THE FORUM
For Collaborative Research℠

HBV Forum 5
Welcoming Remarks

Ryan Anderson

The Forum for Collaborative Research

Berkeley School of Public Health

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Agenda

1:30 PM	**HBV Forum 5 Opening**	
	Forum Moderator: Veronica Miller, *The Forum for Collaborative Research*	
1:30 PM	Welcome and Introduction	Ryan Anderson, *The Forum for Collaborative Research* Harry Janssen, *Toronto Center for Liver Disease, University Health Network* Anuj Gaggar, *Gilead Sciences Inc.*
1:40 PM	**Insights and Challenges in Drug Development for Treating Hepatitis Delta**	
	Session Co-moderator: Marion Peters, *University of California, San Francisco*	
1:45 PM	HDV Therapy - Relevant Recent Findings and Suggested Endpoints	Jeffrey Glenn, *Stanford University Medical Center*
1:55 PM	Molecular Insights into the Synergisms between IFN and the Entry Inhibitor Myrcludex B	Stephan Urban, *Heidelberg University Hospital*
2:05 PM	Clinical Challenges in the Development of HDV Infection	Heiner Wedemeyer, *Essen University Hospital*
2:15 PM	Panel Discussion	Eric Donaldson, *US Food and Drug Administration* Jeffrey Glenn, *Stanford University Medical Center* Stephan Urban, *University Hospital Heidelberg* Heiner Wedemeyer, *Essen University Hospital* Gabriel Westman, *Swedish Medical Products Agency*
3:00 PM	**HBV Forum Working Group Updates**	
3:00 PM	Surrogate Endpoints Working Group Update	Oliver Lenz, *Janssen*
3:10 PM	Association between HBsAg Loss and Long-term Clinical Outcome in Chronic Hepatitis B: A Systematic Review and Meta-analysis	Ryan Anderson, *The Forum for Collaborative Research*
3:30 PM	**Break**	

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Agenda

4:00 PM	Liver Safety Assessment in Chronic Hepatitis B Drug Development: Recommendations from an Expert Panel	Maria Beumont, *Janssen Pharmaceuticals*
4:20 PM	Immune Monitoring Working Group Update	Sara Ferrando-Martinez, *AstraZeneca*
4:40 PM	**Interpretations of the Data from Trials Stopping Long-term Treatment with Nucleos(t)ide Analogues in Patients with Chronic HBV Infection**	
	Session Co-moderator: Bruce Given, *Arrowhead Pharmaceuticals*	
4:45 PM	Expert Perspectives, Relevant Recent Findings and Panel Discussion	Stephanie Buchholz, *Federal Institute for Drugs and Medical Devices (BfArM)* Russell Fleischer, *US Food and Drug Administration* Harry Janssen, *Toronto Centre for Liver Disease, University Health Network* Marion Peters, *University of California, San Francisco* Su Wang, *World Hepatitis Alliance*, *Hepatitis B Foundation*
5:55 PM	**Wrap-up**	Veronica Miller, *The Forum for Collaborative Research*
6:00 PM	**Adjourn and Evening Networking Reception**	

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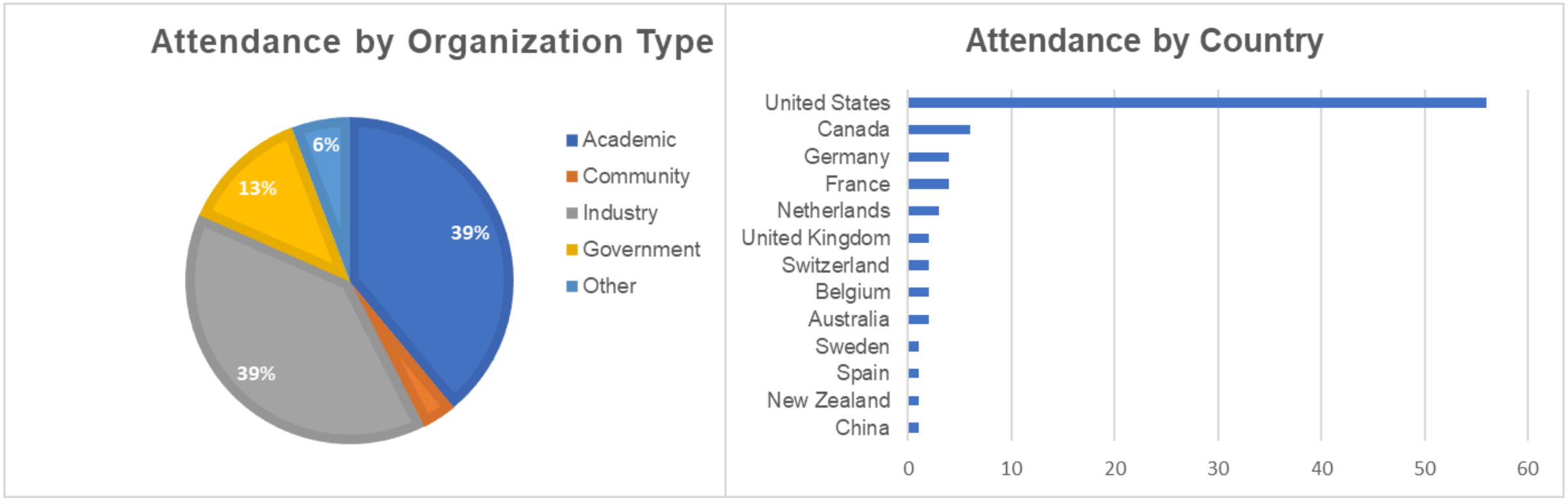
HBV Forum 5 Participation

- 91 attendees; 73 in-person, 18 remote



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HBV Forum

- **What**: a platform for ongoing multi-stakeholder dialogue to identify barriers, prioritize research and identify solutions to accelerate therapeutic development for HBV
- **Who**: regulatory agencies, professional societies, patient representatives, academic and clinical researchers, industry organizations (pharmaceutical, device, diagnostic, biotech)
  - Scientific experts with commitment to advancing the field
  - Not a venue for marketing, investors, journalists
  - Participation in the HBV Forum is by invitation

HBV Forum

- **How**: provide a neutral, independent, safe space for discussion and deliberation across stakeholder groups working in HBV field
  - Focus on developing consensus, increasing synergy and collaboration, and reducing duplication and uncertainty
- **Why**: “Once new drug candidates and therapeutic strategies are identified, their efficient, safe development is in the best interest of all stakeholders, most of all, the patients”

Rules of the Room

- "What's said in the room, stays in the room"
  - Comments/questions are not for attribution
  - Please do not post content of discussion to social media

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HBV Forum Steering Committee (28 members)

Regulatory
- Filip Josephson, *EMA*
- Poonam Mishra, *FDA*

Professional Societies
- Markus Cornberg, *EASL*
- Anna Lok, *AASLD*

Academia
- Carol Brosgart, *UCSF*
- Henry Chan, *The Chinese University of Hong Kong*
- Jordan Feld, *University of Toronto*
- Robert Fontana, *University of Michigan*
- Seng Gee Lim, *National University of Singapore*
- Adam Gehring, University of *Toronto*
- Robert Gish, *Stanford*
- Harry Janssen, *Toronto Centre for Liver Disease*
- Veronica Miller, *The Forum for Collaborative Research*
- Marion Peters, *UCSF*
- Teresa Wright, *Veterans Administration Medical Center*
- Fabien Zoulim, *INSERM*

Community
- Joan Block, *Hepatitis B Foundation*
- Michael Ninburg, *Hepatitis Education Project*

Industry
- Maria Beumont-Mauviel, *Janssen*
- Gavin Cloherty, *Abbott*
- Sara Ferrando-Martinez, *AstraZeneca*
- Anuj Gaggar, *Gilead*
- Bruce Given, *Arrowhead*
- Wolfgang Jessner, *Roche*
- Oliver Lenz, *Janssen*
- Ed Marins, *Roche*
- Rick Pesano, *Quest*
- Cristos Petropoulos, *LabCorp*

Foundation/Consortia
- Timothy Block, *Hepatitis B Foundation*
- Peter Revill, *ICE-HBV*

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HBV Forum Steering Committee: New Members

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Achievements

- **Surrogate Endpoints WG**
  - Comprehensive literature review and meta-analysis – HBsAg loss and long-term clinical outcomes
    - EASL ILC 2019: Accepted as a late-breaking abstract
    - Manuscript is currently being written
- **Liver Safety Monitoring sWG**
  - Manuscript for peer review publication in preparation

Treatment Combinations Working Group Output

Challenges, Considerations, and Principles to Guide Trials of Combination Therapies for Chronic Hepatitis B Virus

Ryan Taylor Anderson, Seng Gee Lim, Poonam Mishra, Filip Josephson, Eric Donaldson, Bruce Given, Veronica Miller

Table 1. Guiding Principles for Combination Drug Development in Chronic Hepatitis B

1.	Provide a solid scientific rationale for pursuing the proposed combination based on appropriate nonclinical studies.
2.	Perform a careful comparison of the nonclinical toxicology findings with the candidate combination drugs to determine if target organs of toxicity overlap. Where appropriate, conduct combination toxicology evaluations.
3.	Review clinical adverse events and/or pharmacologic effects information to evaluate areas of overlapping toxicity. If found, address the potential impact on the clinical trial design to assure patient safety and whether additional nonclinical evaluations are indicated.
4.	Review the routes and mechanisms of absorption, metabolism, and elimination of the candidate drugs to assess the potential for pharmacokinetic drug interactions. Likewise, assess the impact of each drug on metabolic pathways and transporters, again with an eye toward identifying any possible pharmacokinetic interactions. This work might identify the need for nonclinical or clinical assessments of such interactions.
5.	Confront the issue of anticipated ALT increases and any special concerns, such as known potential for hepatotoxicity. Ensure that the protocol includes appropriate measures for the early recognition and evaluation of such increases and appropriate stopping rules to ensure safety of trial participants.
6.	Exclude patients with advanced cirrhosis until combinations have demonstrated adequate efficacy and an acceptable safety profile. Furthermore, patients with decompensated cirrhosis (Child-Pugh B/C) should not be an initial clinical target for hepatitis B virus cure trials until safety in compensated cirrhosis has been established.

Working Group Members: Ibironke Addy, MBBS, MSc, AiCuris; Nezam Afdal, MD, Spring Bank Pharmaceuticals; Ryan Taylor Anderson, MS, Forum for Collaborative Research; Tanvir Bell, MD, US Food and Drug Administration; Carol Brosgart, MD, University of California, San Francisco; Nathaniel Brown, MD, Hepatitis B Foundation; Eric Donaldson, PhD, US Food and Drug Administration; Jordan Feld, MD, PhD, Toronto Western Hospital Liver Center; Anuj Gaggar, MD, PhD, Gilead Sciences, Inc.; Ed Gane, MBChB, MD, FRACP, MNZM, Auckland City Hospital; Bruce Given, MD, Arrowhead Pharmaceuticals; Pedro Goicochea, MSc, MA, Forum for Collaborative Research; Radhakrishnan Iyer, PhD, Spring Bank Pharmaceuticals, Inc.; Chris Kukka, Hepatitis B Foundation; Pietro Lampertico, MD, PhD, University of Milan; Seng Gee Lim, MD, National University of Singapore; Stephen Locarnini, PhD, Victorian Infectious Diseases Reference Laboratory; Uri Lopatin, MD, Assembly Biopharmaceuticals; Mala Maini, PhD, University College of London; Eduardo Bruno Martins, MD, DPhil, Consultant; Patricia Mendez, MD, Arbutus Biopharma, Inc.; Veronica Miller, PhD, Forum for Collaborative Research; Jules O'Rear, PhD, US Food and Drug Administration; Sandra Palleja, MD, PPD, Inc.; Daniela Paulsen, AiCuris; Jean-Michel Pawlotsky, MD, PhD, Henri Mondor University Hospital; Kimberly Struble, PharmD, US Food and Drug Administration; David Suhy, PhD, Benitec Biopharma Ltd; John Sullivan-Bolyai, MD, MPH, ContraVir Pharmaceuticals, Inc.; Andrew Vaillant, PhD, Replicor; Cynthia Wat, MFPM, Roche; Kelly Wong, PhD, Novartis Institutes for BioMedical Research; Teresa Wright, MD, AGAF, San Francisco Veterans Affairs Hospital.

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Thank you!

- **Presenters and Panelists**
  - Jefferey Glenn
  - Stephan Urban
  - Heiner Wedemeyer
  - Eric Donaldson
  - Gabriel Westman
  - Marion Peters
  - Maria Beumont
  - Sara Ferrando-Martinez
  - Harry Janssen
  - Stephanie Buchhlolz
  - Russell Fleischer
  - Su Wang

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Thank you!

- **Forum Staff**
  - Katherine Barradas
  - Terry Daniels
  - Luis Javier Hernandez
  - Vincent Keane
  - Veronica Miller
  - Brenda Rodriguez
  - Jessica Weber

- **Prism Event Management**
  - Paula Blay
  - Mairead O'Reilly
  - Sarah Matthews
  - Penny Jekyll
  - Ian McConnell

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HBV Forum Leadership

- **Academic co-chair:**
  Harry Janssen
  Director
  Toronto Centre for Liver Disease

- **Industry co-chair:**
  Anuj Gaggar
  Vice President Clinical Research
  Gilead Sciences

- **Forum co-chair**:
  Veronica Miller
  Executive Director
  The Forum for Collaborative Research