Team Science: The Key to Non Invasive Biomarkers Development for NASH

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Foundation for NIH
Mission

- The mission of the Foundation for the National Institutes of Health (FNIH) is to support the mission of the NIH. The FNIH creates and leads 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?

- Attract and share resources
- Enable insight and innovation
- Establish standards
- Distribute expertise
- Create consensus
- Drive competitiveness in marketplace
- Disseminate knowledge
- Enhance credibility
- Reduce costs
- Support training & education
- Manage complexity

Accelerating Medicines Partnership

NIH (OD), NIA, NIAMS, NIDDK, NINDS, 12 companies, 10 not-for-profit organizations

Partnership for Accelerating Cancer Therapies

NCI, PhRMA, 12 pharmaceutical companies

Grand Challenges in Global Health (GCGH)

Bill & Melinda Gates Foundation

Alzheimer’s Disease Neuroimaging Initiative (ADNI)

NIA, NIBIB, 25+ companies, 3 not-for-profit organizations

The Biomarkers Consortium

FDA, NIH, CMS, PhRMA, BIO, pharmaceutical and nutrition companies, not-for-profit organizations

Lung-MAP: Master Lung Protocol Trial

NCI (SWOG), FDA, Friends of Cancer Research, 5 companies to date

Helping End Addiction Long-Term (HEAL) Partnership Committee

NIH contract
Biomarkers Consortium

13 years of collaboration, research and progress

TA Aligned Steering Committees

- Metabolic Disorders
- Inflammation & Immunity
- Neuroscience
- Cancer

- >50 publications
- 800+ citations
- 59 member organizations

14 therapeutics advanced based on tools generated
9 clinical tools being used in drug development
5 FDA guidance documents supported by work of the BC
1 Clinical safety biomarker Qualification
The consortium approach is encouraged by the FDA

“Because of the substantial work needed to achieve qualification, CDER [Center for Drug Evaluation and Research] encourages the formation of collaborative groups to undertake these tool-development programs... A variety of projects undertaken by consortia have demonstrated the usefulness of this approach.”

Updated FDA Draft Guidance published January 2014
“at this time, reliable diagnosis and staging of NASH can only be made by histopathological examination of the liver biopsy specimen. Liver biopsy, however, is an invasive procedure that can be associated with occasional morbidity, and in rare circumstances, mortality.”

“....therefore noninvasive biomarkers are needed (including imaging biomarkers) to supplant liver biopsy and provide a comparable or superior ability to accurately diagnose and assess various grades of NASH and stages of liver fibrosis”
NIMBLE Approved Project Plan accounts for methodological elements needed to meet evidentiary standards

Stage 1

- Retrospective Analysis of Existing Datasets/Cohorts
- Methodology Studies for Imaging Modalities

Stage 2

- Prospective Study for characterization of biomarker performance
- Circulating / Imaging / Others

Selection of robust candidate biomarkers advancing to Stage 2

Project Milestone
NIMBLE Cross-Stakeholder Team Science

NIMBLE Project Partners

- Academic Institutions*
- Pharmaceutical companies**
- Diagnostic companies***
- Patient Advocacy

NIMBLE Project Organization

- NIMBLE Program Overall Leadership Team
  - Project Co-chairs: Arun Sanyal, Sudha Shankar, Roberto Calle
  - Members: Claude Sirlin, Anthony Samir, Rohit Loomba, Sarah Sherlock
  - Program Officer: Tania Kamphaus
  - Project Management: Helen Heymann, Emily Morgan, Sidra Iqbal
  - FDA liaison: Lara Dimick
  - Patient Advocacy: GLI (Donna Cryer)

- Circulating & Functional Markers Work Stream
  - Co-chairs: Rohit Loomba, Sudha Shankar, Arun Sanyal

- Imaging Markers Work Stream
  - Co-chairs: Claude Sirlin, Anthony Samir, Sarah Sherlock

- Pathology Expert Team
  - Cynthia Guy
  - Melissa Contos
  - Others TBD

- Data Analysis & Statistical Modeling Expert Team
  - Nancy Obuchowski (Cleveland Clinic)
  - Santos Carvajal-Gonzalez (Pfizer)
  - Statistical CRO
  - Academic collaborators

Roles and Management

* Engage in project execution, steering of project. FNIH manages research agreements and Conflict of Interest
** Provide funding and actively involved in steering of project. FNIH manages funding and deliverables
*** Provide blinded assays only (all in kind). Not involved in steering. FNIH manages sample and data chain of custody
NIMBLE is working and collaborating with LITMUS and Working in Concert with Regulators to Accelerate Biomarker Development

Feedback on LOI application
Consensus on case definitions
Helping regulators gain content expertise

Liver Forum

NIMBLE
FNIH-BC

LITMUS
IMI

FDA
Milestone 1A
- Select candidate circulating markers
- QC of extant biobanked samples
- Assessment of analytical performance of assays

Milestone 1B
- Generate draft letter of intent
- Acceptance of letter of intent

Milestone 2A
repeatability / reproducibility of candidate imaging markers

Milestone 2B
preliminary assessment of the correlation of the candidate markers with histologic diagnosis

Milestone 2C
White paper defining markers selected for stage 2 (circulating and imaging)
LOI accepted by FDA

• NIMBLE Letter of Intent (LOI) -
  • Submitted: 02-26-2019
  • Confirmation of Receipt: 02-26-2019
  • Initial Feedback: April 2019
  • Revised LOI submitted October 15 2019
  • LOI accepted by FDA on February 20, 2020

https://www.fda.gov/drugs/cder-biomarker-qualification-program/biomarker-qualification-submissions
Coming up…

Q4 2020
- Early read from Retrospective Study
- Submission of LOI 2 (Imaging)

Q1 2021
- Early reads from Imaging Studies
- 1.1 (US) & 1.2 (MR)

Q3 2021
- NIMBLE Proposal for go/no-go to Stage 2
- Qualification Plan

Q4 2021
- White Paper
- Prospective Study Initiated

Q1 2022
- Full Qualification Plan for FDA

Ongoing Conversations and Collaborations
- Steering committee updates
- Continuous FDA engagement
- Liver Forum and community updates
- Patient Groups engagement
FNIH NIMBLE Contact Information

For further questions please contact:

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Backup Slides
Mitigation Factors to respond to Covid-19 delay

• Prioritize sample release from cohort/biorepository

• Align with labs and continuously monitor changing scenario – identify when labs can safely accept samples and able to process (e.g., potential backlog)

• Continue Statistical Planning, revising contracts, IRB, Protocols,

• Ongoing interactions of FNIH with Key Collaborator labs to keep posted on developments
Biomarkers Consortium Private Sector Members  (as of 10-10-19)

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