



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

# Biomarkers Working Group

## HBV Forum 10

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# Background

- Clarity is urgently needed to understand the landscape of HBV biomarkers measured in trials of novel therapies.
  - *Which markers are being measured in trials?*
  - *What is the meaning (clinically or virologically) of measured biomarkers?*
  - *Through what methods are markers being measured?*
  - *How are their endpoints defined?*
  - *To what extent are biomarkers data publicly available?*

# Rationale



- The HBV Forum's role is to:
  - 1) assess what has been done in a very rapidly moving field
  - 2) identify gaps
  - 3) facilitate collaboration and synergy
- Conduct a review of Phase 2, 2a, 2b trials and collate biomarkers information in a repository of study-level data
  - Develop a shared tool for all stakeholders
  - Goal is to facilitate more efficient clinical development

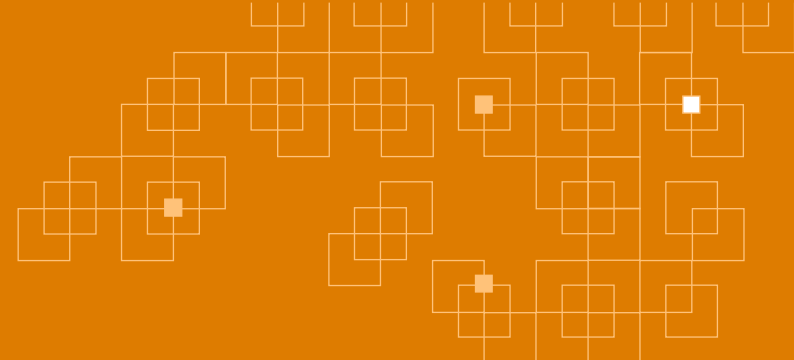
# Methods: Exploratory Phase



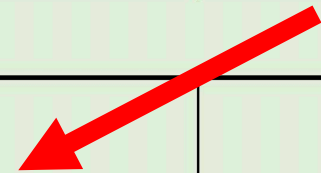
- Initial exploratory phase with the following trials:
  - REEF-2 (Janssen)
  - B-CLEAR (GSK)
- Helped structure the ‘landscaping’ approach and identify what columns of study-level information are most relevant

Clinical Trial Information					
Study & Sponsor	Combination Trial? (excludes NrtI or IFN as backbone drugs)	Backbone Drug(s) (NrtI, IFN, or placebo)	Novel Investigational Compound(s)	Drug Category (antiviral or immune modulator)	Mechanism of Action
REEF-2 Trial (Janssen)	YES	ETV, TDF, TAF	JNJ-3989	antiviral	siRNA
			JNJ-6379	antiviral	CAM-E
B-Clear Trial (GSK)	NO	ETV, TDF, TAF, 3TC, ADV, FTC	bepirovirsen	antiviral	ASO

Study & Sponsor	HBsAg Inclusion Criteria	HBV DNA Inclusion Criteria	HBeAg Status (Positive, Negative, BOTH)	HBeAg Assay (Quantitative or Qualitative)	HBeAg Assay Used
REEF-2 Trial (Janssen)	HBsAg > 100 IU/mL	HBV DNA < 60 IU/mL	Negative	Qualitative	not specified
B-Clear Trial (GSK)	HBsAg > 100 IU/mL	HBV DNA < 90 IU/mL (if on NrtI) HBV DNA > 2000 IU/mL (if not on NrtI)	BOTH	Quantitative	Diasorin LIAISON HBeAg



A	AC	AD	AE	AG
	Primary Efficacy Endpoint Definition			
Study & Sponsor	Primary Efficacy Endpoint Definition	Time Frame Assessing Primary Efficacy Endpoint	HBsAg Assay Used	HBsAg Assay LLOQ
REEF-2 Trial (Janssen)	HBsAg seroclearance < 0.05 IU/mL	24 weeks after stopping ALL treatment	Abbott Architect Platform	0.05 IU/mL
B-Clear Trial (GSK)	HBsAg < 0.05 IU/mL and HBV DNA < 20 IU/mL	24 weeks after investigational treatment cessation	Roche Elecsys HBsAg II quant II	0.05 IU/mL

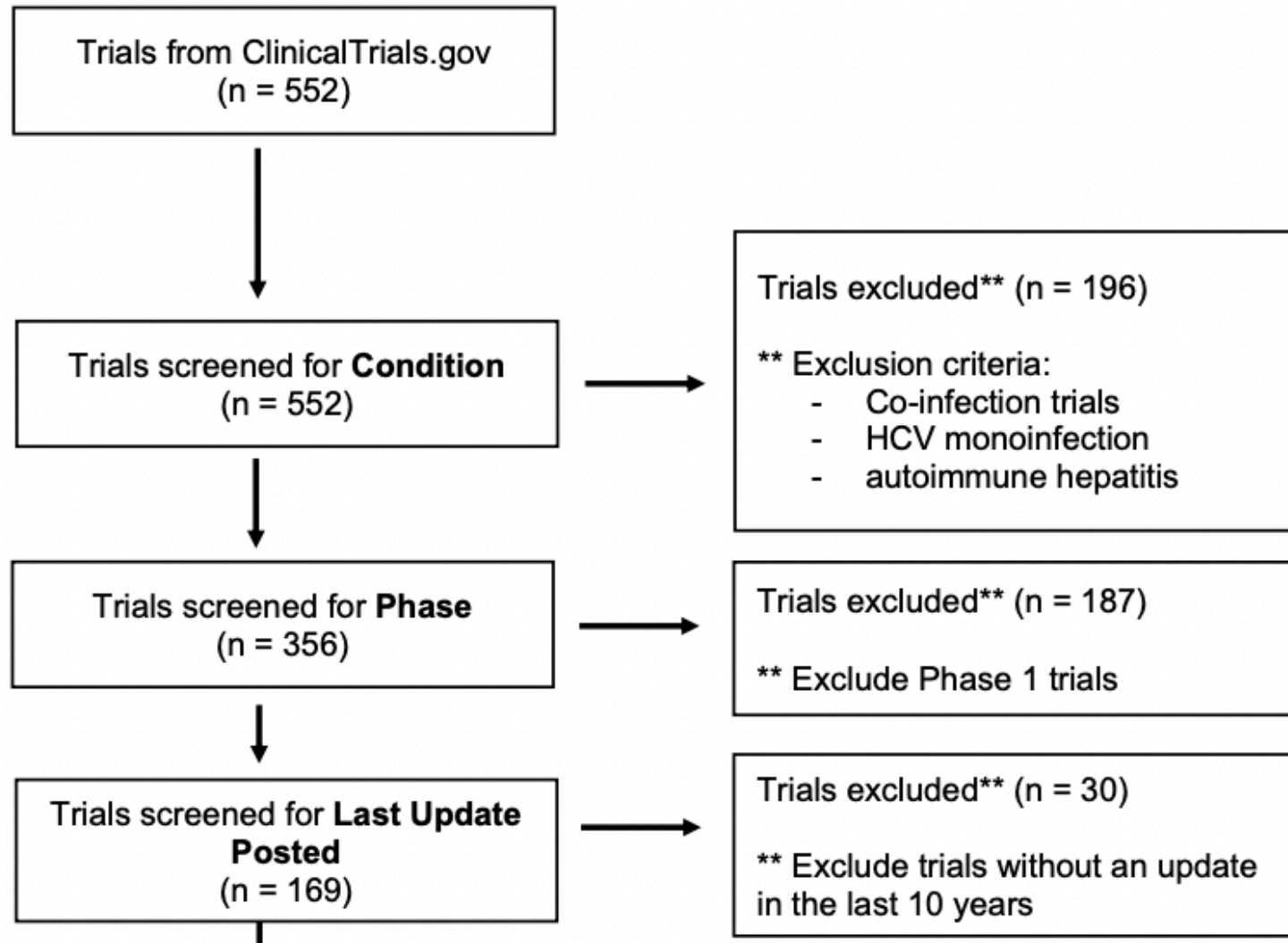


# Methods: Trial Identification

- 552 trials were identified through a search on ClinicalTrials.gov with the following terms:
  - Condition or disease: chronic hepatitis B
  - Study type: interventional studies
  - Recruitment status: recruiting, active, not recruiting, enrolling by invitation, suspended, terminated, withdrawn
  - Age group:  $\geq 18$
  - Phase: 1, 2, 3 \*
  - Funder type: any

*\* Phase 1 was included in the search because some trials are coded as both Phase 1 | Phase 2*

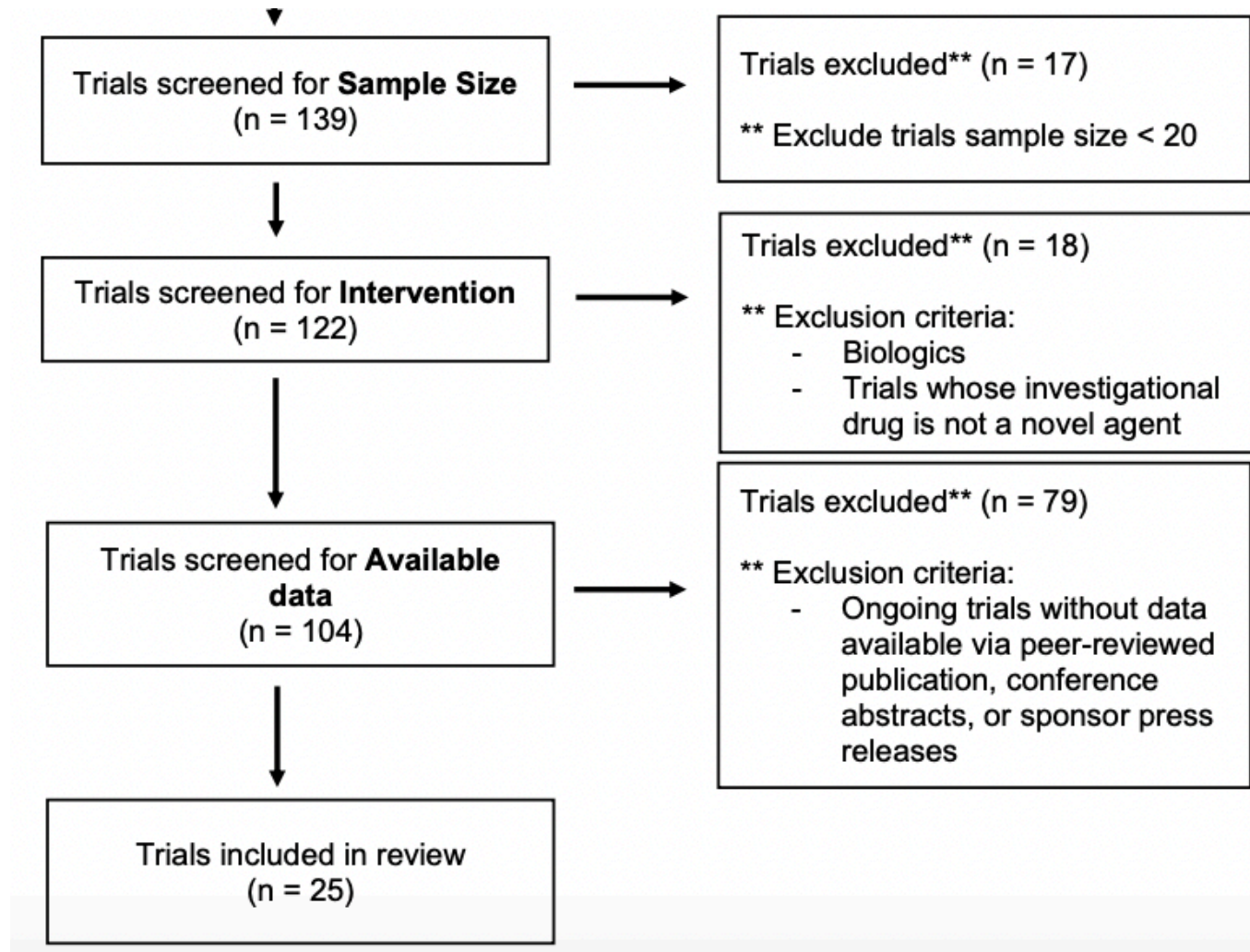
# Screening (1)



xxx



# Screening (2)



xxx

# Lessons Learned



- Dearth of information in the public domain
  - biomarkers data and assays used
- Methods to measure transcriptional markers not standardized
  - HBV RNA, HBcrAg
- Immunologic markers are measured but may not be reported
- Field should leverage data from trials of discontinued agents

# Future Directions

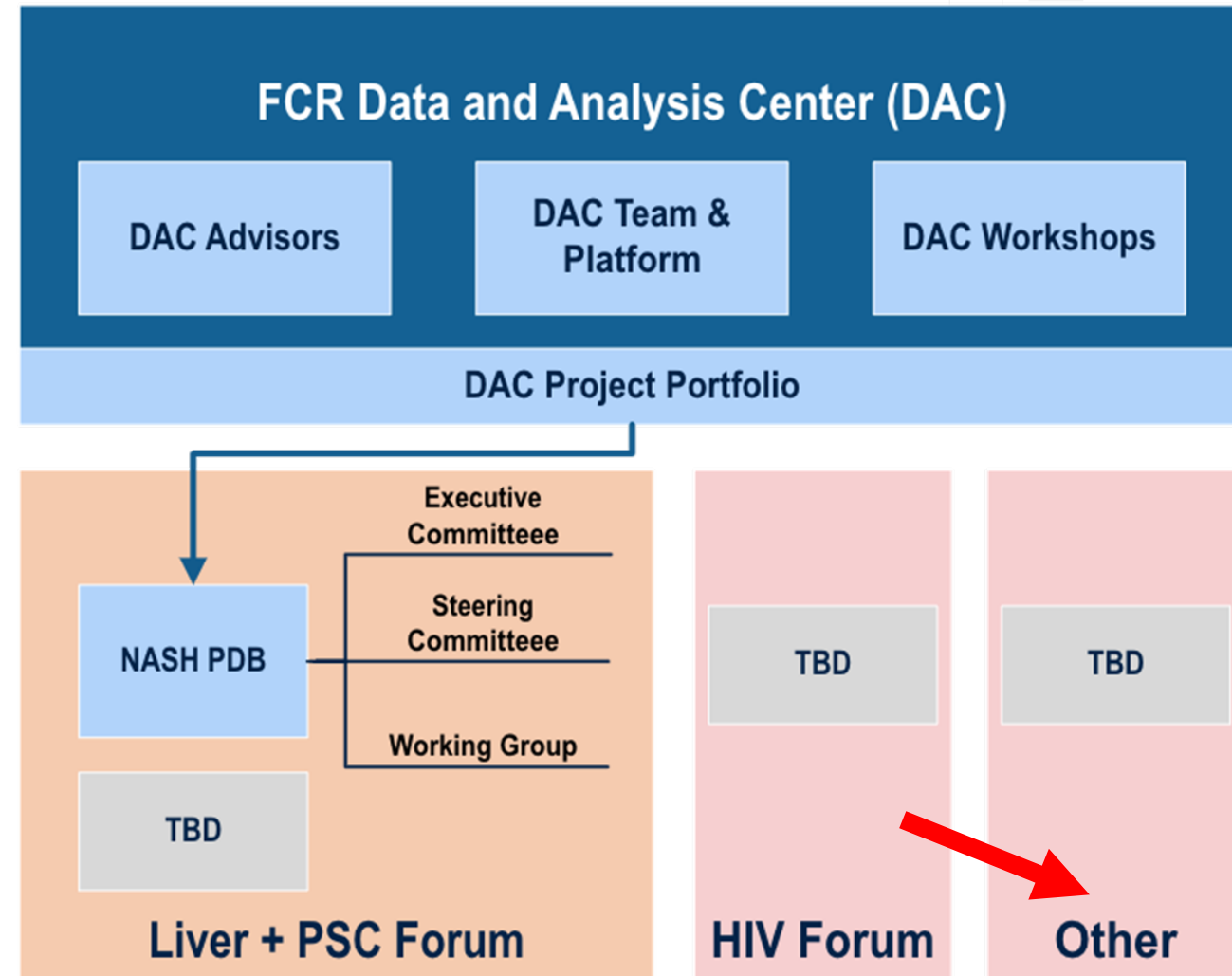
1. Continue landscaping exercise to add information on the 25 trials already in the review
2. Add new trials to the sheet as data from ongoing trials become available
3. Outreach to industry sponsors for information not in the public domain
4. Assess interest and feasibility in acquiring datasets from discontinued trials

# Forum Data & Analysis Center



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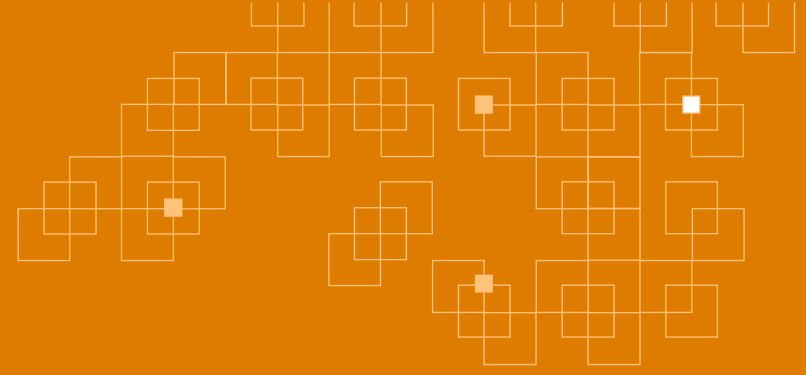
- Neutral venue for data sharing, ongoing discussion, evaluation, and innovation in data use and analytics
- Serves the needs of industry, regulatory agencies, and patients in advancing data science for drug development
- A safe approach for data sharing across sectors (e.g., private and publicly held data)
- Find more info at <https://forumresearch.org/data-center>



# Acknowledgements



- Thank you to:
  - Trial sponsors who have provided key information thus far
  - Markus Cornberg and Doug Mayers, Working Group Co-Leads
  - Mayland Treat, Graduate Student Researcher



# Open Discussion