

**THE FORUM**  
For Collaborative Research<sup>SM</sup>

# Updates from NASH Biomarkers Consortia

## **NIMBLE**

Roberto Calle, FNIH Biomarkers Consortium  
Rohit Loomba, University of California, San Diego

# NIMBLE

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## Non-Invasive BioMarkers of MetaBolic Liver Disease

LIVER FORUM 8  
APRIL 10, 2018

Drs. Rohit Loomba, Sudha Shankar & Roberto Calle  
For the NIMBLE Project Team

The logo for The Biomarkers Consortium. It features the word "THE" in a small, blue, sans-serif font above the word "biomarkers" in a larger, blue, sans-serif font. The letter "i" in "biomarkers" has a small blue circle above it. Below "biomarkers", the word "CONSORTIUM" is written in a smaller, blue, sans-serif font.

**THE**  
**biomarkers**  
**CONSORTIUM**

# FNIH - Biomarkers Consortium



Established by Congress in **1996** as a not-for-profit organization to support NIH in its mission by advancing biomedical research and training collaborations among government, universities, industry and not-for-profit organizations

\$875 Million raised since **1996** with **>550** projects supported and **93%** of funds going directly to project support. Rated as **Outstanding** by **Charity Navigator**.

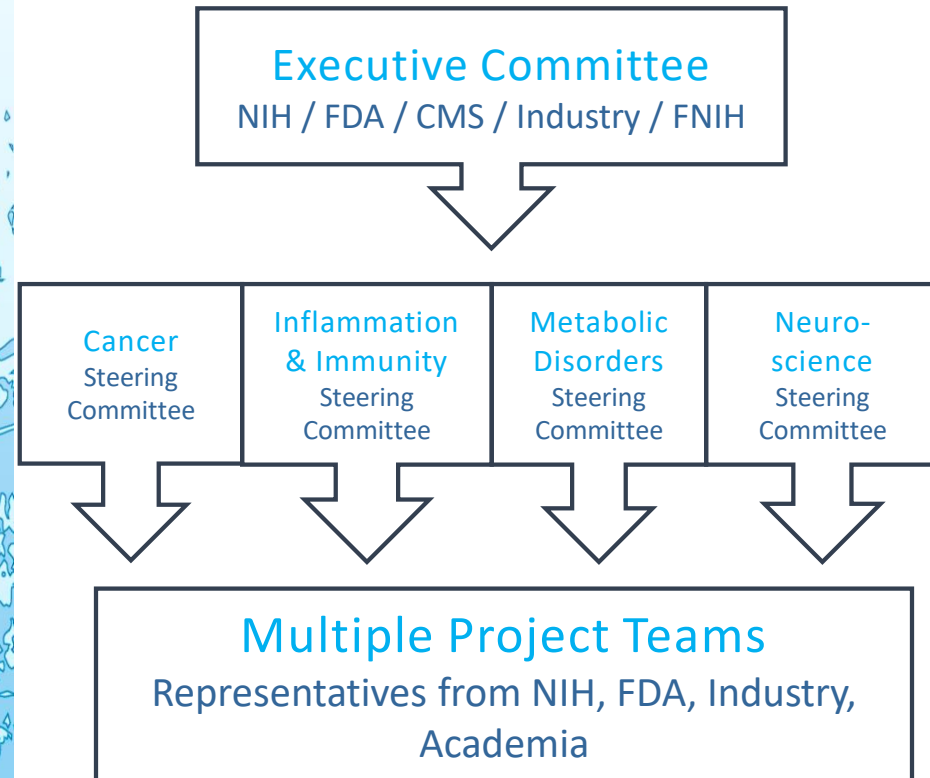
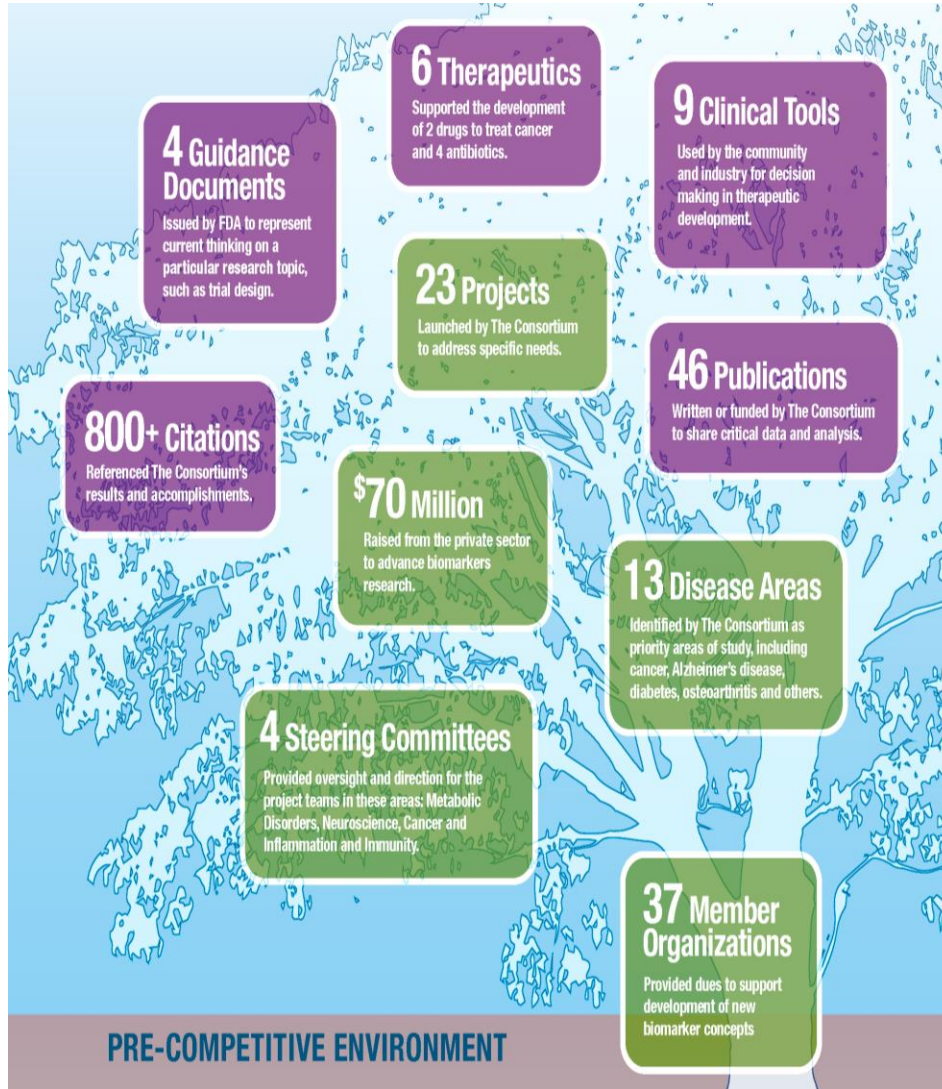
## Biomarkers Consortium Mission Statement

To **discover, develop, and seek regulatory approval for biomarkers** to support and accelerate development of new drugs, preventive medicine, and medical diagnostics by **combining the forces of the public and private sectors**.

## Biomarkers Consortium Goals

- **Facilitate** development of **evidence to help qualify biomarkers** for specific applications in diagnosing disease, predicting therapeutic response or improving clinical practice;
- Generate **pre-competitive** projects; makes consortium project **results broadly available to the entire scientific community**

# 10 years of collaborative research and progress



# Metabolic Disorders Steering Committee Project Portfolio

Completed Projects	Active Projects	Pipeline (in development)	Pre-Launch Phase
<ul style="list-style-type: none"> <li>▪ Adiponectin</li> <li>▪ Carotid MRI Reproducibility</li> <li>▪ Sarcopenia 1 Consensus Definition</li> </ul>	<ul style="list-style-type: none"> <li>▪ Atherosclerosis <i>In-Silico</i> Modeling</li> <li>▪ Beta Cell 1 Clinical Studies</li> <li>▪ Bone Quality</li> <li>▪ Cardiac Troponin</li> <li>▪ Sarcopenia 2 Consensus Definition</li> </ul>	<ul style="list-style-type: none"> <li>▪ Beta Cell 2 - Prospective</li> <li>▪ Bone Quality 2 – FDA BQP Initiative</li> </ul>	<ul style="list-style-type: none"> <li>▪ NIMBLE Program</li> </ul>

# NIMBLE's Goal

To advance qualification of one or more, fit-for-purpose, non-invasive tools, that integrate circulating and quantitative imaging markers:



## Context of Use priorities for NIMBLE:

- In a patient with clinical risk factors for NASH → To diagnose NASH and determine stage of disease (F2 fibrosis or higher i.e. high-risk NASH)
- In a patient diagnosed with NASH\* → for detection and quantification of change in NASH status (NASH present vs absent, change in disease activity) and stage (fibrosis stage) in response to pharmacologic intervention

# NIMBLE Program Stages

## Program Launch



QC datasets & samples

### STAGE 1 – Retrospective analysis & method studies

Biomarker selection  
For Stage 2  
Regroup with FDA

1. Retrospective analysis of existing samples
2. Methodology imaging studies

White Paper

Cross-sectional analysis of baseline data

### STAGE 2 – Prospective study including selected markers

Pubs & final data release

Planning

Study Execution & Interim Readout

Analysis & Reporting

Cross-Sectional

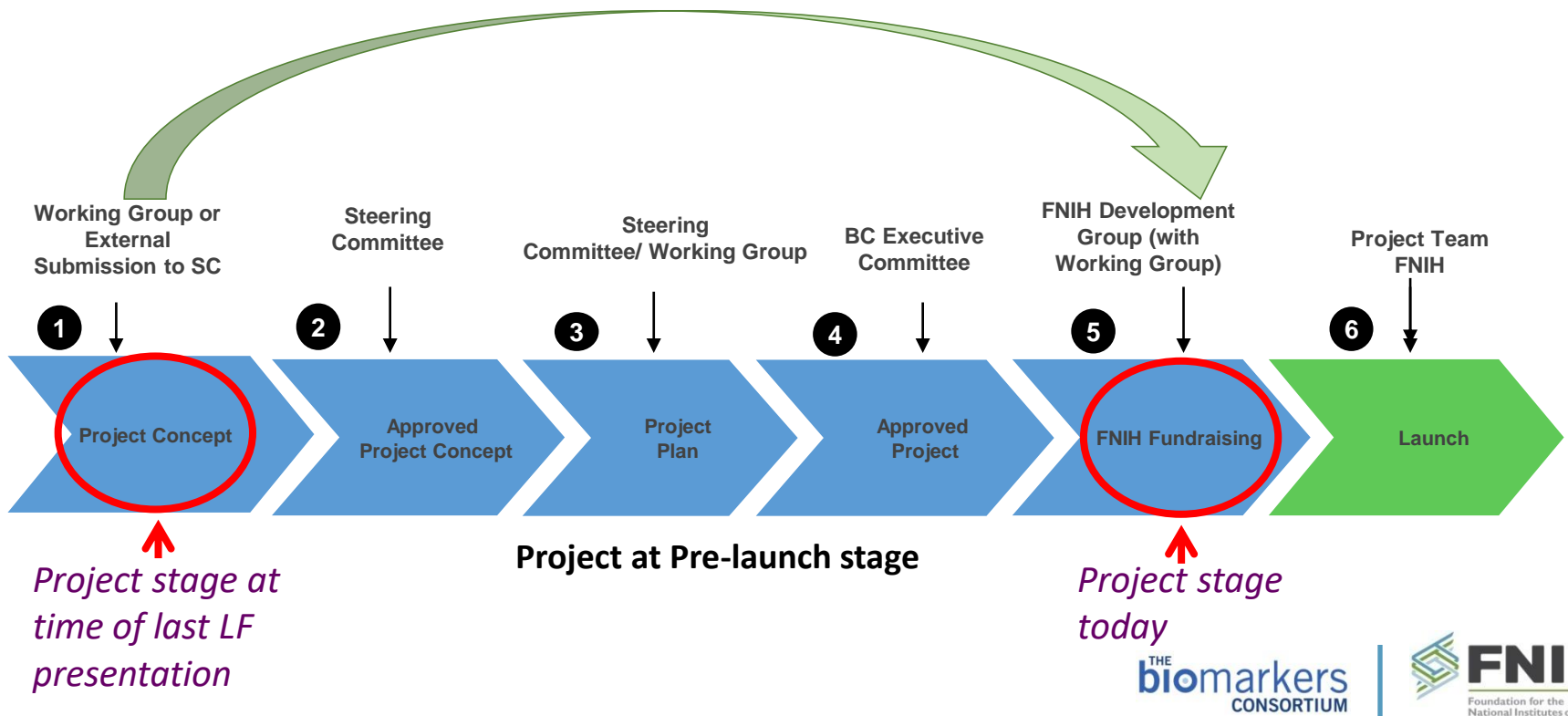
Longitudinal, interventional trial

# Progression of Project Development through FNIH Biomarkers Consortium

## ■ Working Group stage: fully endorsed project

### ■ Partners can provide:

- Financial support – 9 companies already committed to financially support NIMBLE → sufficient for full project implementation
- In-kind support (e.g., assay platforms, reagents, samples, relevant data sets, instruments) that can be quantified financially





## Key characteristics of NIMBLE Consortium

- **Industry-academic collaboration**
- **Innovative team science**
- **Focus**
- **Deliverables with track-record**
  - ✧ Share
- **Advance the field**

# NIMBLE Program Team Structure: Founded in a Collaborative Innovative Team Science Model

## NIMBLE Project Team

Project Team Co-chairs: Arun Sanyal, Sudha Shankar & Roberto Calle

Work Stream Co-Chairs: Claude Sirlin, Anthony Samir, Rohit Loomba

Project Team Members: Representatives from supporting companies and academia

Scientific Program Manager: Tania Kamphaus

### Circulating & Functional Markers Work Stream

**Rohit Loomba – Co-chair**

*Sudha Shankar (NGMBio)*

*Manal Abdelmalek (DCRI)*

*Mohammad Siddiqui (VCU)*

*Representatives from companies  
contributing assays*

*Others TBD*

### Imaging Markers Work Stream

**Claude Sirlin (UCSD)– Co-chair**

**Anthony Samir (Harvard/MGH) – Co-chair**

*Sarah Sherlock (Pfizer)*

*Roberto Calle (Pfizer)*

*Representatives from companies  
contributing imaging technology*

*Others TBD*

### Pathology Platform Team

*Cynthia Guy (DCRI)*

*Melissa Contos (VCU)*

*Others TBD*

### Clin Ops Platform Team

*TBD*

### Statistics Platform Team

*Santos Carvajal-Gonzalez*

*(Pfizer)*

*Others TBD*

# Focus and Clarity in the NIMBLE Mission

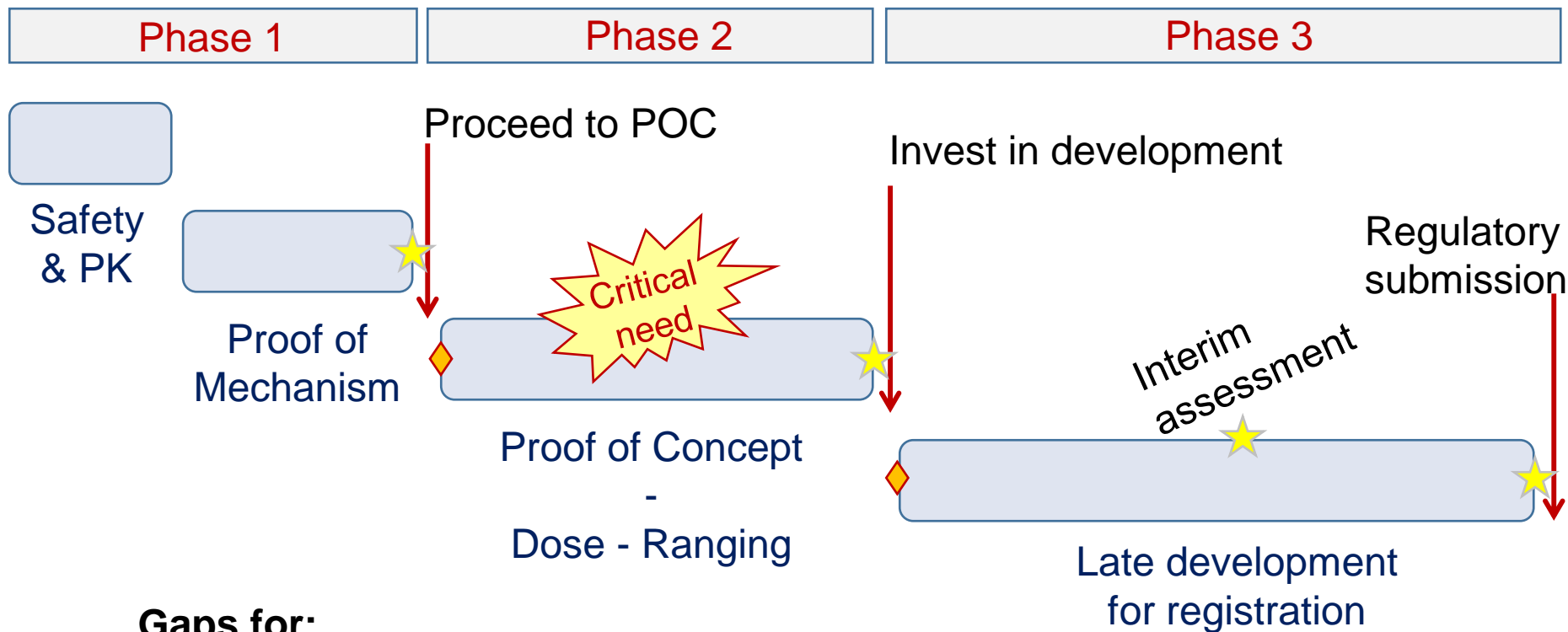
**Two focused but clinically important goals that are relevant to drug development and to clinicians**

■ **Who should be treated?**

■ **Is the patient responding to the treatment?**

- **Improvement in disease state**
- **Worsening in disease state**

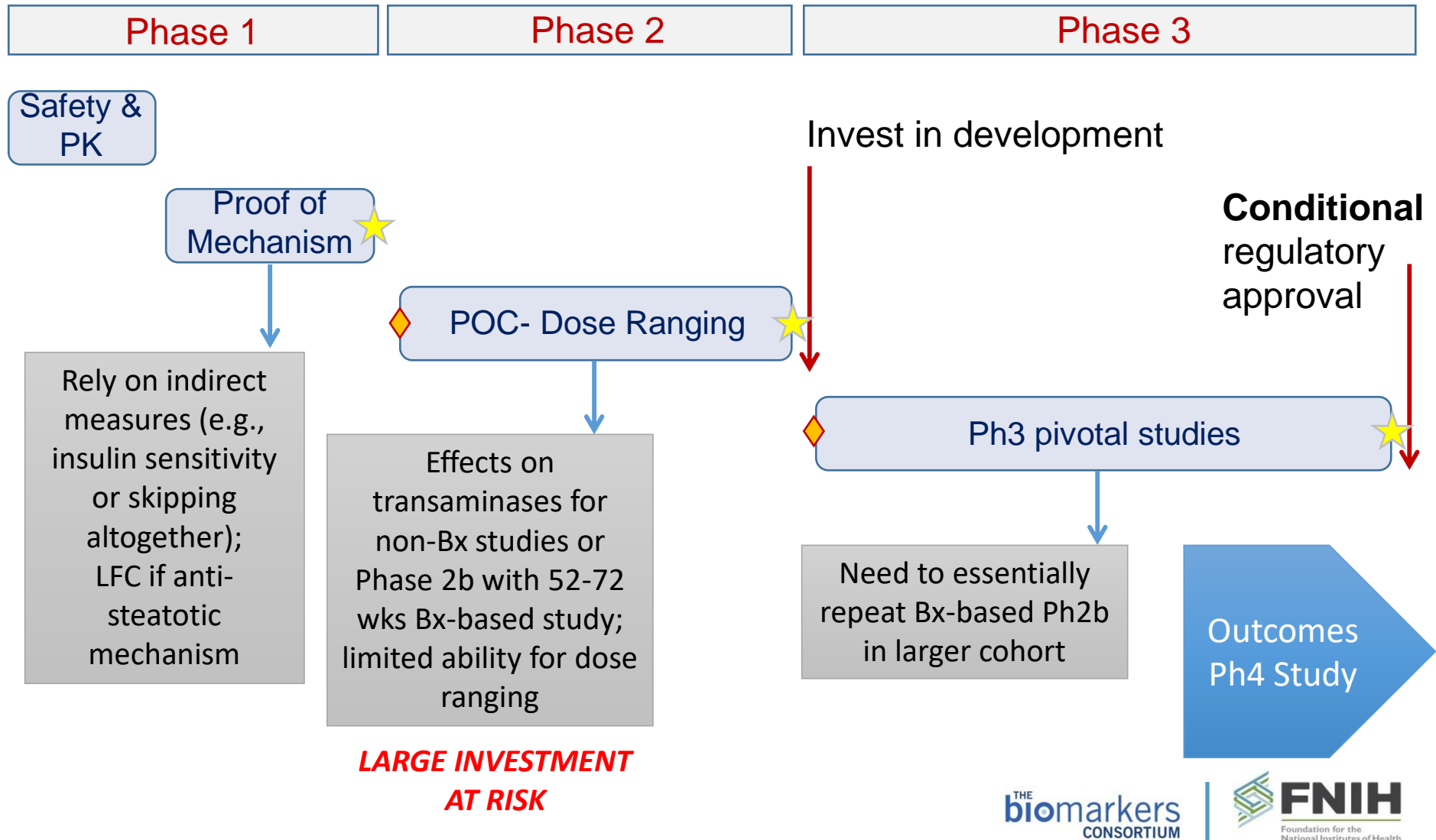
# Drug Development – Urgent Unmet Need for Noninvasive Biomarkers for NASH



## Gaps for:

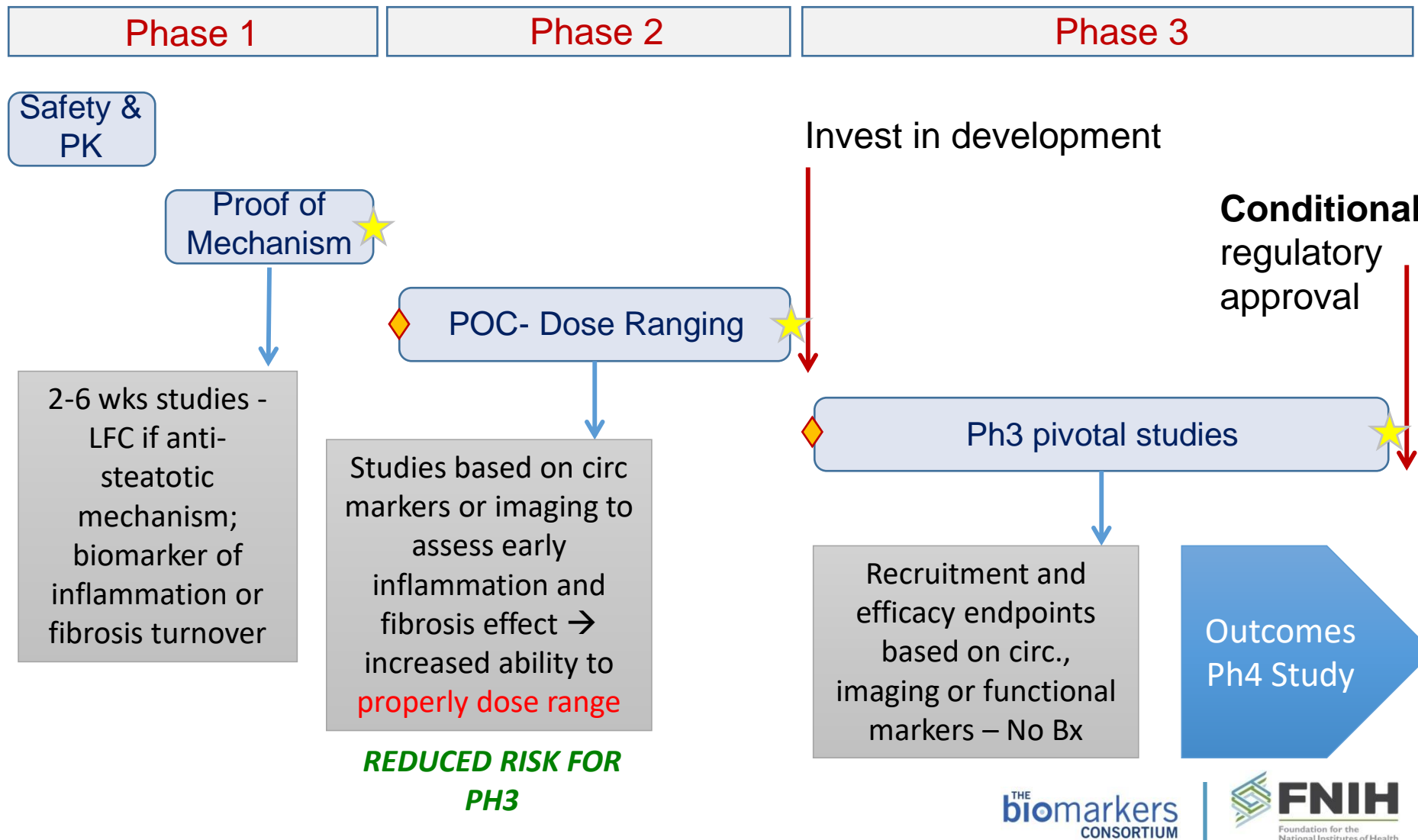
1. Recruitment of right population (enriched)
2. Non-invasive & short duration POC and dose ranging
3. Interval evaluation during development w/o Bx
4. Regulatory approval without Bx (aspirational)

# Development of New Therapeutics – Present State



# Development of New Therapeutics – Future State 1

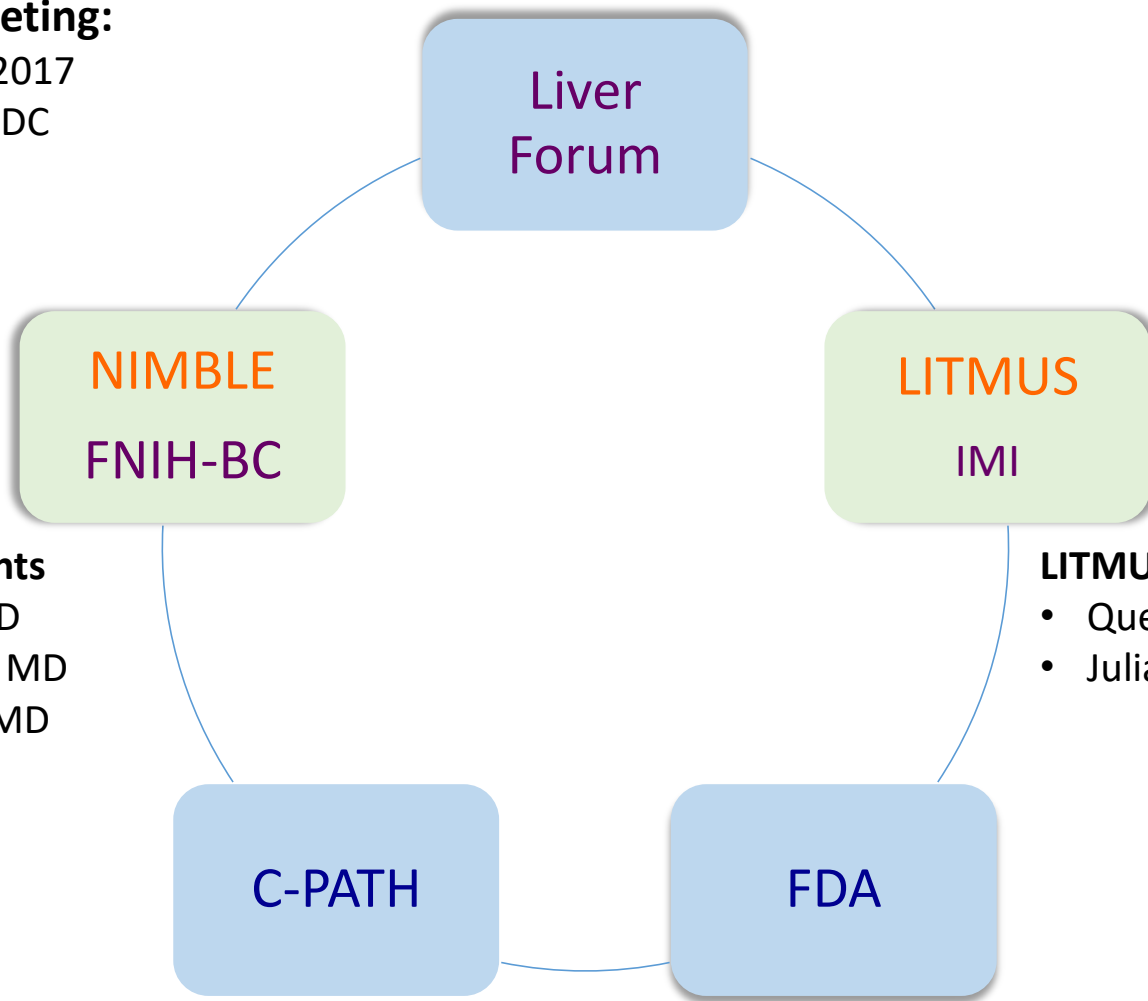
Eliminate the need for liver biopsy inclusion and assessing treatment response in Phase 2 trials



# Collaborative approach to develop and qualify non-invasive tests for NASH: formation of a coalition for NASH biomarkers

## Kick-off meeting:

October 18, 2017  
Washington, DC



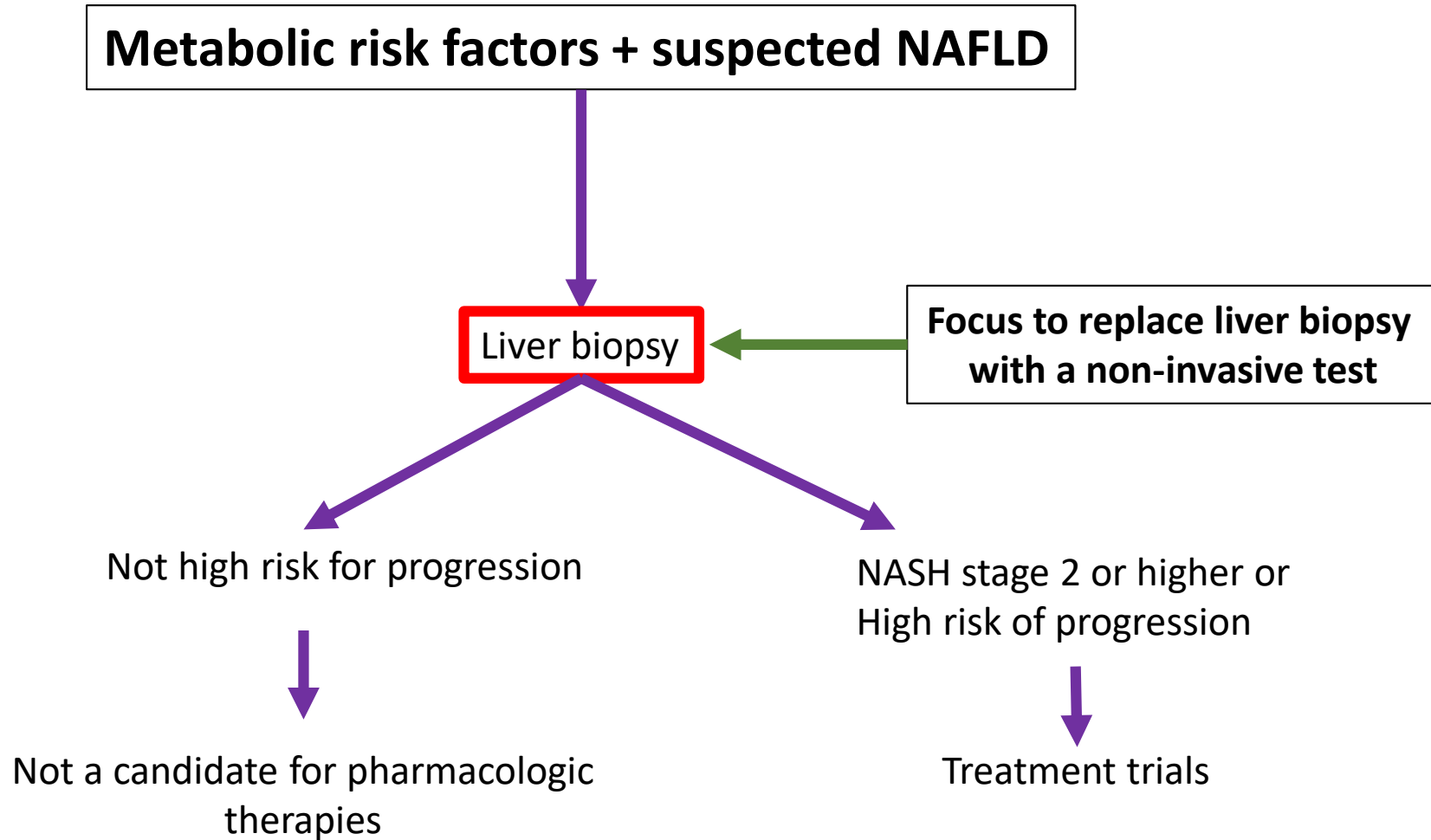
### NIMBLE Participants

- Arun Sanyal, MD
- Sudha Shankar, MD
- Roberto Calle, MD

### LITMUS Participants

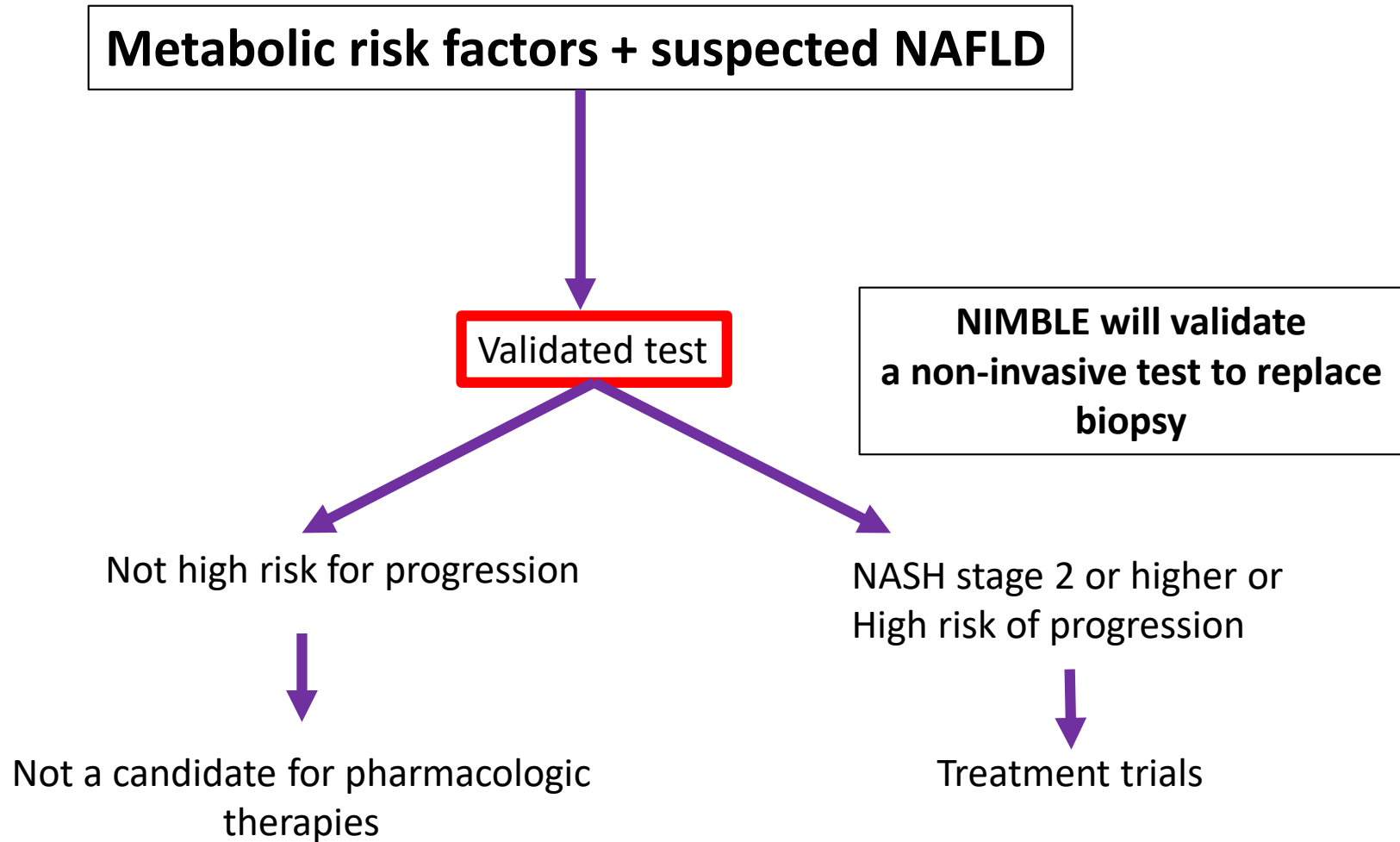
- Quentin Anstee, MD, PhD
- Julia Brosnan, PhD

# Clinical Care of NASH – Present State





# Clinical Care of NASH – Future State



# SHARING OF NIMBLE LEARNINGS

- **Standardization of methodology, analysis and interpretation**
- **Publication of findings and recommended standards in peer-reviewed journals**
- **Aim to establish follow up to NIMBLE with collaborations to corroborate findings**
  - Other large NASH Biomarkers Consortia, e.g., LITMUS
  - Emerging databases and cohorts in other countries

## NIMBLE Team's Collaborative Vision

- **Industry-academic collaboration**
- **Innovative team science**
- **Focus**
- **Deliverables**
- **Advance the field**

**Welcome open collaboration across silos between pharma, biotech, diagnostics, imaging companies, regulators, and academics**