Novel Alternative Methods (NAMs) Validation and Qualification Network (VQN) Public-Private Partnership Plan Update

SACTAM Presentation

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Building Bridges to Breakthroughs

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

The Foundation for the National Institutes of Health (FNIH) is a non-profit organization chartered by the U.S. Congress and launched in 1996 to support the mission of NIH.

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

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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

$1.55B private funds raised

122 active partnerships

$.90 of every dollar directly supports programs

We accelerate prevention, new therapies, diagnostics & potential cures

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

We advance global health & seek equity in care

- MATERNAL & CHILD HEALTH
- GENECONVENE GLOBAL COLLABORATIVE
- GRAND CHALLENGES IN GLOBAL HEALTH

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

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

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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

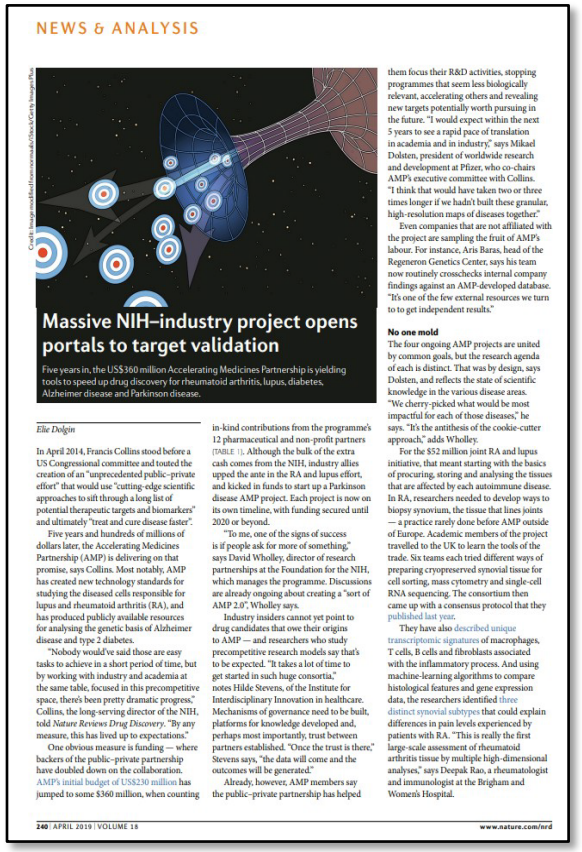
Funded exclusively by private organizations

BIOMARKERS CONSORTIUM

IMPROVING HEALTH THROUGH MEANINGFUL MEASUREMENTS

Grand Challenges in Global Health

The Accelerating Medicines Partnership® (AMP®) Program



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.

240 | APRIL 2019 | VOLUME 18 www.nature.com/nrd

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 targets, biomarkers and development paradigms
  - Developing leading-edge tools and technologies
  - Collecting large scale datasets and supporting analytics for open analysis by the public
  - Generating consensus platforms and procedures

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AMP® Program Development

AMP® By the Numbers

12

Projects

$915M

Total Investment

10+

Years

36

Industry Partners

16

NIH Institutes and cross-institute programs

43

Non-Profits

https://fnih.org/our-programs/accelerating-medicines-partnership-amp/

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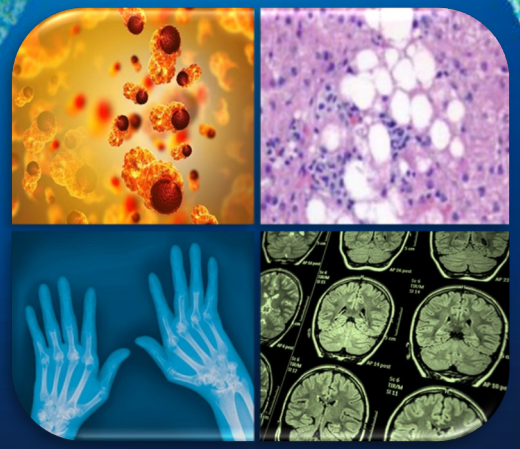
The Biomarkers Consortium

Advancing Precision Medicine



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IMPROVING HEALTH THROUGH MEANINGFUL MEASUREMENTS

Driving principles of the Biomarkers Consortium

- BC projects bridge the gap between basic research and practical needs for advancing drug development and regulatory science.

- Drug development tool projects are developed collaboratively with involvement from academic, government, and industry scientists. Projects can be generated in any therapeutic area and often consult with patients and advocates.

- All work is pre-competitive, and results are released to the public as early as possible.

- All projects have specific, well-defined goals and are milestone-driven, including interim "go/no-go" funding gates.

Biomarkers Consortium

18+ years of collaboration, research, and progress

60+ active partners

40+ projects

$108M private funds raised

- **2** Biomarkers accepted by FDA for use as a surrogate endpoint
- **1** Qualified composite safety biomarker
- **14+** Therapeutics advanced based on tools generated
- **9** FDA Guidance documents supported by work of the BC
- **9** Clinical tools being used in trials for drug development

>50 publications
800+ citations

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Public Private Partnerships: Role of the FNIH

The 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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Potential NAMS PPP

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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.
- Collection and dissemination of **training modules** will support education and adoption of NAMs in the broader community.

Complement-ARIE

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.

https://commonfund.nih.gov/complementarie

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Role of the NAMs VQN Steering Committee

Work with the Complement-ARIE to collaborate on a VQN Design Phase

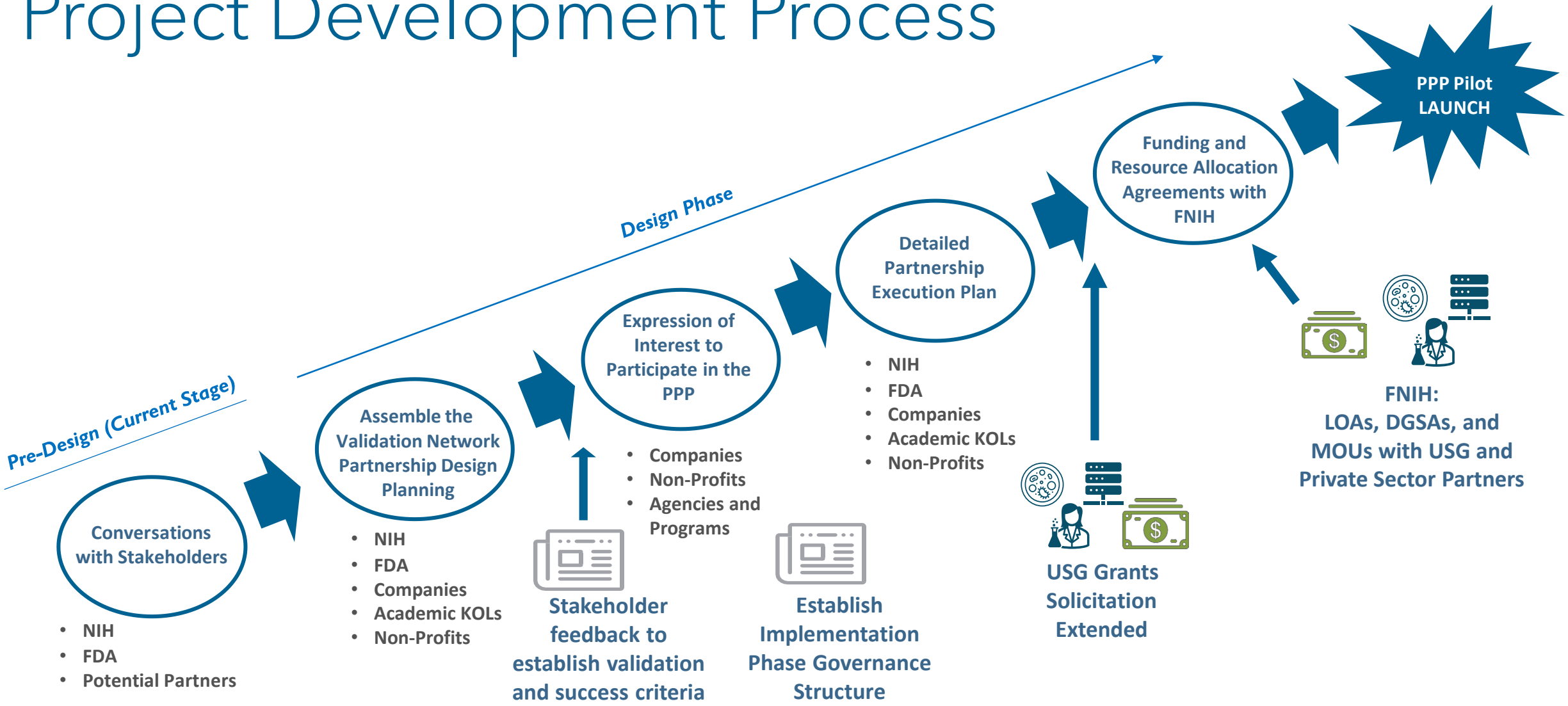
FNIH has launched in the NAMs VQN Steering Committee (SC) in advance of the RFC for the following purposes:

- Stand up working groups to focus on development of project proposals in the NAMs area that could collaborate with Complement-AIRE or operate through existing BC, AMP and other mechanisms
- Build a set of cohesive projects validate and support adoption of NAMs

SC will be instrumental for:

- Proposal Evaluation
- Project Development
- Assembling Funding and Partnership

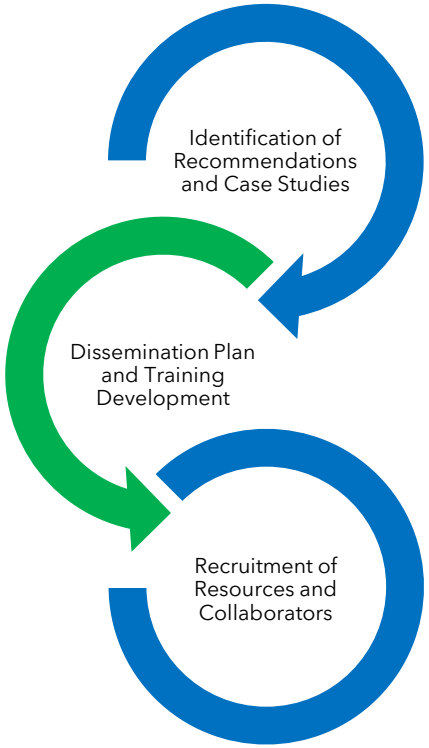
Project Development Process



Design Phase

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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Design Phase Activity

- Convene workshop with industry, academia, NGOs, CROs, and federal partners:
  - FDA, EPA, NSF, ARPA-H, BARDA, VA, DARPA, NIST, NASA, ICCVAM, 3Rs Consortium, IQMPS, HESI, C-Path, HIS, industry and civil society partners.
- Identify and confirm interest of 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.
  - 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 initiate recommendations
  - Review training efforts for educational dissemination

White Paper Development

- An aggregation of interest and scope
- An advertisement for inclusion
- A baseline for negotiation
- A project team charter with:
  - Budgets
  - Timelines
  - Scoping parameters
  - Milestones
  - Expected outputs

Budgeting

- Design Phase
  - Requests NIH to work across agencies to solicit $300,000 in contributions
  - FNIH will work with private sector partners to request $200,000 in industry support

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

- Implementation Phase Plan Expects:
  - $3-4M per year in Public Funding
  - $6–8M per year in Private Sector

Decide How to Assemble Working Groups

- Technology
  - In chemico
  - In silico
  - In vitro
- Sector
  - Bio-Medical
  - Chemical
  - Environmental
- Use-Case
  - Safety
  - Toxicology
- Therapeutic Area
  - Cancer
  - Metabolics
  - Inflammatory Process
  - Neuroscience
  - Rare Disease
- Tissue
- Species
- Other?

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Next Steps

- Current ongoing efforts:
  - FNIH Polling NAMs VQN SC participants for feedback on working group structure
  - Soliciting support from private sector partners and interest in continued participation
- Q4 2024
  - Establish Working Groups and self-select membership
  - Re-engage the full Steering Committee (SC) on a bi-monthly basis to assess progress
  - Work with Complement-AIRE on the pending documentation for collaboration
- Q1 2025 – Begin Design Phase in earnest

Discussion

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