



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

# Case Definitions

## Working Group Update

Stephen Harrison, MD  
*Pinnacle Clinical Research*

# Case Definitions Update

- **Defining Improvement in NASH for Treatment Trial Endpoints: Recommendations from the Liver Forum**
  - **Writing Team:** Amanda Cheung, Brent Neuschwander-Tetri, David Kleiner, Mary Rinella, Stephen Harrison, Vlad Ratziu, Arun Sanyal, Sophie Megnien, Veronica Miller, on behalf of the Case Definitions Working Group
  - **Purpose:** Summary of currently available surrogate markers, highlighting clinically meaningful changes that can be used to identify beneficial effects of therapeutic agents and allow comparability across trials
  - Multiple rounds of review developing consensus
  - Currently undergoing final review
  - To be submitted to Hepatology

# Currently Accepted Surrogate Endpoints

- Resolution of NASH without worsening of fibrosis
  - Disappearance of hepatocyte ballooning (reduction to grade 0) and the resolution or persistence of minimal lobular inflammation (grade 0 or 1)
- Improvement of fibrosis without worsening of NASH
  - Improvement by at least one stage using the Brunt criteria

*The clinical significance of such changes still needs to be demonstrated through long term outcome studies*

# Recommendations

- Manuscript includes proposed definitions for:
  - Resolution of NAFLD, Improved NAFLD, Improved NASH, Resolution of NASH, Worsened NASH, Improved Fibrosis, Worsened Fibrosis, Improved Portal Hypertension
- Recommendations for each clinical trial phase (2a, 2b, 3, 4)
- Includes exploratory measures
  - Blood-based tests, Imaging, Biopsy, Clinical