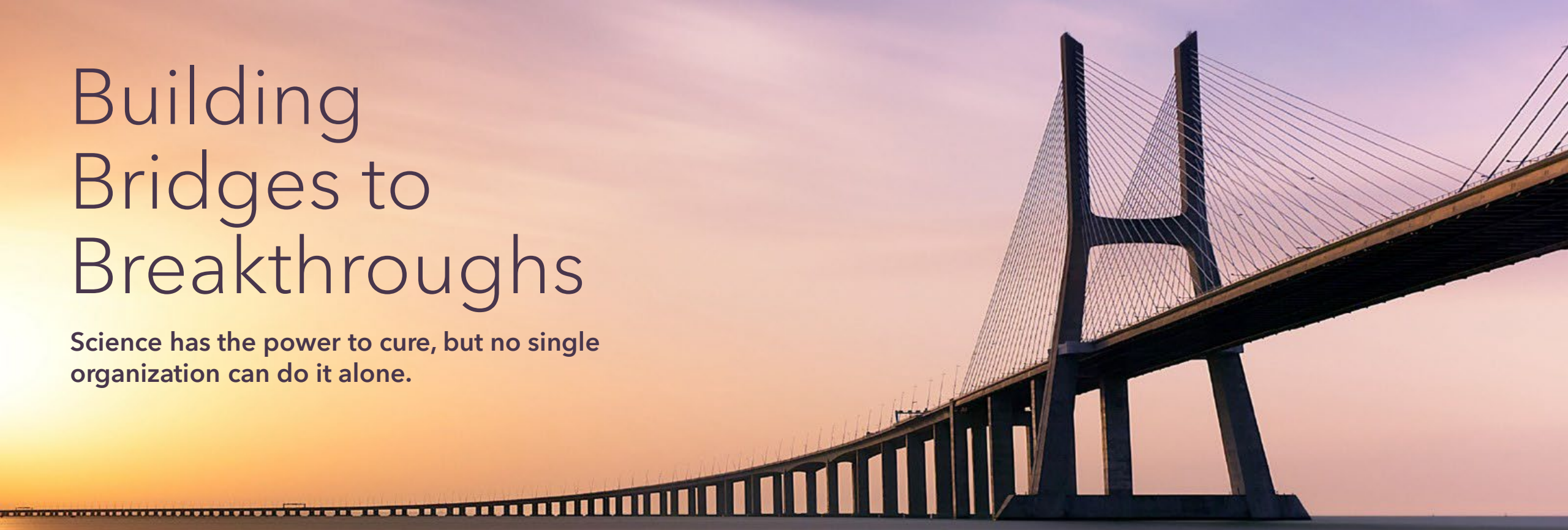
ICCVAM Public Forum

May 20 – 21, 2024

FNIH

Building Bridges to Breakthroughs

Science has the power to cure, but no single organization can do it alone.



We connect world-leading NIH researchers with the ingenuity and expertise of public and private sector leaders to accelerate medical breakthroughs.

FNIH is a non-profit organization chartered by congress and launched in 1996 to support the mission of NIH.

FNIH

Partnering with world-class organizations to tackle the most pressing health challenges

PUBLIC

We support the mission of the nation's premier biomedical research agency, driving discoveries that improve health and save peoples' lives.

BIOPHARMA

We collaborate with leading R&D organizations to advance research that will lead to new therapies, diagnostics, and potential cures.

FOUNDATIONS

We work with foundations to address urgent issues in global health and accelerate biomedical innovation across a range of diseases.

Biomedical innovation to improve health

FNIH creates and leads alliances and public-private partnerships that advance breakthrough biomedical discoveries and improve the quality of people's lives.

$1.5B
private funds raised

122
active partnerships

We accelerate prevention, new therapies, diagnostics & potential cures

- ACCELERATING MEDICINES PARTNERSHIP (AMP)
- BIOMARKERS CONSORTIUM
- BESPOKE GENE THERAPY CONSORTIUM (BGTC)
- PARTNERSHIP FOR ACCELERATING CANCER THERAPIES (PACT)
- ACCELERATING COVID-19 THERAPEUTIC INTERVENTIONS & VACCINES (ACTIV)

We advance global health & seek equity in care

- MATERNAL & CHILD HEALTH: A-PLUS
- GENECONVENE GLOBAL COLLABORATIVE

We power science by celebrating & training the next generation of scientists

- LURIE PRIZE IN BIOMEDICAL SCIENCES
- TRAILBLAZER PRIZE FOR CLINICIAN SCIENTISTS
- CHARLES A. SANDERS PARTNERSHIP AWARD

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Public Private Partnerships: Role of FNIH

FNIH convenes the best minds around the world to tackle complex health problems through partnership and collaboration.

GOVERNANCE

Establish and manage a variety of structures appropriate to each partnership

POLICY MANAGEMENT

Provide safe harbor for interactions between companies, government, and academic entities

Policies support NIH ethical and policy standards

PROGRAM MANAGEMENT

Drive stakeholder consensus about appropriate scientific selection and execution of projects

FUNDRAISING & RELATIONSHIP MANAGEMENT

Directly solicit contributions

Steward and manage donor funds

PROJECT MANAGEMENT

Ensure projects meet established deliverables and "go/no go" milestones

INTELLECTUAL PROPERTY MANAGEMENT

Provide "pre-competitive" structures for handling intellectual property, if needed

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FNIH Partnerships Cover a Spectrum of Designs

Funded exclusively by public organizations

ACTIV

Funded by both public and private organizations

LUNG-MAP

ADNI

Funded exclusively by private organizations

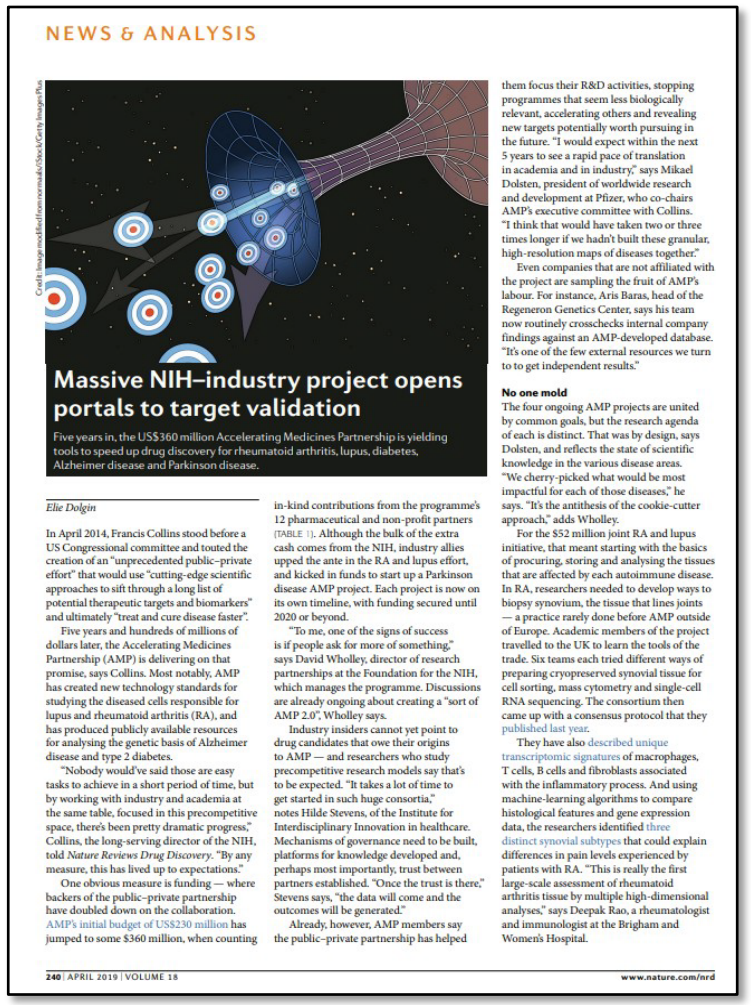
BIOMARKERS CONSORTIUM

IMPROVING HEALTH THROUGH MEANINGFUL MEASUREMENTS

Grand Challenges in Global Health

ACCELERATING MEDICINES PARTNERSHIP (AMP)

Accelerating Medicines Partnership® (AMP®)



NEWS & ANALYSIS

Massive NIH–industry project opens portals to target validation

Five years in, the US$360 million Accelerating Medicines Partnership is yielding tools to speed up drug discovery for rheumatoid arthritis, lupus, diabetes, Alzheimer disease and Parkinson disease.

Elie Dolgin

In April 2014, Francis Collins stood before a US Congressional committee and touted the creation of an "unprecedented public–private effort" that would use "cutting-edge scientific approaches to sift through a long list of potential therapeutic targets and biomarkers" and ultimately "treat and cure disease faster".

Five years and hundreds of millions of dollars later, the Accelerating Medicines Partnership (AMP) is delivering on that promise, says Collins. Most notably, AMP has created new technology standards for studying the diseased cells responsible for lupus and rheumatoid arthritis (RA), and has produced publicly available resources for analysing the genetic basis of Alzheimer disease and type 2 diabetes.

"Nobody would've said those are easy tasks to achieve in a short period of time, but by working with industry and academia at the same table, focused in this precompetitive space, there's been pretty dramatic progress," Collins, the long-serving director of the NIH, told *Nature Reviews Drug Discovery*. "By any measure, this has lived up to expectations."

One obvious measure is funding — where backers of the public–private partnership have doubled down on the collaboration. AMP's initial budget of US$230 million has jumped to some $360 million, when counting in-kind contributions from the programme's 12 pharmaceutical and non-profit partners (TABLE 1). Although the bulk of the extra cash comes from the NIH, industry allies upped the ante in the RA and lupus effort, and kicked in funds to start up a Parkinson disease AMP project. Each project is now on its own timeline, with funding secured until 2020 or beyond.

"To me, one of the signs of success is if people ask for more of something," says David Wholley, director of research partnerships at the Foundation for the NIH, which manages the programme. Discussions are already ongoing about creating a "sort of AMP 2.0", Wholley says.

Industry insiders cannot yet point to drug candidates that owe their origins to AMP — and researchers who study precompetitive research models say that's to be expected. "It takes a lot of time to get started in such huge consortia," notes Hilde Stevens, of the Institute for Interdisciplinary Innovation in healthcare. Mechanisms of governance need to be built, platforms for knowledge developed and, perhaps most importantly, trust between partners established. "Once the trust is there," Stevens says, "the data will come and the outcomes will be generated."

Already, however, AMP members say the public–private partnership has helped them focus their R&D activities, stopping programmes that seem less biologically relevant, accelerating others and revealing new targets potentially worth pursuing in the future. "I would expect within the next 5 years to see a rapid pace of translation in academia and in industry," says Mikael Dolsten, president of worldwide research and development at Pfizer, who co-chairs AMP's executive committee with Collins. "I think that would have taken two or three times longer if we hadn't built these granular, high-resolution maps of diseases together."

Even companies that are not affiliated with the project are sampling the fruit of AMP's labour. For instance, Aris Baras, head of the Regeneron Genetics Center, says his team now routinely crosschecks internal company findings against an AMP-developed database. "It's one of the few external resources we turn to to get independent results."

No one mold

The four ongoing AMP projects are united by common goals, but the research agenda of each is distinct. That was by design, says Dolsten, and reflects the state of scientific knowledge in the various disease areas. "We cherry-picked what would be most impactful for each of those diseases," he says. "It's the antithesis of the cookie-cutter approach," adds Wholley.

For the $52 million joint RA and lupus initiative, that meant starting with the basics of procuring, storing and analysing the tissues that are affected by each autoimmune disease. In RA, researchers needed to develop ways to biopsy synovium, the tissue that lines joints — a practice rarely done before AMP outside of Europe. Academic members of the project travelled to the UK to learn the tools of the trade. Six teams each tried different ways of preparing cryopreserved synovial tissue for cell sorting, mass cytometry and single-cell RNA sequencing. The consortium then came up with a consensus protocol that they published last year.

They have also described unique transcriptomic signatures of macrophages, T cells, B cells and fibroblasts associated with the inflammatory process. And using machine-learning algorithms to compare histological features and gene expression data, the researchers identified three distinct synovial subtypes that could explain differences in pain levels experienced by patients with RA. "This is really the first large-scale assessment of rheumatoid arthritis tissue by multiple high-dimensional analyses," says Deepak Rao, a rheumatologist and immunologist at the Brigham and Women's Hospital.

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For an overview of the AMP Initiative, see:
Nature Reviews Drug Discovery - February 27, 2019
https://www.nature.com/articles/d41573-019-00033-8

Precompetitive public-private collaboration started in 2014

Unite resources of NIH and private partners to improve our understanding of disease pathways and transform current models for developing new treatments by:

- Identifying new biomarkers and targets
- Developing leading-edge tools and technologies
- Collecting large scale datasets and sharing broadly to research community
- Generating consensus on platforms and procedures

Launched initiatives:

- Alzheimer's Disease 1.0 (2014)
- Type 2 Diabetes (2014)
- Rheumatoid Arthritis & Systemic Lupus Erythematosus (2014)
- Parkinson's Disease (2018)
- Schizophrenia (2020)
- Alzheimer's Disease 2.0 (2021)
- Common Metabolic Diseases (2021)
- Bespoke Gene Therapy Consortium (2021)
- Autoimmune and Immune-Mediated Diseases (2021)

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AMP® by the Numbers

9
Programs

$772M
Total Investment

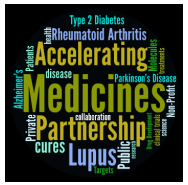
8+
Years

28
Industry Partners

15
NIH Institutes and cross-institute programs

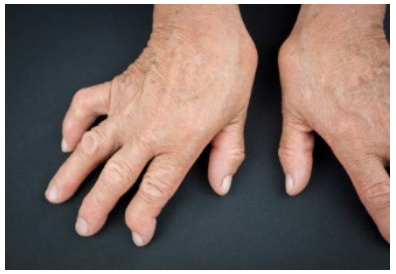
27
Non-Profits

As of April 2022



Alzheimer's Disease

Type 2 Diabetes



Autoimmune Diseases

Parkinson's Disease

Industry members

abbvie
Biogen
gsk
Lilly

janssen
Lilly
MERCK
Pfizer
SANOFI

abbvie
Bristol-Myers Squibb
MERCK
janssen
Pfizer
SANOFI
Takeda

Celgene
verily
gsk
Pfizer
SANOFI

Government members

NIH National Institute on Aging
NIH National Institute of Neurological Disorders and Stroke
FDA U.S. FOOD & DRUG ADMINISTRATION

NIH National Institute of Diabetes and Digestive and Kidney Diseases

NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIH National Institute of Allergy and Infectious Diseases

NIH National Institute on Aging
NIH National Institute of Neurological Disorders and Stroke
FDA U.S. FOOD & DRUG ADMINISTRATION

Non-profit members

alzheimer's association
GEOFFREY BEENE
USAgainst Alzheimer's
we can stop it by 2020.
Alzheimer's Drug Discovery Foundation

American Diabetes Association.
JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

LUPUS RESEARCH ALLIANCE
LUPUS FOUNDATION OF AMERICA
Arthritis Foundation
Rheumatology Research Foundation
Advancing Treatment | Finding Cures

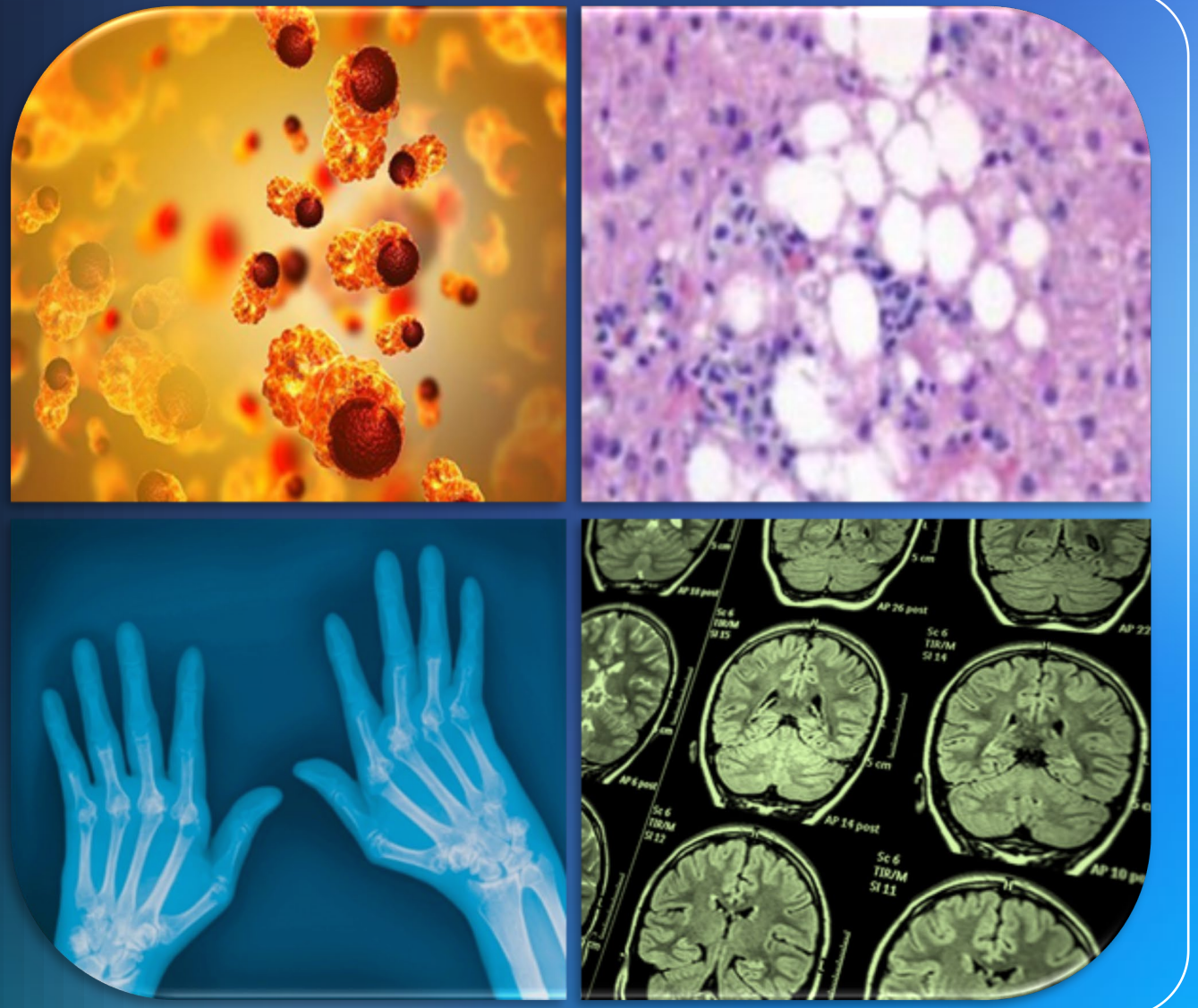
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

PhRMA
RESEARCH · PROGRESS · HOPE
FNIH
Foundation for the National Institutes of Health

The Biomarkers Consortium

BIOMARKERS CONSORTIUM

IMPROVING HEALTH THROUGH MEANINGFUL MEASUREMENTS



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Biomarkers Consortium

Vision

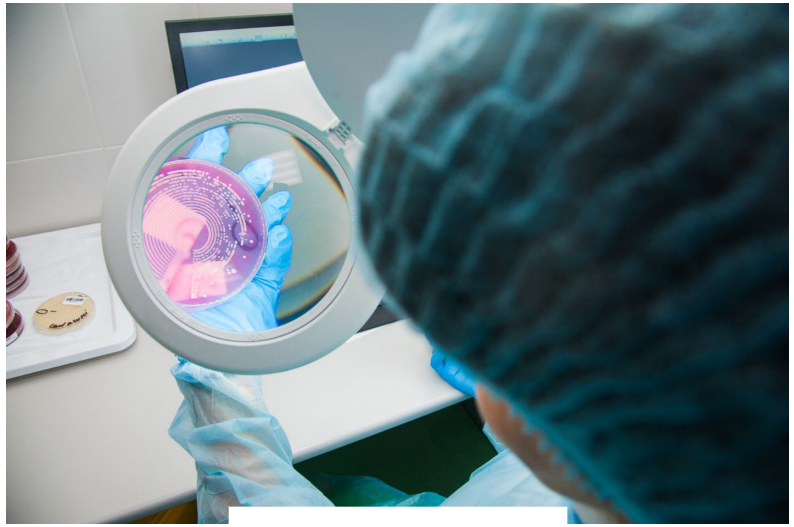
- Improving health through meaningful measurements

Mission

- To create and lead cross-sector efforts that validate and qualify biomarkers and other drug development tools to accelerate better decision making for the development of new therapeutics and health technologies.

Goals

- Facilitate the development and the seeking of regulatory approval for biomarkers using new and existing technologies;
- Develop evidence to help qualify biomarkers for specific applications in diagnosing disease, predicting therapeutic response or improving clinical practice;
- Generate information useful to inform regulatory decision making;
- Make consortium project results broadly available to the entire scientific community.



Biomarkers Consortium

15 years of collaboration, research, and progress

9 clinical tools being used in drug development

5 FDA guidance documents supported by work of the BC

1 qualified composite biomarker

>50 publications

800+ citations

14 therapeutics advanced based on tools generated

60+ member organizations

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Biomarkers Consortium Private Sector Members (as of December 6, 2023)

Represent large and small companies, trade groups, and not-for-profit organizations

Who we are: Executive Committee

Experienced leaders from public, private, and non-profit sectors

Doug Lowy, MD
Interim Chair, Deputy Director, National Cancer Institute

Diana W. Bianchi, MD
Director, National Institute of Child Health and Human Development (NICHD)

Barbara D. Buch, MD
Associate Director for Medicine Center for Biologics Evaluation and Research (CBER), FDA

Lindsey A. Criswell, MD, MPH, DSc
Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)

Jennifer D. Davidson Hamilton, PhD
Vice President and Head, Precision Medicine Regeneron Pharmaceuticals, Inc.

Gregory Friberg, MD
Vice President and Therapeutic Area Head (Hematology / Oncology / Bone) for Global Development

Joshua Gordon, MD, PhD
Director, National Institute of Mental Health (NIMH)

Rob Iannone, MD
Executive Vice President, Research and Development and Chief Medical Officer, Jazz Pharmaceuticals

Shari M. Ling, MD
Deputy Chief Medical Officer, Centers for Medicare and Medicaid Services

Doug Lowy, MD
Deputy Director, National Cancer Institute (NCI)

Vasum Peiris, MD, MPH, FAAP, FACC, FASE
Chief Medical Officer for Pediatrics and Special Populations, Center for Devices and Radiological Health (CDRH), FDA

Francisca Reyes Turcu, MD
Team Lead, Molecular Pathology and Cytology Branch Center for Devices and Radiological Health (CDRH), FDA

Mary Thanh Hai, MD
Deputy Director for Clinical, Office of New Drugs, FDA

Ellen V. Sigal, PhD
Chairperson and Founder, Friends of Cancer Research

David Strauss, MD, PhD
Division Director, Division of Applied Regulatory Science, U.S. FDA

Bruce J. Tromberg, PhD
Director, National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Michael S. Vincent, MD, PhD
Senior Vice President, Chief Scientific Officer, Pfizer

John Wagner, MD, PhD
Chief Medical Officer, Koneksa

Jeff Siegel
Director of the Office of Drug Evaluation Sciences (ODES) in the Office of New Drugs (OND), CDER, FDA

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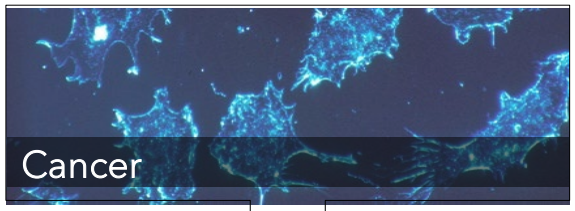
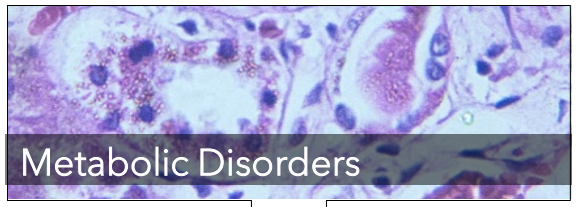
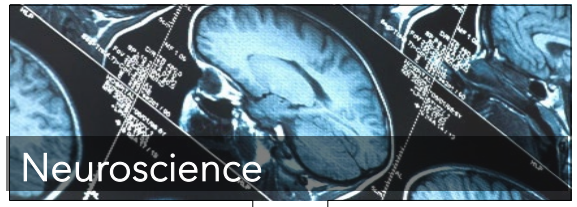
Biomarkers Consortium Governance

Executive Committee
NIH / FDA / CMS / Industry / FNIH

Steering Committees







Multiple Project Teams
Representatives from NIH, FDA, Industry, Non-Profits, and Academia

Working Groups and Project Development Teams
Representatives from NIH, FDA, Industry, Non-Profits, and Academia

Complement-ARIE

Complement Animal Research in Experimentation

Better model and understand human health and disease outcomes across diverse populations.

Develop NAMs that provide insight into specific biological processes or disease states.

Validate mature NAMs to support regulatory use and standardization.

Complement traditional animal models and make biomedical research more efficient and effective.

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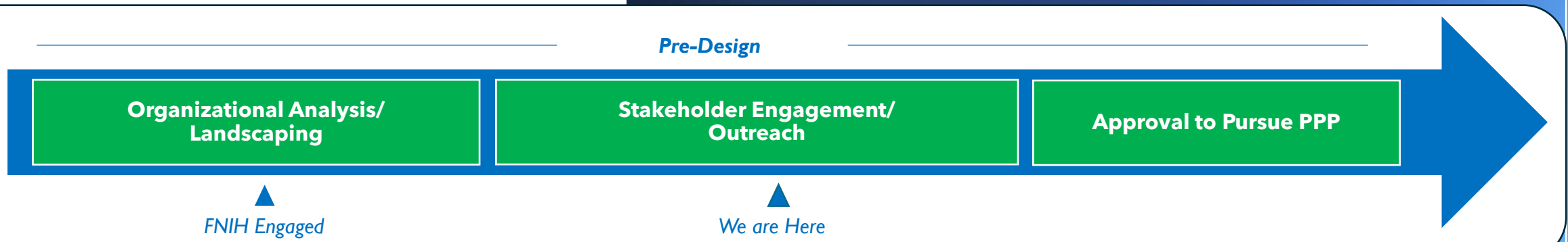
Potential of a NAMs PPP

- Creation of a public-private partnership (PPP) will establish a **community platform and a replicable process for NAMs validation**.
- Partnership with **novel existing technologies,** testing refinement initiatives and regulatory networks, will support development of a **multistakeholder validation process**.
- Provision of **process recommendations and public guidance to support implementation of NAMs** will complement existing models used in biomedical research.

Pre-Design



Assess feasibility and utility of proposed PPP

1. Organizational analysis and landscaping
2. Stakeholder engagement and outreach
3. NIH and FNIH establish PPP

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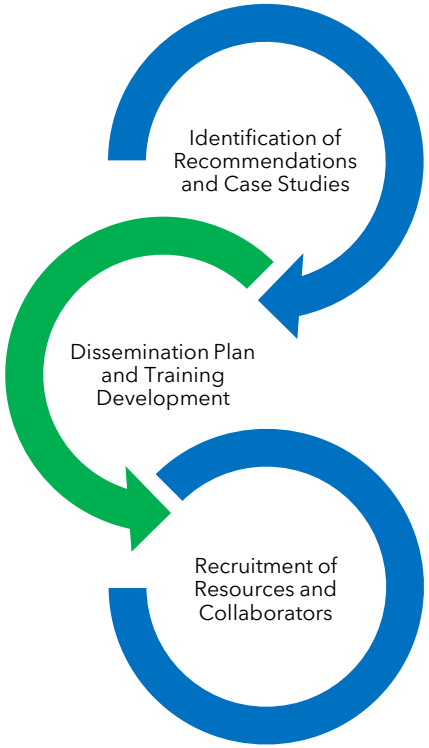
Design

2024 - 2025

Validation Network Convening and Phase 1 Design



- Develop success criteria: Establish minimum information for identification of NAMs for validation and/or qualification.
- Develop governance structure: Plan, develop network with FNIH, Industry, NGOs, federal partners and regulators.
  - Identify primary "customers" and associated regulatory agencies.
  - Conduct workshops and other activities to identify industry/agency priority needs.
  - Seek feedback on scope of validation and qualification efforts.
  - Define pre-competitive data sharing capacity for stakeholders.
- Issue RFPs to solicit nominations of "late-stage" NAMs to address priority needs.

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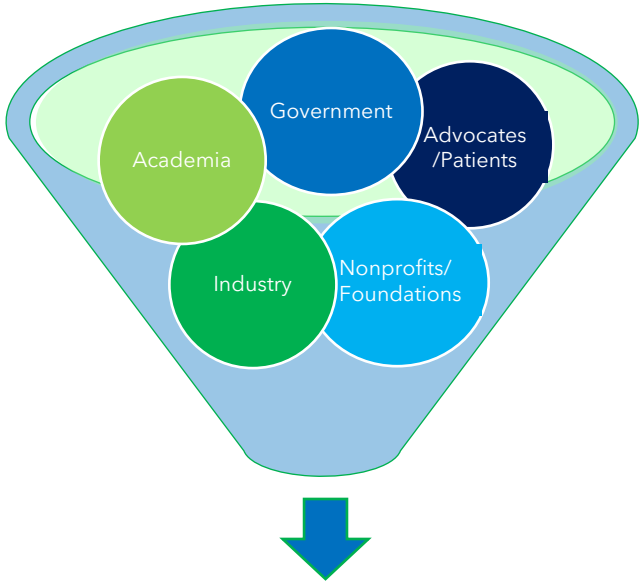
Implementation

2025 - 2029

Implementation of PPP Governance and Execution of Partnership



Validation Process, Guidance Evaluation

- Establish validation management teams.
  - Select 4-8 late-stage NAMs for validation.
  - Design validation studies in collaboration with agencies/end-users.
- Establish data sharing process with the NAM Data Hub and Coordination Center.
- Apply reporting standards to NAMS from Tech Dev Centers.
- Nominate mature NAMs from Tech Dev Centers for Validation Network.
- Establish training opportunities with PPP partner groups.
- Maintain Steering Committee annual engagement with stakeholders and NAMs developers to guide priority needs.

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The Role of FNIH

- Partnership development and convening of key stakeholders
- Program development, coordination, administration, fundraising and fund distribution
- Management of external collaboration
  - Selection of award(s)
  - Management of the application and peer review process
  - Management of grant/contract administration (e.g., budget, contracting, tracking of milestones, payments, and renewal)
- Financial monitoring and oversight
- Communications / media support
- Governance for IP, data access, and confidentiality
- Reporting overall scientific and/or financial activities to partners

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THANK YOU

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dconnors@fnih.org

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February 14, 2024

Back Up

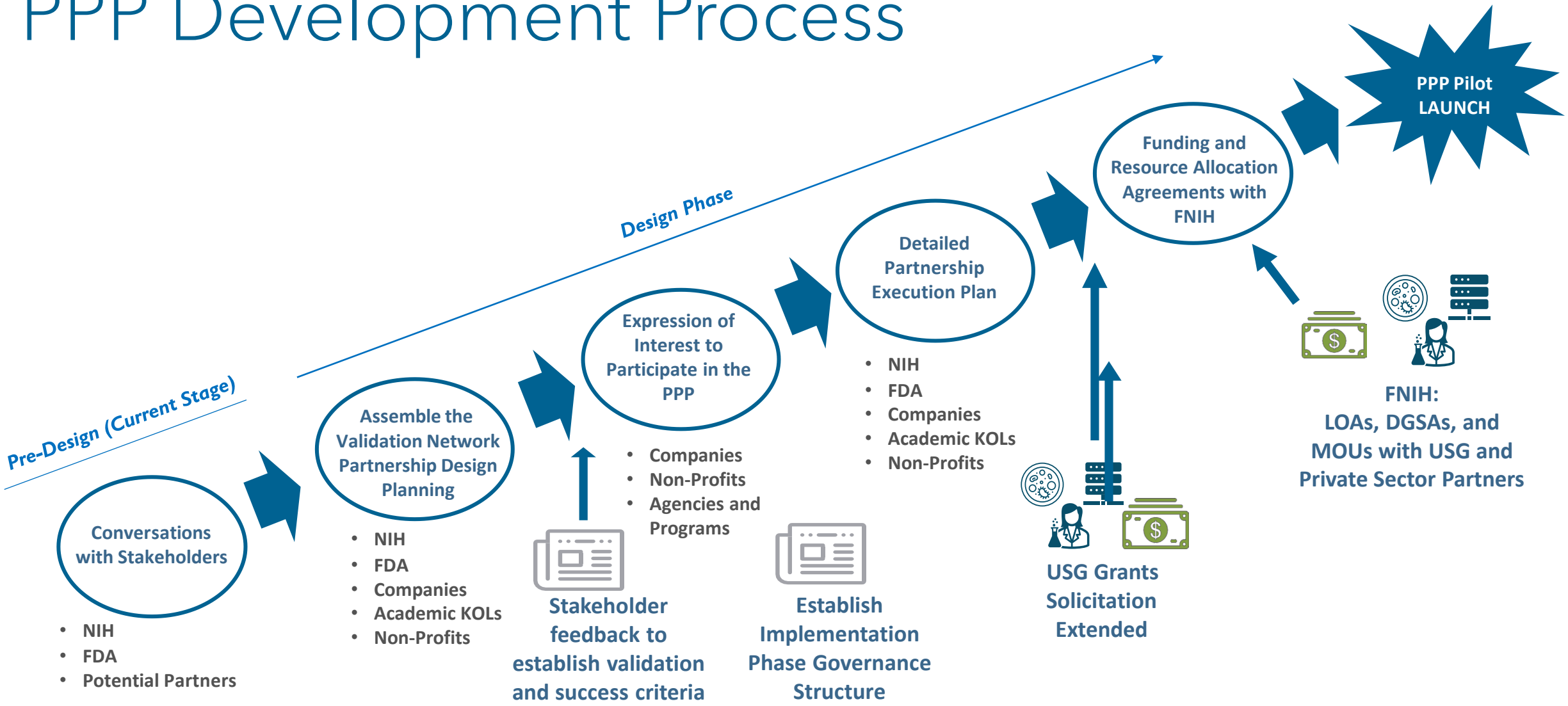
FNIH

February 14, 2024

FNIH PPP Objectives

- Validation network for regulatory implementation from July 2024 through Phase 1 July 2025 to 2028. Budget: $3-4M per year.
  - Establish common data elements
  - Standardize reporting
  - Apply validation/qualification frameworks
  - Accelerate deployment and regulatory implementation with an emphasis on combinatorial NAMs
  - Streamline regulatory frameworks to accelerate implementation and adoption of NAMs
- Outreach, development, and training network
  - Promote the development of an inclusive, diverse biomedical research workforce with the skills to build and use NAMs
  - Community engagement, evaluation and management of societal and ethical considerations

PPP Development Process



Design Phase Activities

- Convene a high-level executive stakeholder meeting to refine the plan for partnership
- Convene 2 public workshops to acquire multidisciplinary community input on the design of the partnership
- Establish one virtual meeting each month for each Working Group to carry out specific tasks needed to develop the Implementation Phase
- Prepare a detailed Implementation plan for the project with WG chairs
- Assemble necessary partners and contractual agreements for the Implementation Phase

Design Phase Budget

- NIH to work across agency relationships to solicit $5000 contribution from each
  - $300,000 in agency support
- FNIH to work with private sector partners to establish interest and gain initial design support
  - $200,000 in company support
- FNIH to support contracting with project partners and establish a milestone approach at completion of Design Phase to fund Implementation. Assumes Go/No-Go for Phase 2.

Design Phase	Total Design Phase Budget
Budget	
Personnel	$232,656
Meetings & Travel	$150,000
FNIH Direct Costs	$382,656
Indirect Costs	$76,531
Total Design Phase Cost	$459,187

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Design Phase Criteria (Year 1)

- Convene workshops with industry, academia, NGOs, CROs, and federal partners:
  - FDA, EPA, NSF, ARPA-H, BARDA, VA, DARPA, NIST, NASA, and ICCVAM
  - Include 3Rs Consortium, IQMPS and HESI members with C-Path and HSI support
- Identify and confirm potential industry and federal partners, with a focus on pre-competitive and collaborative approaches.
- Coordinate with ICCVAM workgroup to identify regulatory needs and support validation efforts (e.g., via VMTs).
  - Identify existing recommendations and international standards for dissemination.
- Determine scope of validation efforts, data-sharing, and reporting standards.
- Identify funding streams: lab work, chemical sourcing, data analysis, reporting, peer review, etc.
- Governance/criteria for selection of use cases – refine goals for the network.
  - Establish Steering Committee and Working Groups to establish and validate recommendations.
  - Review training efforts for educational dissemination.

Implementation Phase Criteria (Years 2 - 5)

- Coordination with:
  - Industry, NGOs, CROs and federal partners.from Design Phase for support
  - ICCVAM WG to bring in expertise and augment the network beyond biomedical partners
  - NICEATM to input validated NAMs in CAMERA (Collection of Alternative Methods for Regulatory Application)
  - International stakeholders, such as OECD, HESI, 3Rs and IQMPS Consortia, and regulatory agencies for global harmonization
- Establish:
  - Steering Committee to guide and support timely decision making and implementation
  - Select 8 use case validation and qualification studies (across NAMs categories) and review with stakeholders
  - Nominate mature NAMs from Tech Dev Centers for Validation and Qualification Network
  - Training opportunities with partner groups
- Interact with
  - NAM Data Hub and Coordination Center to ensure data accessibility and sharing
  - NAM Technology Development Centers (established through NIH granting) to apply reporting standards
  - Regulators, industry, CROs in NAMs dev (e.g., via ICCVAM MDF)
- Potential for an Implementation Phase 2 (Years 6 – 10)