



PARIS MASH MEETING

11th edition

**Organized by
Arun Sanyal & Lawrence Serfaty**

**September 11 & 12, 2025
Institut Pasteur, Paris**





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MASH
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**Liver Forum Updates
Veronica Miller, PhD
Forum for Collaborative Research
UC Berkeley School of Public Health**



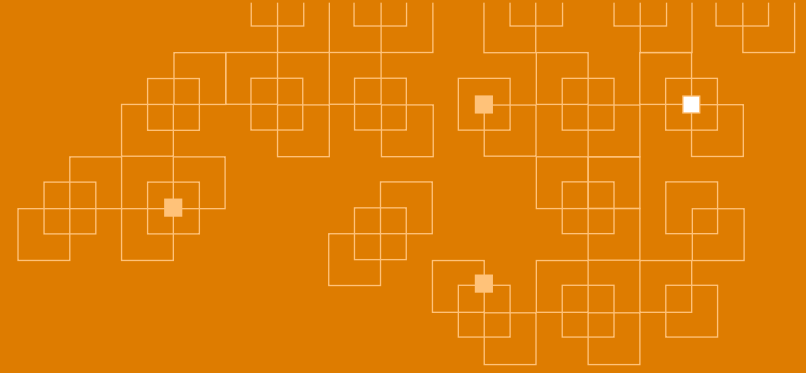
PEDDLE Working Group: Where We Are, and What's Next

Founding Co-Chairs:

Michael Betel | Fatty Liver Alliance

Henry E. Chang | Fatty Liver Foundation

Rosemarie Sellati | Regeneron Pharmaceuticals, Inc

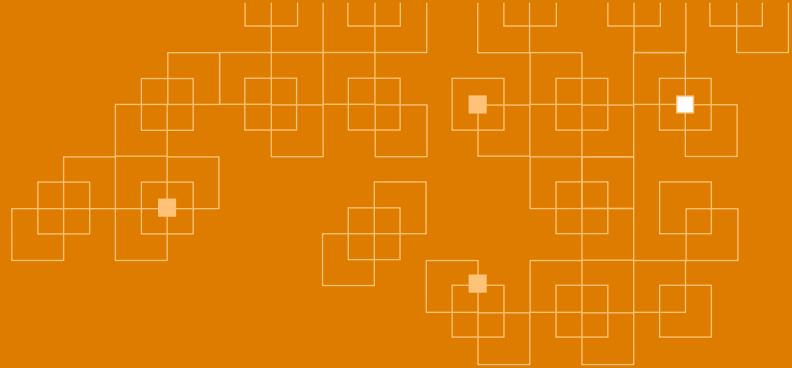


NIT as Endpoints Update



PEDDLE

Patient Engagement in Drug
Development: Leading through Example



THE FORUM

For Collaborative ResearchSM

Berkeley's Hub for Regulatory Science

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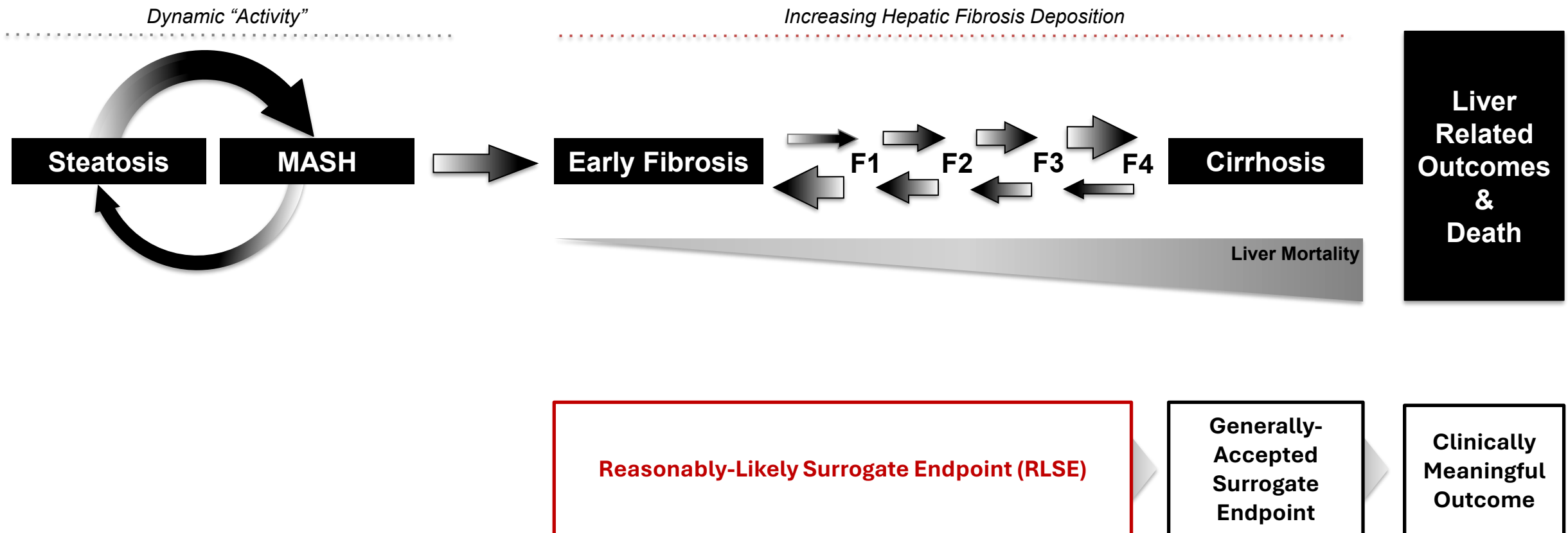
LF RLSE Project Timeline

-LF15
 - Continuous efforts to assess status of NIT data as “fit-for-purpose” for accelerated approval
 - “Show us the data”
- LF16 – Washington, DC
 - Standardizing NASH NITs
- LF17 – Paris, France
 - Forum RLSE Proposal Presentation 1
- LF18 – Washington, DC
 - Presentation 2
- LF19 – Paris France
 - Presentation 3

Multiple interactions with regulators

Clear signals that FDA DHN is prepared to consider NITs

MASLD Natural History



Proposal: A Non-Invasively Assessed Fibrosis RLSE

1. Change in Hepatic Fibrosis should be the basis for a NIT-based RLSE.

- Non-invasive Fibrosis biomarkers have robust evidence of high **diagnostic** and **prognostic** performance as well as demonstrating **sensitivity to change** in multiple studies.
- To establish Treatment Response it is proposed to demonstrate **concordance of change in two biomarkers at the individual patient level**.

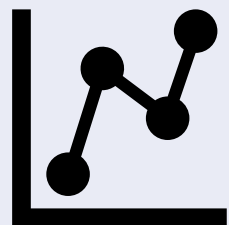
2. Change in Liver Fat Content (steatosis) and/or markers of Disease Activity may provide supportive evidence of treatment effect but do not form part of the proposed RLSE.

- Steatosis and Activity biomarkers have evidence for diagnostic performance and sensitivity to change, but **lack strong evidence of prognostic performance**.

OUTLINE



Literature Review Methods



NIT data: i) Prognosis-predicting Liver Related Events (LRE) and ii) response to treatment

- LSM
 - VCTE
 - MRE
- Plasma markers of fibrosis
 - ELF
- Hepatic fat content
 - MRI-PDFF

Summary of Literature Review (Manuscripts)-9/7/25

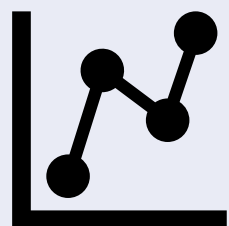
Topic	Total NIT papers	Prognosis: Baseline +/- change NIT and LRE	Treatment: NIT changes
VCTE	37	17	20
MRE	18	8	10
ELF	33	5	28
MRI-PDFF	24	0	24
ALL	68*	29*	39*
Total Patients	39,372	29,912	9,460

*multiple NIT may be present in one study

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Full presentation + references



- See Liver Forum 19 (September 10) materials

<https://www.forumresearch.org/liver-forum/liver-forum-meetings/liver-forum-meetings-meetings>

High-Level Summary

- VCTE Prognostic ✓ ✓ ✓
- VCTE Treatment Change ✓ ✓ ✓
- MRE Prognostic ✓
- MRE Treatment Change
- ELF Prognostic ✓ ✓
- ELF Treatment Change ✓ ✓

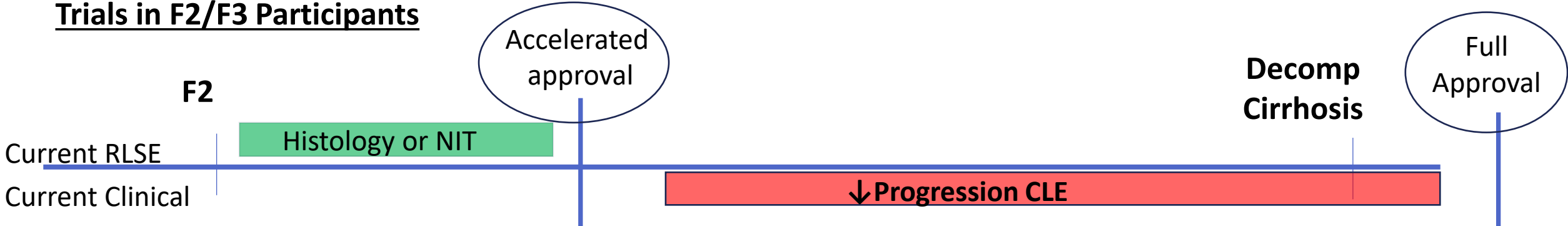
In the news

- FDA DHN paper
 - Hepatology
- Biomarker Qualification Program
 - LOI Determination Letter

- Until clinical benefit confirmed, drugs are not SOC
- Demonstrating that NITs correlate with histology (or histologic response to therapy) may also be useful to support the mechanistic rationale by showing that the NIT may reflect the primary causal pathway(s) in MASH pathogenesis.
- A description of the mechanism of action of the drug, and how that relates to the understanding of the disease and the attributes measured by NITs should also be described
- Use of NITs to identify progression to cirrhosis could also be considered for development as a VSE.

-  Improve
-  Stable
-  Worsen

Trials in F2/F3 Participants

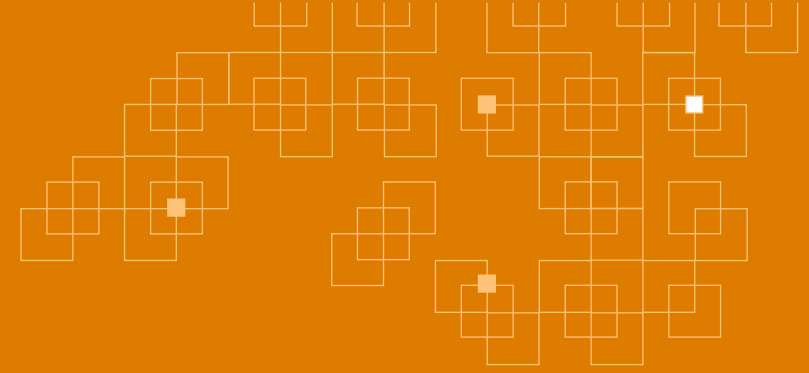


Trials in F4 Participants



Data requirements

- RLSE →→→→→VSE
- Increase certainty (decrease uncertainty)
- “Validate” the relationship between NIT and clinical benefit
 - Increase certainty
 - Decrease uncertainty
- In context of clinical benefit confirmatory trials
- Consistency across different drugs
 - MOA*



Pediatric Working Group Updates

Standardization of Clinical Trial Design for Youth-Onset MASLD

Miriam Vos, MD, MSPH, FAHA, FAASLD

Bryan Rudolph, MD, MPH

Looking Back 1 Year Ago

Why This Group is Needed:

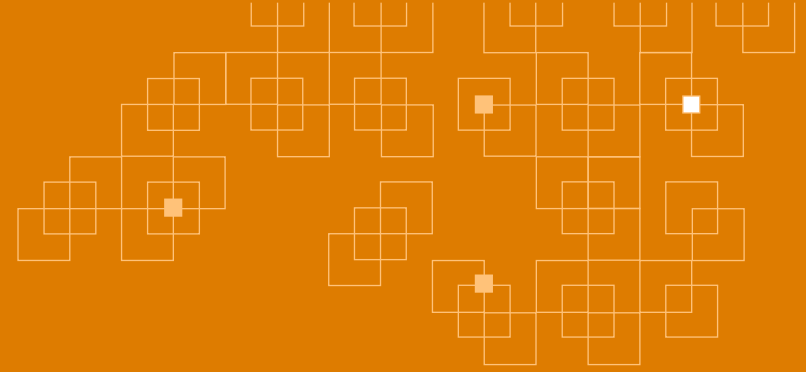
- Approved medications in adults will soon need trials in pediatric patients with MASH
- Regulatory guidance (EMA and FDA) differ
- 5-11-fold increased risk of increased mortality in children and high burden of comorbidities (e.g., diabetes)
- Prior pediatric Liver Forum consensus documents needs updating

Process:

- Sept 2024: first meeting to discuss literature vis-à-vis prevalence, NITs, outcomes
- Subsequent meetings (N=5) focused on reaching consensus on optimal trial design
- Goal: produce a standardized framework for pediatric clinical trial

Evolving Consensus

- Study inclusion criteria
 - diagnostic
 - Primary study endpoints
 - MRI-PDFF, ALT, and GTT
 - Focus on safety
 - Encourage standardization
 - Eg biomarkers for cross-study comparison
 - Recognize gaps in knowledge
 - Encourage collaborative research
- WG Participants:
 - Ped hepatologists
 - Pharma/biotech
 - Regulators
 - FDA;EMA
 - Patients



LF MASH Database

The Data & Analysis Center (DAC) Team



Veronica Miller, PhD
Director, Forum
Principal Investigator



Margot Yann, PhD, MEng
Director, DAC
Principal Data Scientist



Richard Haubrich, MD
Consultant



Alice Kang, MPH, CPH
Sr. Project Manager



Sunil Gupta
SAS, CDISC Consultant



Zach Rooney, MSCS
IT System Analyst



Debajyoti Debnath, MS
Research Associate

John Sninsky PhD
Advisor

Recruiting Now:

- **Research Data Analyst**
- **Data Engineer**

LF MASH Data Collaboration



- Phase 1
 - Placebo data from completed trials
 - = MASH PDB
- Phase 2
 - Treatment data from completed trials
 - Facilitate RLSE-VSE development across programs

MASH PDB Project



THE FORUM
For Collaborative ResearchSM

MASH PDB Working Group - Open to all Liver Forum Members!

Co-Chairs

- Manal Abdelmalek, Academic co-Chair
- Michael Cooreman, Industry co-Chair

Executive Committees

- Quentin Anstee
- Bettina Hansen
- Veronica Miller
- Arun Sanyal
- Henry Chang

Steering Committees

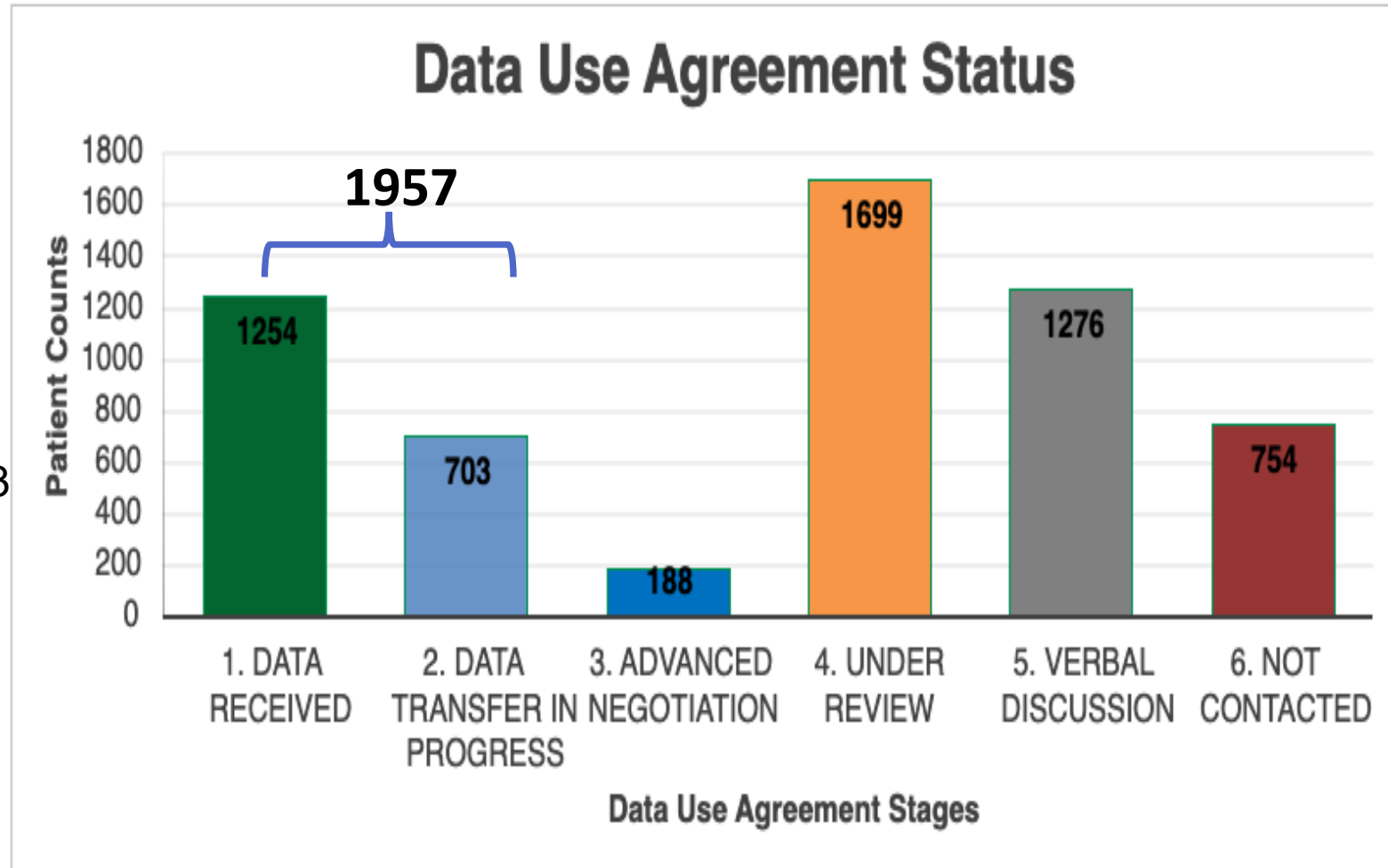
Data Contributors & Experts across stakeholder groups

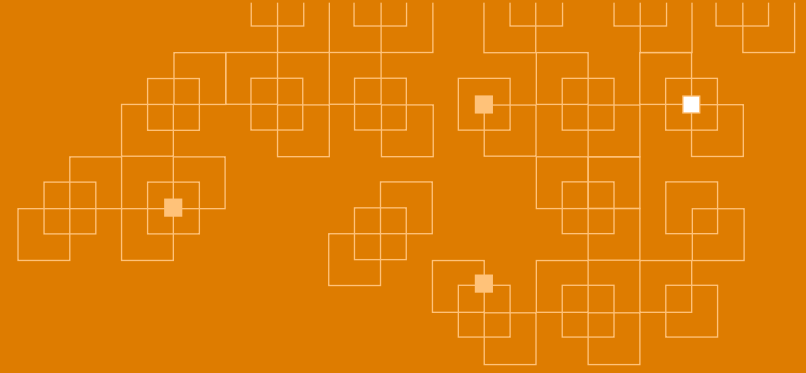
Thank you for the PDB Leadership!

Data Sources & Data Availability

As of September 9, 2025

- Invited to participate
 - All completed phase 2 and phase 3 studies
- Potential # of patients: 5874
 1. Data Received: 1254
4 companies & NIDDK
 2. Signed, data transfer in progress: 703
2 companies
 3. Advanced negotiations: 188





Merci!

**NIDDK, Enyo, Mirum, Abbvie, Akero
Ipsen, Pfizer**

Progress

- Comprehensive data harmonization process
 - Based on CDISC standards
- Data integration
- Descriptive data overview

Proposed analysis (Phase 1)



- Natural history
 - Placebo “response” – histology and NIT
 - Contribute to NIT-Endpoint conversations
- Supplemental external controls
 - Including digital twin generation
- Bespoke analyses for specific programs

Liver Forum Sponsors



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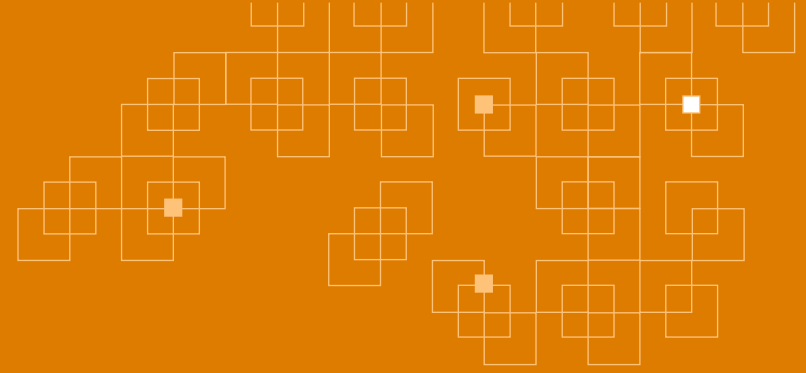
RECTIFY
PHARMA

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Takeda



Thank you!
Veronicam@berkeley.edu