Session 1: Welcome & Updates

- Acknowledgments
- Operating Principles
- Liver Forum Goals & Objectives
  - Updates since Liver Forum 1
- Objectives for Liver Forum 2
Steering Committee

- Co-chairs
  - Gary Burgess, Vectura
  - Arun Sanyal, VCU
- FDA
  - Lara Dimick, CDER/DGIEP
  - Ruby Mehta, CDER/DGIEP
- EMA
  - Elmer Schabel, BfArM
- Carol Brosgart, UCSF
- Laurent Castera, Hôpital Beaujon
- Stephen Harrison, Brooke Army Med Center
- Markus Peck, MedUni Wien
- Scott Friedman, Mount Sinai
- Veronica Miller, HIV Forum
- Massimo Pinzani, UCL
- Detlef Schuppan, Mainz Uni Med Center/BIDMC
- Jeff Bornstein, Biogen Idec
- Eric Hughes, BMS
- David Shapiro, Intercept
- Bill Baldyga, Patient Representative
- Tracy Swan, Patient Advocate
Forum Staff

- *Rob Besaw, MPH
- *Brenda Rodriguez, MBA, MSc
- Nivedha Panneer, MPH
- Ben Hauschild, MPH
- Myrna Cozen, MPH
  - Visiting Scholar
- Students, Interns, Fellows
Last but NOT Least!

- Margie and David Poole and IHL team
Liver Forum
Operating Principles

Neutrality & Independence
Transparency & Accessibility
Inclusiveness & Collaboration
Efficiency & Productivity
Neutrality & Independence

- Ownership
  - Collective ownership
  - Equal voice
  - Safe space for discussion, dialogue, and deliberation

- Leadership
  - Recognized leaders from all stakeholder groups
Neutrality & Independence

- Credibility
  - Recommendations based on sound ethical principles and scientific evidence
  - Let consensus evolve
  - Participation restricted to scientific experts from organizations with commitment to advancing the field
  - Not a venue for marketing, investors, journalists
    - Consensus information publicly available
Transparency & Accessibility

- Funding
  - All members invited to contribute according to ability to pay
  - Voluntary contributions
  - Seek as broad a funding base as possible

- Accountability
  - To member stakeholder groups
  - Frequent evaluation: Meeting the needs?

- Publication/dissemination
Inclusiveness & Collaboration

- Open to all organizations with an authentic commitment to the scientific advancement of the field
  - Value diversity
  - Expert input from all stakeholder groups
- Volunteered contributions by members
- Optimal resource utilization
- Share information as possible
- Avoid unintended duplication
Efficiency & Productivity

- Sustained disease specific focus
- Synchronous work process
  - “Information Democracy”
- Cross-pollination of ideas
- Standardization of research practices
- Design more efficient clinical trials
- Link silos!
Liver Forum Rules

- In-person collaborative sessions (vs meetings)
  - Closed – by invitation, guided by inclusiveness principle
  - Public dissemination only after vetting by participants

- Chatham House Rules
  - Comments are not for attribution

- Everyone brings expertise
  - Experts do not officially represent organizations or agencies
  - Comments are off-the-record

- Everyone contributes
  - No passive observers
Manage Enthusiasm

• Maximum 2 experts from each company for in-person meetings
• More opportunity for involvement within working groups
The Liver Forum
Goals & Objectives
The Liver Forum: Overall Goals

- Independent and neutral venue
  - ongoing multi-stakeholder dialogue
  - facilitate more efficient regulatory path for diagnosis and treatment of NASH and fibrosis

- Facilitate best science-based decisions, in real time, regarding efficacy and safety
  - Break down inefficiencies
  - Increase clarity
  - Benefit to the whole field, especially the patient
**Pragmatic Goals**

- Work towards acceptance of biomarkers (all diagnostic modalities) for
  - Defining disease stage
    - Diagnostic and prognostic
    - Patient selection; inclusion/exclusion criteria
  - Intervention
    - Predictive, pharmacodynamic, and endpoint surrogate markers
- Facilitate the establishment of a natural history cohort
  - Placebo arm data, other data sources
Liver Forum 1
November 2014

- Official launch of The Liver Forum
  - Meet and get to know the players
  - Understand process and governance
- Understand regulatory perspectives
  - EMA and FDA
- Recommend initial working groups
Progress since LF 1

- Published LF1 meeting report
- Recruited new members
- Membership survey
  - elicit feedback
  - volunteers for working groups members and leadership
- Established Working Groups
  - Recruit leadership
  - Recruit working group members
  - Initiate discussions & deliberation towards first series of manuscripts
- Establish funding base
- Recruit additional staff
Liver Forum 2 Objectives

- Update on EU and US regulatory perspective/experience in this field
- Update on preliminary deliberations within working groups
  - Various stages
- Feedback on strategy/approach for working groups
- Feedback on strategies moving forward
Session 2:
Regulatory Perspectives & Updates

Moderators: Gary Burgess, Arun Sanyal
Presenters/Discussants:
Elmer Schabel, BfArM/EMA
Lara Dimick, FDA
Sessions 3, 4, 5: Working Group Updates
WORKING GROUPS

- Data Standardization
  - Joanne Imperial, Andrew Muir
- Definition of Disease Stages
  - Stephen Harrison and Sophie Megnien
- Pediatric Issues
  - Joel Lavine, Krishna Polu, Miriam Vos
Why, What, and How

- Address gaps identified during Liver Forum 1
- Work towards overall goal of biomarker acceptance
- Start with small steps
  - What do we need to/can we put in place to help achieve the larger goal?
- WG’s are interrelated
  - Strategic to focus on specific angle/perspective, then integrate
Biomarkers & Endpoints (Chris Leptak, LF 1)

Disease focused
- Natural history
- Absence of intervention
- Diagnostic
- Prognostic

Response to Intervention
- Predictive
  - Efficacy
  - Safety
- Pharmacodynamic
  - Dose selection
- Efficacy
  - Predicts clinical outcome
Baseline

Diagnostic Prognostic

Natural History

End of Follow Up

Clinical Endpoint

Adult

Pediatric
Baseline
Diagnostic Prognostic

Predictive
Intervention

PD Efficacy
Natural History

End of Follow Up
Clinical Endpoint

Adult
Pediatric
Session 3: Toward Data Driven Collaboration

Moderators: Veronica Miller, David Shapiro

Presenters/Discussants:
Bettina Hansen; Borje Darpö
Joanne Imperial; Scott Friedman; Rohit Loomba, Rob Myers
DATA STANDARDIZATION
WORKING GROUP

- Co-chairs: Joanne Imperial, Andrew Muir
- Working Group members:
  - Manu Chakravarthy
  - David DeBrota
  - Lara Dimick-Santos
  - Dean Hum
  - Sophie Megnien
  - Dan Peres
  - Stephen Rossi
  - David Shapiro
  - Brent Tetri
Toward Data-Driven Collaboration

- What can we learn from studies of surrogate endpoints in PBC trials?
- What can we learn from standardization of ECG/QT criteria for inclusion in NASH trials?
- Working group strategy and feedback
Proposed Strategy

• Create overview of baseline variables in current clinical trials
  – What is level of variability?
  – Stratification?

• Explore potential of endpoints for future trials
  – Static vs. dynamic

• Consider multi-sponsor sub-studies within academic networks
  – Explore different funding mechanisms
Session 4: Speaking a Common Language: Definitions

Moderators: Markus Peck, Arun Sanyal

Presenters/Discussants:
Sophie Megnien, Stephen Harrison
Laurent Castera, Jude Oben, Rebecca Taub
Definitions Working Group

- **Co-Chairs**
  - Stephen Harrison
  - Sophie Megnien
- **Working Group Members**
  - Helena Brett-Smith
  - Tony Coombs
  - Marcelo Costa
  - Lara Dimick
  - Greg Everson
  - Scott Friedman
  - Mike Hambleton
  - Dean Hum

- **Members, continued**
  - Joanne Imperial
  - Ruby Mehta
  - Melissa Palmer
  - Markus Peck
  - Dan Peres
  - Vlad Ratziu
  - Arie Regev
  - David Shapiro
  - Chinwe Ukomadu
  - Teresa Wright
Proposed Strategy

• Summarize current state-of-the-science
  – Where are the gaps, pitfalls?

• To what extent can we standardize/derive consensus based on current science?

• What opportunities exist for advancing the science?
  – Histological, radiological/imaging, functional
  – Dynamic vs. static

• What are the opportunities for collaboration?
Proposed steps

- NASH: define
- NASH: diagnose
- Gaps/Flaws of current methodologies
- Integration of new science into field
Session 5:
Pediatric/Adolescents

Moderators: Carol Brosgart, Gary Burgess
Presenters/Discussants:
Joel Lavine, Krishna Polu, Miriam Vos
Dennis Grasela, Stefan Neubauer
Pediatric Issues
Working Group

- Co-chairs
  - Joel Lavine
  - Krishna Polu
  - Miriam Vos

- Working Group members
  - Rajarshi Banerjee
  - Lara Dimick-Santos
  - Martine Kraus
  - Sophie Megnien
  - Ruby Mehta
  - Christine Murray
  - Stephanie Noviello
  - Debra Silberg
**Pediatric Working Group**

- Proposed Strategies
- Address gaps in knowledge
  - Natural progression, long term consequences
- Biomarkers/diagnostics for pediatric and adolescent population
  - Urgency to replace liver biopsy
- Opportunities for collaboration
Session 6: Summing Up & Next Steps

Gary Burgess
Veronica Miller
Arun Sanyal