Preclinical Profiling of ABI-6250, a Novel Small-Molecule Orally Bioavailable Drug Candidate for the Treatment of Chronic Hepatitis D Virus Infections

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Hepatotropic and GI Viruses; March 20th, 2025

Presenter Disclosures

- Francielle Tramontini Gomes de Sousa is an employee and stockholder of Assembly Biosciences, Inc.

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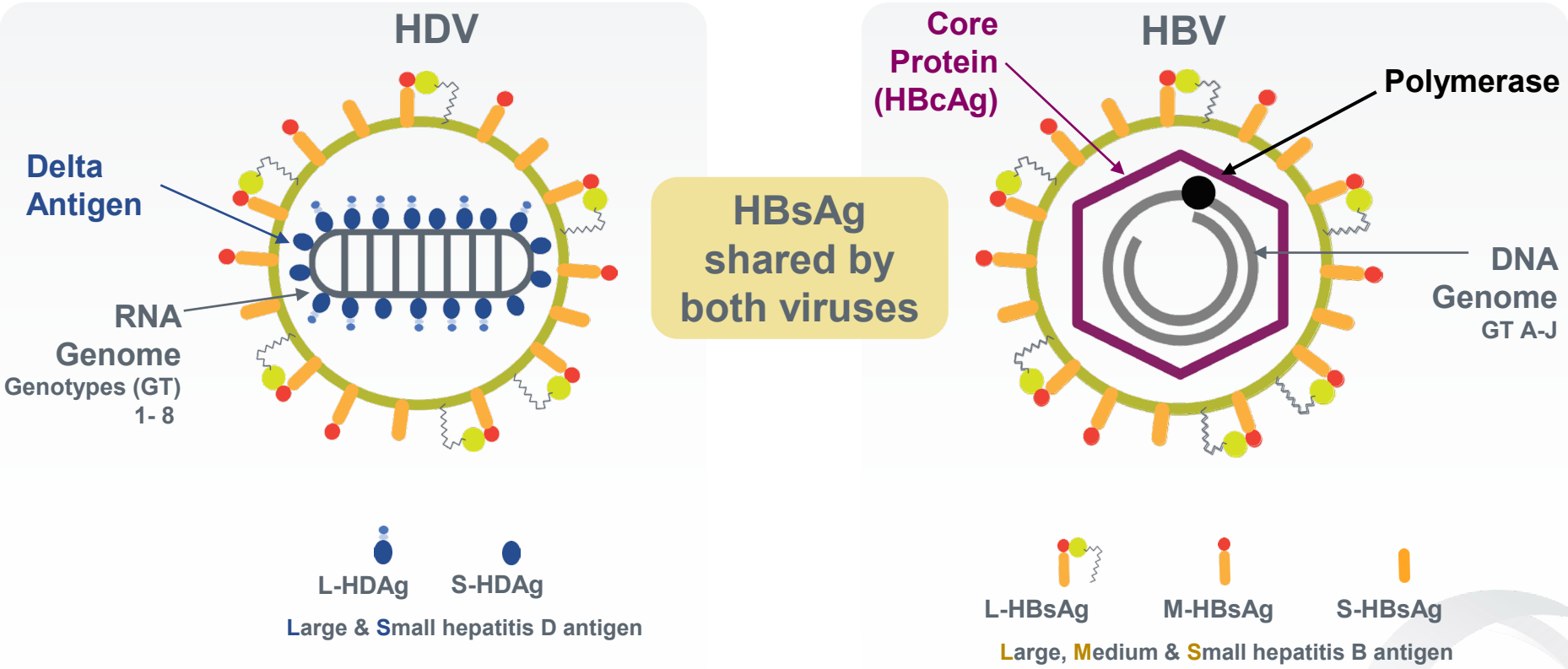
Hepatitis Delta Virus (HDV) and Hepatitis B Virus (HBV)



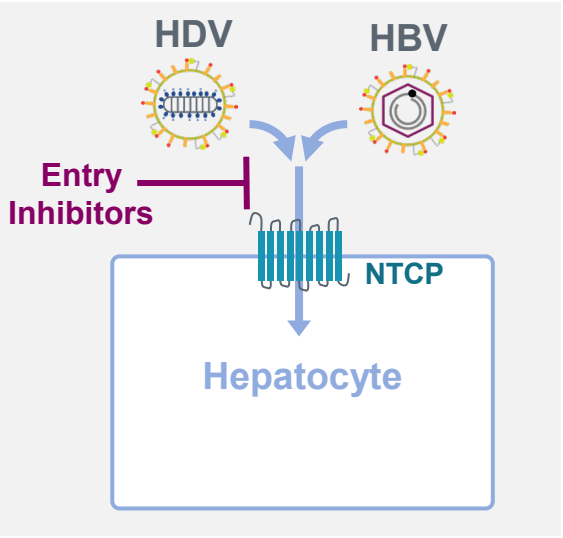
Chronic HDV Infection is The Most Severe Form of Viral Hepatitis with Limited Treatment Options

- Chronic HDV infection affects about 12-72 million patients worldwide[1,2]

- It is the most severe form of viral hepatitis
- Increased risk of cirrhosis & hepatocellular carcinoma (HCC)

- Very limited treatment options for HDV
  - Bulevirtide (BLV):
    - NTCP inhibitor
    - Only approved drug for CHD by the European Medicines Agency (EMA)
    - It requires daily injections

Entry Inhibitors Targeting NTCP Block HDV/HBV Infection



→ There is a need for an orally-bioavailable HDV entry inhibitor

1) WHO. Hepatitis D Fact Sheet. https://www.who.int/news-room/fact-sheets/detail/hepatitis-d 2) Negro F, et al. JAMA. 2023;330(24):2376-87. NTCP, sodium taurocholate cotransporting polypeptide

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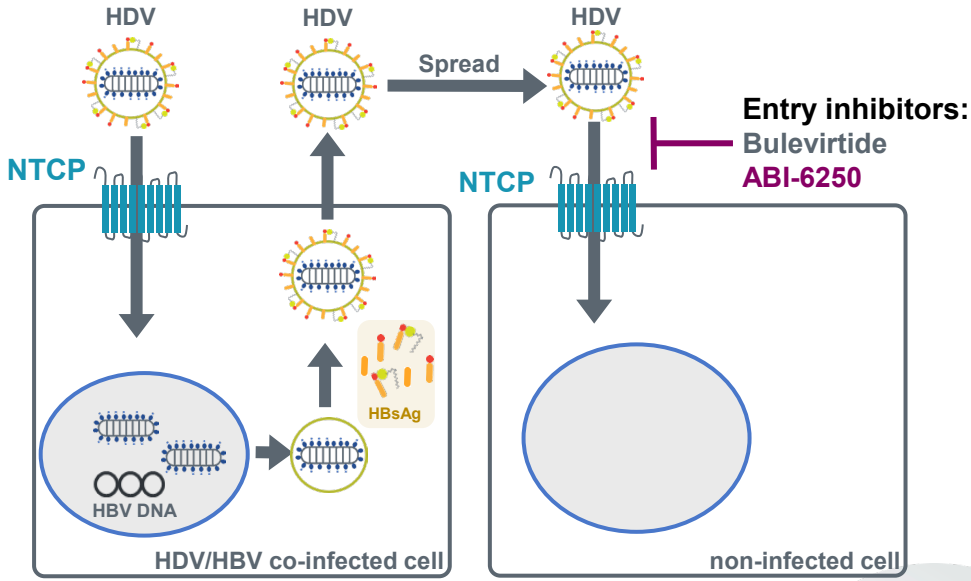

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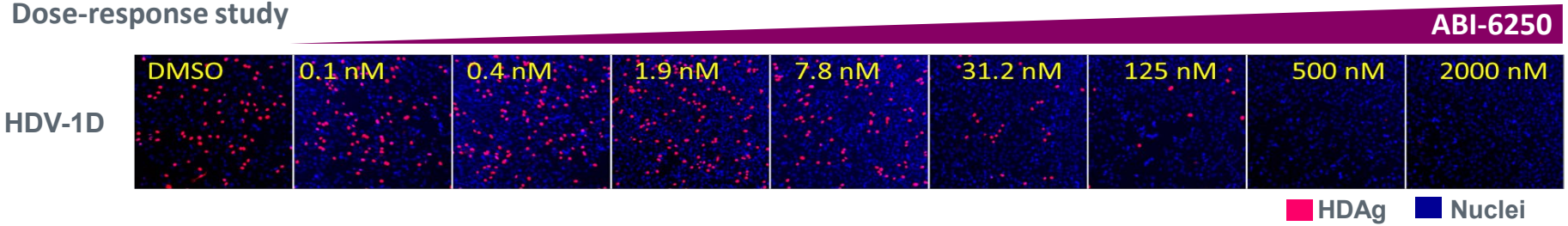
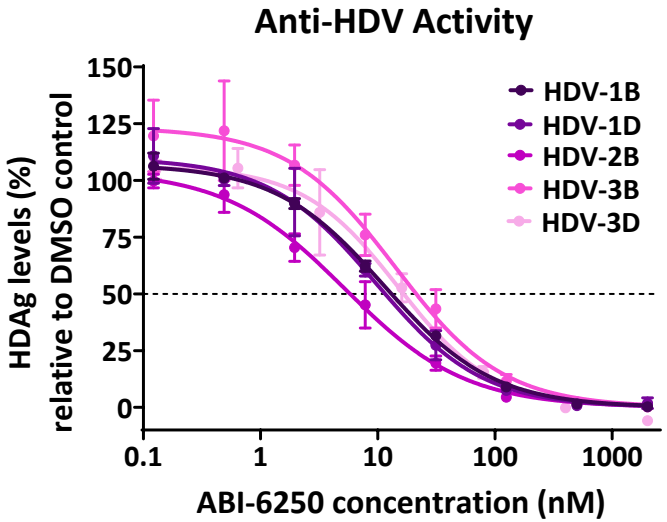
ABI-6250 Potently Inhibits Multiple HDV Genotypes

Dose-response study

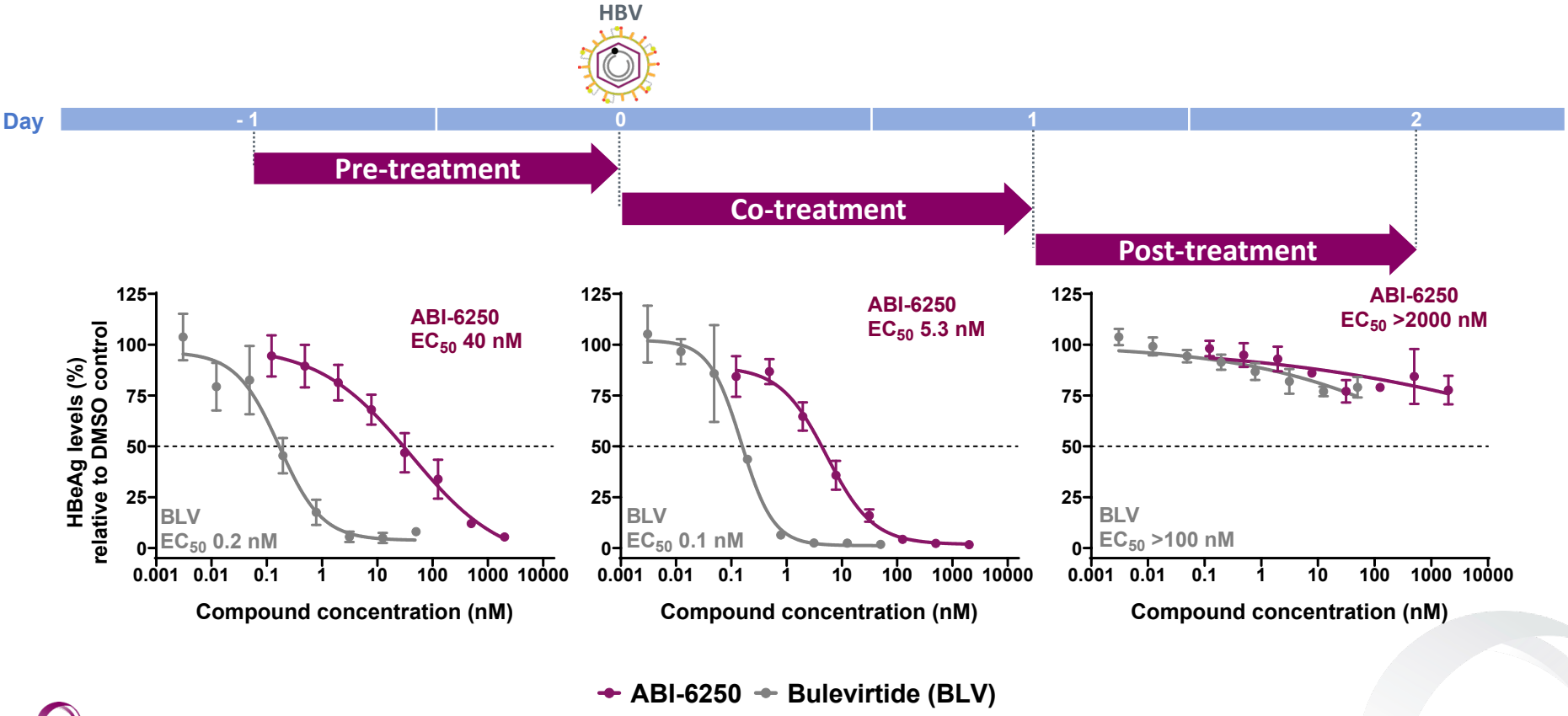




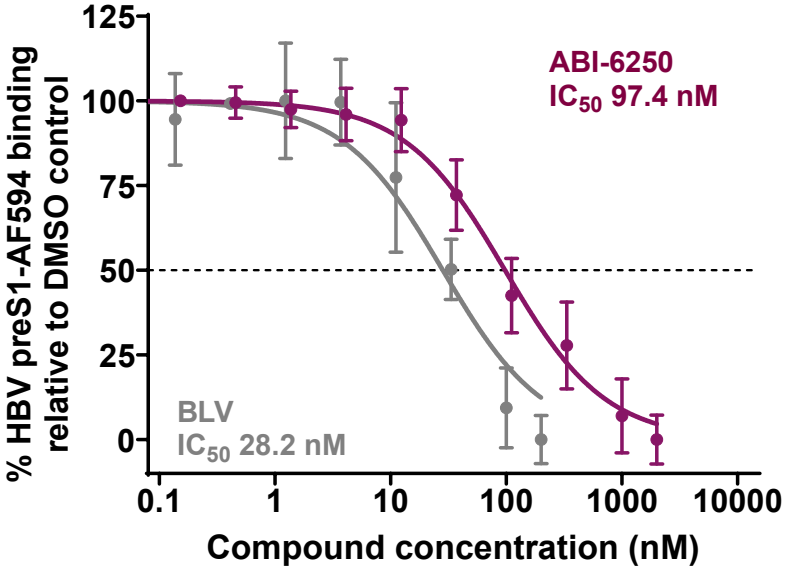
Compound	HDV EC_{50} (nM)		HBV EC_{50} (nM)	
	HepG2-NTCP	PHH	HepG2-NTCP	PHH
ABI-6250	5 – 15 (GT-1, 2, 3, B, D)	11 (GT-3B)	4.7 (GT-D)	14 (GT-A, C, D)
Bulevirtide	0.5 (GT-3D)	0.6 (GT-3B)	0.2 (GT-D)	0.2 (GT-D)

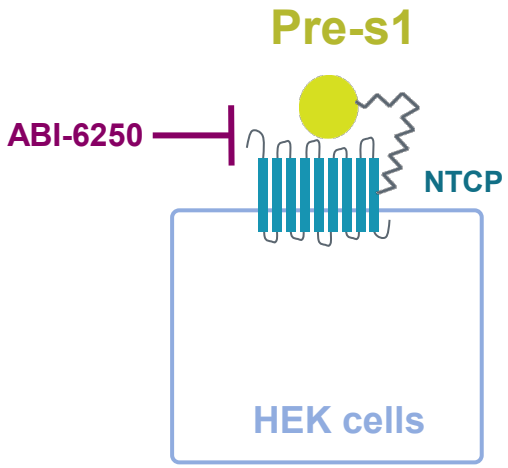
ABI-6250 Inhibits HBV During Pre and Co-treatment

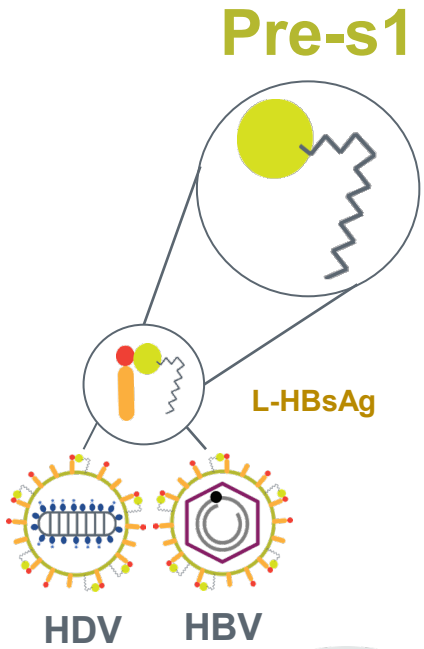
Time-of-addition study



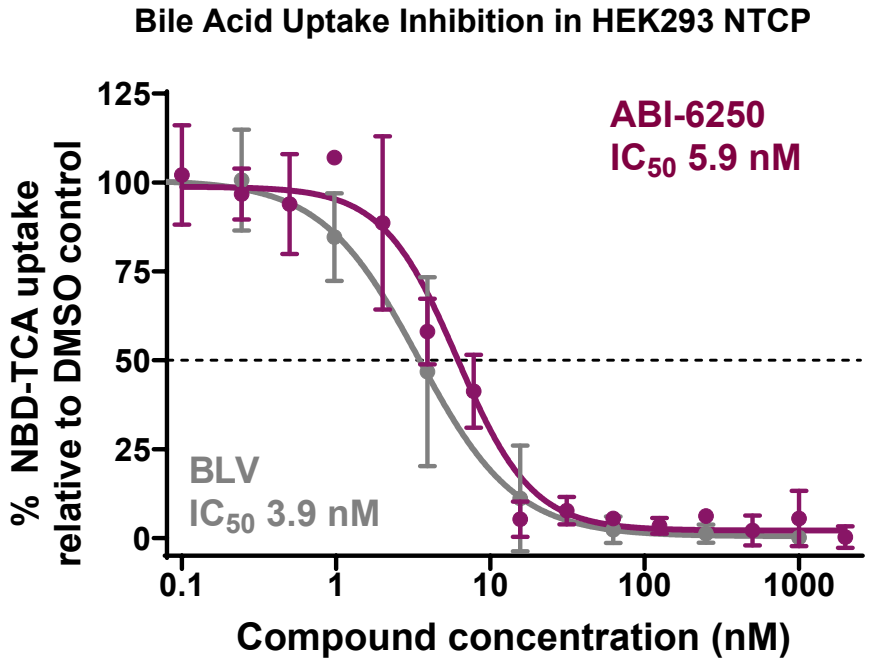
ABI-6250 Interferes with HBV PreS1 Binding to NTCP







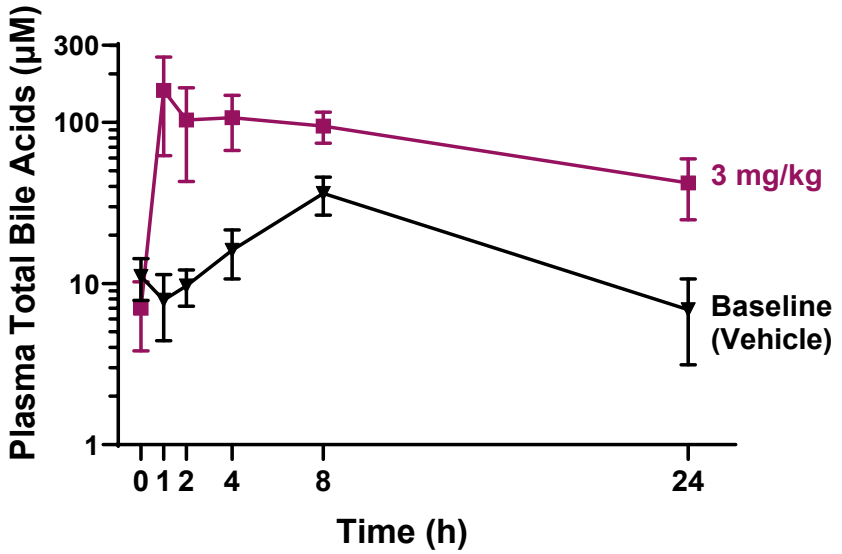
ABI-6250 Inhibits NTCP-Dependent Bile Acid Uptake *In Vitro*



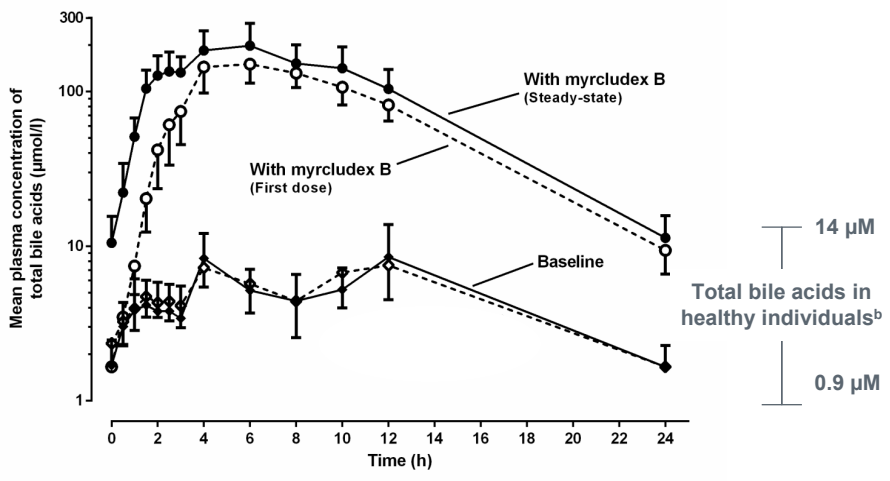
Cell type	Bile Acid IC_{50} (nM)	
	ABI-6250	Bulevirtide
Huh7 NTCP	8.3	4.8
PHH	2.9	1.9

ABI-6250 Elevates Total Bile Acids *In Vivo*

ABI-6250: Single oral dose in non-human primates (NHPs)



BLV: Clinical bile acid elevations in healthy individuals (single 10 mg SC[a])



SC, subcutaneous

[a]Blank et al.; Clin Pharm Therapy, 2017; [b]Liu et al.; SciRep. 2017

Conclusions

- ABI-6250 is a highly potent, specific, orally bioavailable small molecule HDV/HBV entry inhibitor
- At projected clinically relevant concentrations, ABI-6250 elevates total bile acids *in vivo*, indicating selective target engagement
- The PK profile supports low once-daily oral dosing for chronic HDV treatment
- A Phase 1a clinical trial is ongoing

Acknowledgments

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Questions?