Innovative Therapeutics Targeting Serious Viral Diseases

SEPTEMBER 2023

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Industry-leading experts focused on transforming treatment of viral diseases

- Accomplished management team, BOD and R&D organization
- Highly experienced team; collectively over 15 approved drugs in viral disease and hepatitis

High-recurrence genital herpes (HSV-1, HSV-2)

4M patients[1]

Chronic hepatitis D (HDV)

12M patients[3]

Transplant-associated herpesviruses (CMV, HSV-1, HSV-2, VZV)

60,000 patients[2]

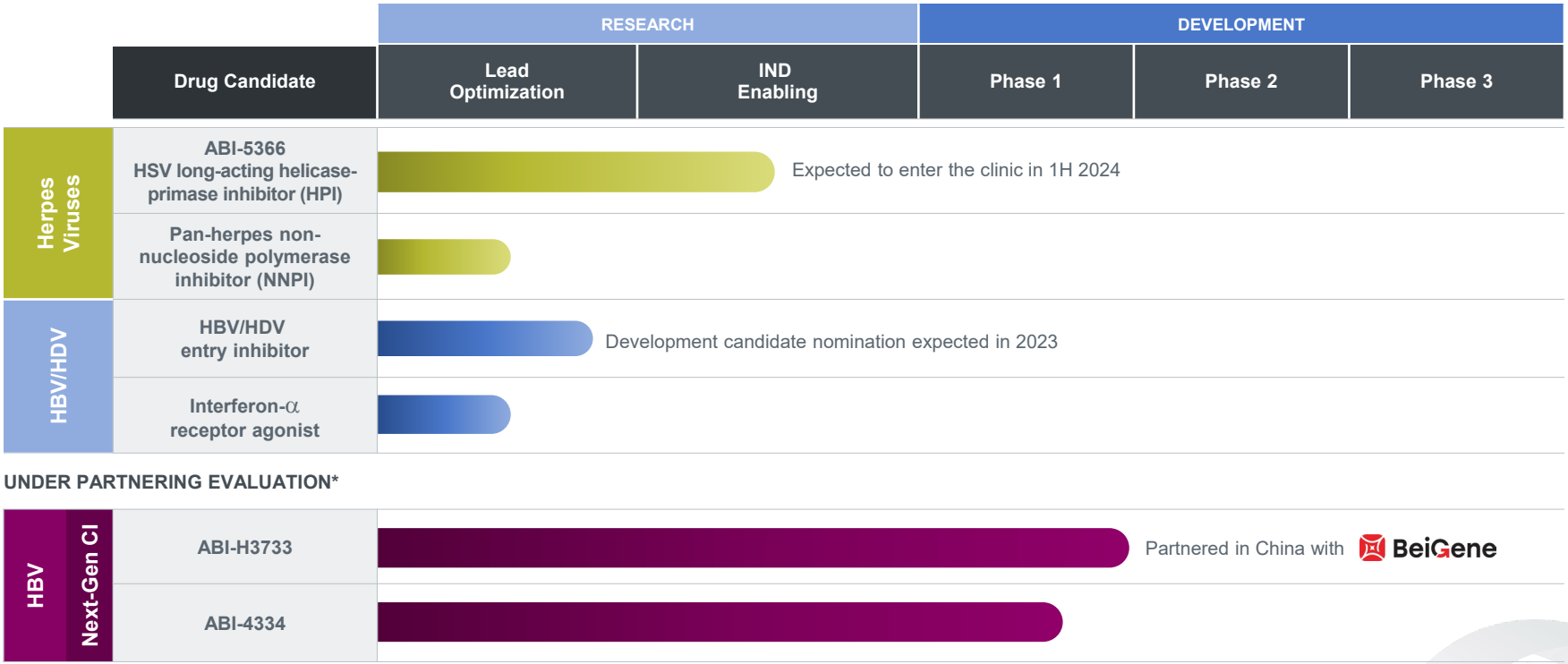
Chronic hepatitis B (HBV)

296M patients[4]

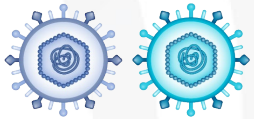
BOD, Board of Directors; CMV, cytomegalovirus; HBV, hepatitis B virus; HDV, hepatitis delta virus; HSV, herpes simplex virus; R&D, research and development; VZV, varicella-zoster virus.

1. Engelberg et al. Sexually Transmitted Diseases. 2003; Benedetti et al. Ann Intern Med. 1999 (estimated for US and EU4/UK; assumes same diagnosis rate for EU4/UK as for US); 2. EBMT, OPTN, UNOS, and IRODAT (US and EU); 3. Stockdale, J Hep. 2020; 4. WHO 2021.

Advancing a portfolio of innovative and differentiated small molecule therapeutics

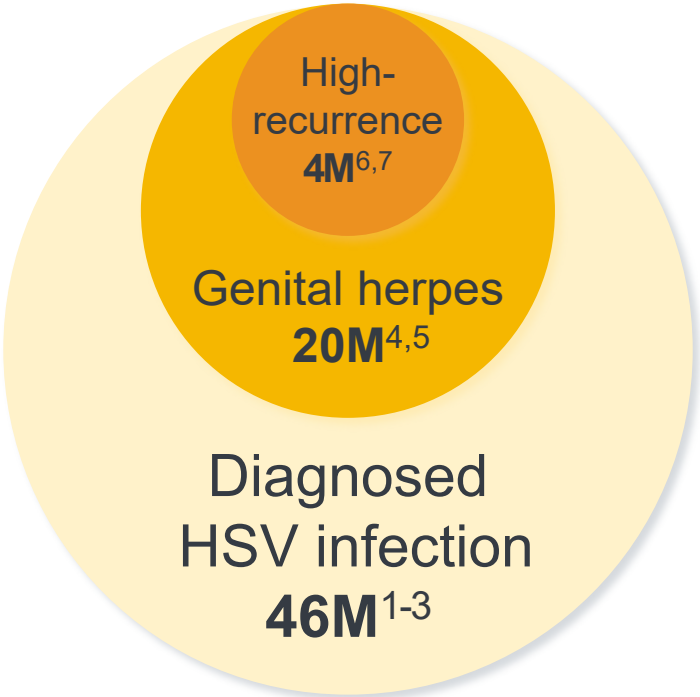


CI, core inhibitor.
*Next-generation core inhibitors; ABI-4334 has completed Phase 1a and ABI-H3733 has completed Phase 1b; Assembly Bio evaluating partnering options prior to further clinical development.



ABI-5366: Long-acting HSV helicase-primase inhibitor (HPI) for high-recurrence genital herpes

High-recurrence genital herpes is a prevalent condition with significant disease burden



- HSV-1 & HSV-2 are common, life-long infections, which are often asymptomatic and frequently go undiagnosed[1]
- Symptomatic genital herpes creates painful sores that can last a week or more[5]
- 5% of HSV-1 patients and 50% of HSV-2 patients experience ≥3 recurrences a year[6,7]
- $1-3 billion market opportunity for high-recurrence

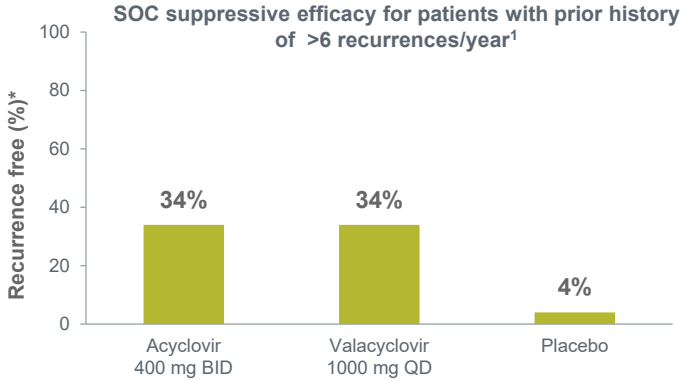
Estimated for US & EU4/UK

1. McQuillan et al. *NCHS Data Brief*. 2018; 2. Yousuf et al. *BMJ Global Health*. 2020; 3. Fanfair et al. *Sex Transm Dis*. 2013 Alareeki et al. *Lancet Reg. Health*. 2022; 4. James. Bull *World Health Organ*. 2020 5. HSV Fact Sheet –WHO ; 6. Engelberg et al. *Sexually Transmitted Diseases*. 2003; 7. Benedetti et al. *Ann Intern Med*. 1999. Assumes same diagnosis rate for EU4/UK as for US

Approved antivirals are only partially effective and daily pill burden is high

INADEQUATE SUPPRESSION

2 of 3* patients are not adequately treated[1]



*Does not adjust for lost to follow-up, discontinuations due to adverse events, and consent withdrawn.

CONTINUED TRANSMISSION

<50% transmission reduction[2]

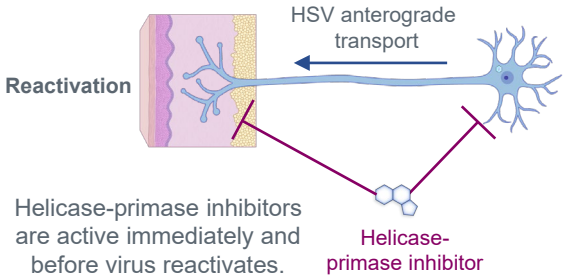
HIGH PILL BURDEN

Must be taken **once or twice daily** for life

1. Valtrex (Valacyclovir) US package insert; 2. Corey, et al. *NEJM*. 2004.

ABI-5366 is designed to provide significant innovation over current standard of care

- Low nanomolar potency *in vitro* against the HSV helicase-primase complex (clinically validated target)
- Favorable preclinical profile for long-acting agent, including exceptionally low clearance; well tolerated in safety studies to date
- Long dosing intervals predicted preclinically, offering potential for increased efficacy and patient uptake

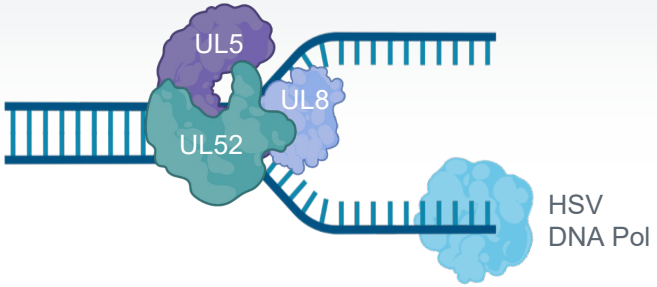


Initiation of clinical studies anticipated 1H 2024

HSV helicase-primase is a clinically validated target

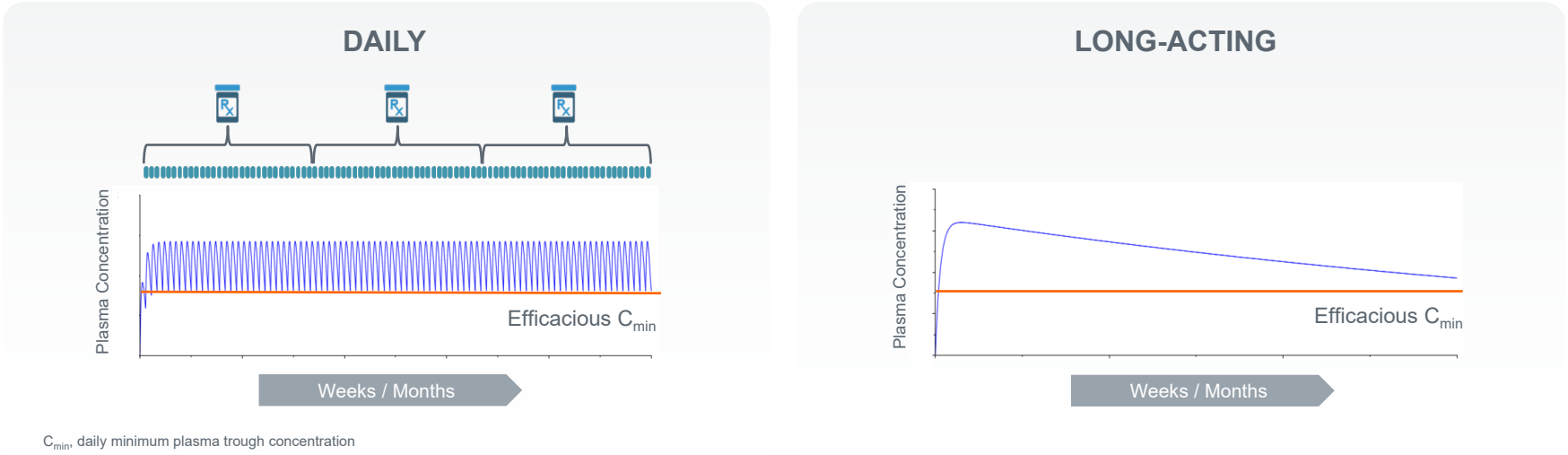
- Helicase-primase inhibitors target an essential HSV enzyme
- Acts immediately, unlike standard of care
- Clinically validated mechanism
  - Pritelivir[1]: greater reductions in HSV shedding, fewer days with lesions & pain vs. valacyclovir
- Active against nucleoside analog resistant HSV

HSV HELICASE-PRIMASE COMPLEX



1. Wald, et al. *JAMA* 2016

A long-acting therapy for genital herpes has the potential to improve efficacy, adherence and uptake



C_{min}, daily minimum plasma trough concentration

- 72% of high-recurrence HSV patients prefer suppressive therapy to episodic[1]
  - Medication non-adherence for chronic illness is ~50% with stigma, AE anxiety, high dosing frequency being key barriers[2]
- Long-acting therapy ⟶ consistent drug levels, better compliance[3] ⟶ improved efficacy
- Reduced dosing frequency ⟶ greater discretion ⟶ lower barrier to continued use

1. Romanowski, et al. Sex Trans Dis. 2003; 2. WHO. Adherence to Long-Term Therapies: Evidence for Action; 3. Okoli, et al. Mental Health Nurs. 2021; Engel, et al. JAMA. 1990.

ABI-5366 has a compelling preclinical profile

Highly potent in antiviral assays

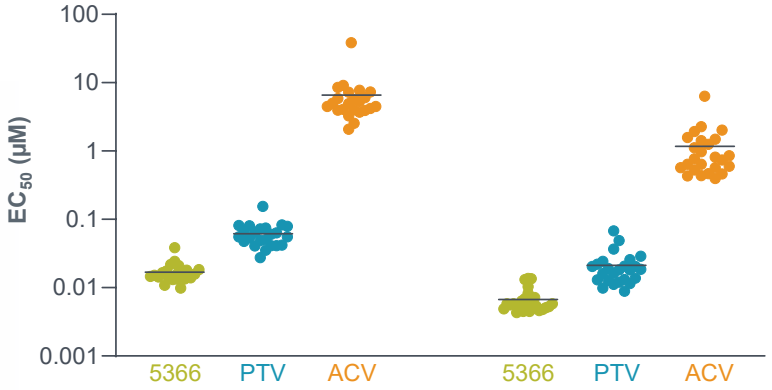
Critical properties for long-acting

- Exceptionally low clearance
- Projected human half-life of >7 days[1]
- Potential for long-acting oral, and injectable (SC/IM) formulations

Excellent preclinical safety profile to date

- No findings in standard *in vitro* safety assessment
- Well tolerated at high exposure in non-GLP tox
- GLP tox studies in process

CLINICAL ISOLATE SENSITIVITY[1]



AVG. EC_{50} (µM)	HSV-2 (n=23)			HSV-1 (n=25)		
	ABI-5366	PTV	ACV	ABI-5366	PTV	ACV
Clinical Isolates	0.017	0.062	6.6	0.007	0.022	1.2
Lab strains	0.010	0.042	1.1	0.019	0.051	3.2

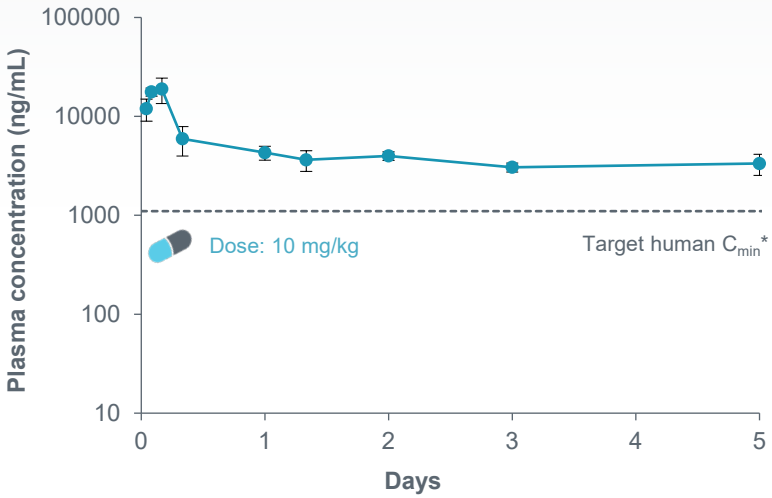
5366 is 4x more potent than pritelivir and 400x more potent than acyclovir in vitro

PTV, pritelivir; ACV, acyclovir.

1. Contreras et al. 2023. IHW

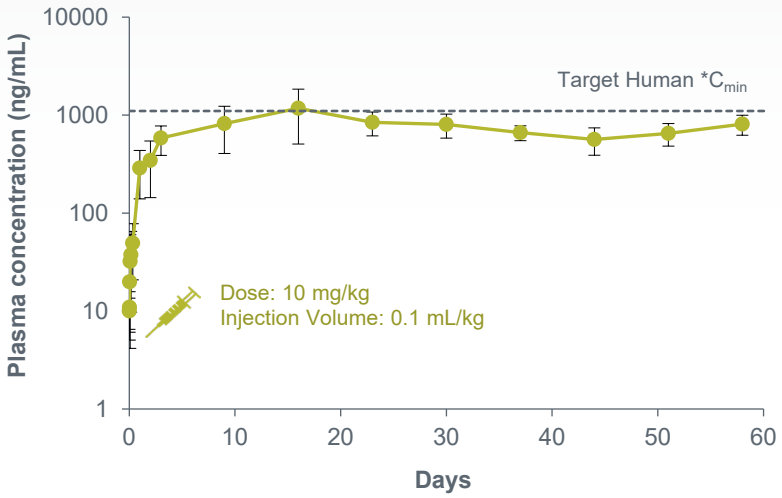
ABI-5366 in preclinical PK studies demonstrates potential for long acting oral and injectable administration

SINGLE ORAL DOSE PK



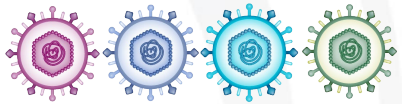
Oral formulation achieved target exposure quickly and maintained for extended time post dosing; study ongoing

SINGLE SUBCUTANEOUS INJECTION PK[1]



Single low volume SC injection without a loading dose demonstrates extended-release profile

1. Contreras et al. 2023. IHW *Target human plasma concentration derived from pritelivir, adjusted for ABI-5366 protein shift and potency



Oral pan-herpes non-nucleoside polymerase inhibitor (NNPI) for transplant-associated herpesviruses

Multiple herpesviruses can cause significant morbidity and mortality in immunocompromised transplant recipients

60,000 patients affected[1]

Among transplant patients:
~60% are CMV positive
~60% are HSV positive
~80% are VZV positive

- Lifelong latent infections; frequently reactivate during immunosuppression
- Uncontrolled viral replication and severe disease during reactivation
- Risk of graft loss
- Risk of death

Patel and Paya. Clin. Microbiol. Rev. 1997; Breuer, *et al.* Mol. Diagn. Ther. 2012; Clark, *et al.* Semin. Respir. Crit. Car Med. 2013; Haidar and Singh. Curr. Opin. Infect. Dis. 2019; Beyar-Katz *et al.* Clin. Microbiol. Infect. 2020; Kwon et al. Transp. Infect. Dis. 2021; Wutzler et al. Vaccine 2001; Bauer et al. BMC Infect. Dis. 2010; Reynolds et al. Public Health Rep. 2010; Lanzieri et al. Int. J. Gynaecol. Obstet. 2016; Lachmann et al. PLoS One 2018; Patton et al.Clin. Infect. Dis. 2018; Ayoub et al. BMC Med. 2019; Zuhair et al. Rev. Med. Virol. 2019; Zhang et al. Virol. J. 2022

1. EBMT, OPTN, UNOS, and IRODAT (estimate for transplanted-associated herpesvirus reflects US and EU only).

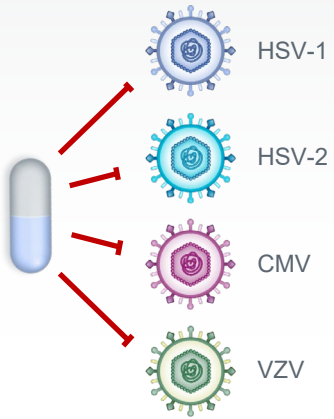
Assembly Bio's oral pan-herpes polymerase inhibitor program is designed to provide significant innovation over current standard of care

Multiple herpes viruses can cause significant morbidity and mortality in immunocompromised patients

Current antivirals are not broad spectrum and have tolerability and drug interaction limitations in immunosuppressed patients

An oral pan-herpesvirus inhibitor meeting our target profile would be a significant advance over currently used therapies

- Potential to greatly simplify treatment (1 agent to control 4 viruses)
- Potential to improve tolerability and eliminate drug-drug interactions



Three series of potent, broad-spectrum herpes virus inhibitors identified; aim to advance compounds into preclinical safety testing in 2H 2023

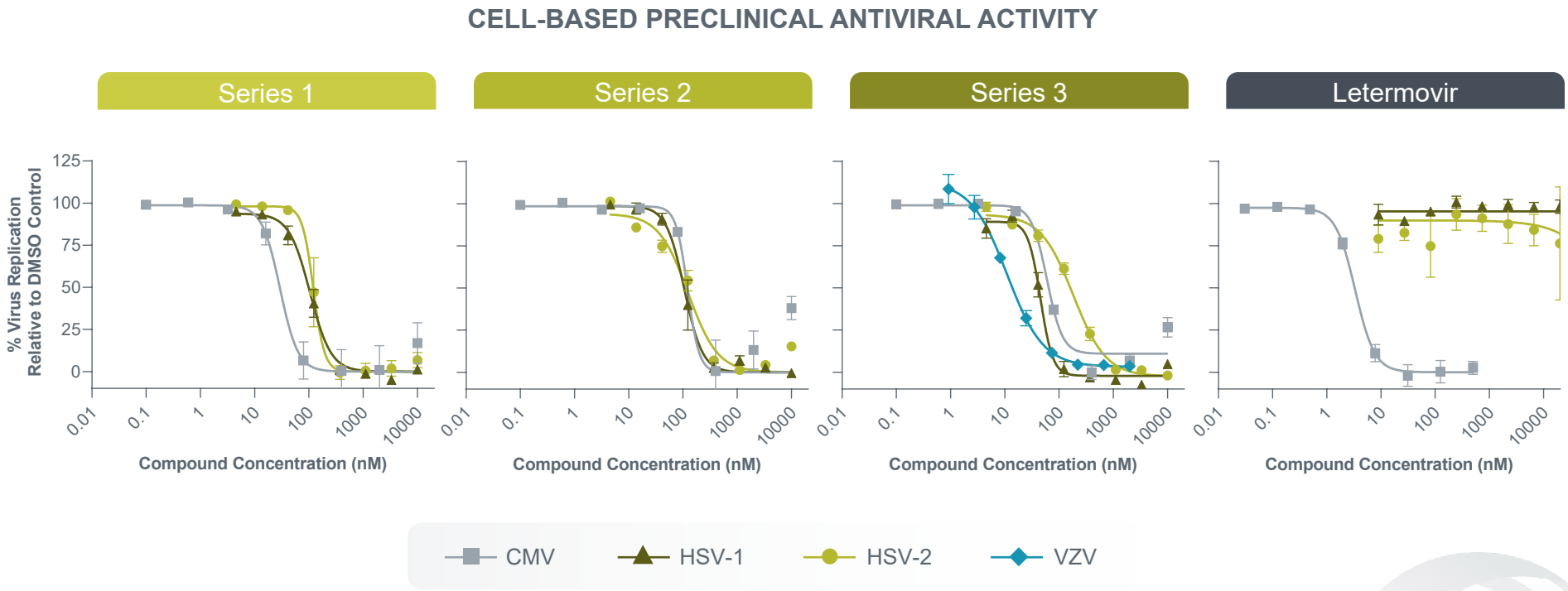
Approved antivirals are not broad spectrum and have tolerability and drug interaction limitations in immunosuppressed patients

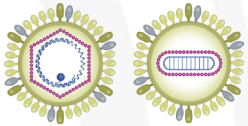
TARGET	DRUG	Approved for Use		
		CMV	HSV-1/-2	VZV
Polymerase	Acyclovir Famciclovir	✗	✓	✓
	Foscarnet*, **	✓	✓	✗
	Ganciclovir*, ** Cidofovir*, **	✓	✗	✗
Viral Kinase	Maribavir	✓	✗	✗
Terminase	Letermovir*			

*Drug-drug interactions **Black box warning

An oral pan-herpes antiviral could greatly simplify treatment.

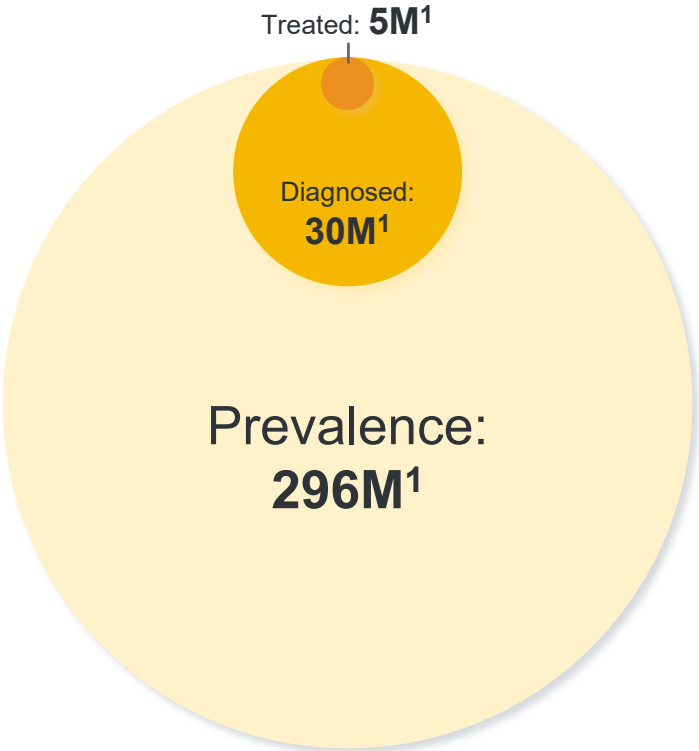
Novel, potent, broad-spectrum herpesvirus polymerase inhibitors have been identified





Oral entry inhibitor for hepatitis B and D

Hepatitis B is a major global public health problem

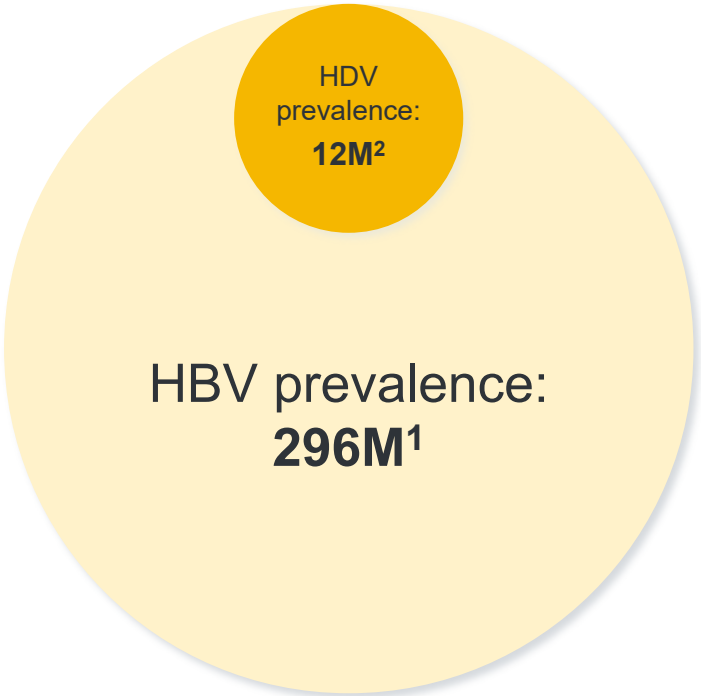


- Up to 1M people/year die from HBV-related causes
- Treatments are life-long and reduce but do not eliminate the virus, resulting in very low cure rates
- No new MOAs approved for HBV in >25 years
- Opportunity to improve outcomes and increase number of patients diagnosed and treated with development of finite and curative therapies

MOA, mechanism of action.

1. WHO (2021).

Hepatitis D impacts a subset of hepatitis B patients and increases disease burden



HDV infection occurs only with HBV infection; envelope with HBsAg shared by both viruses

HDV causes 18% of cirrhosis and 20% of hepatocellular carcinoma associated with HBV[2]

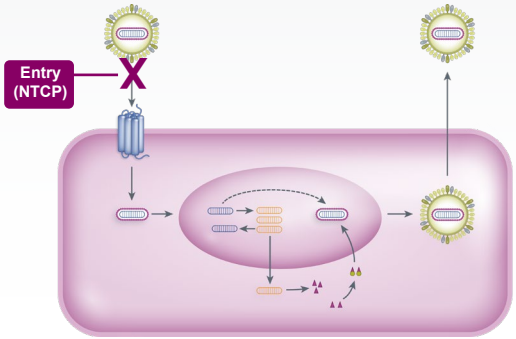
Very limited treatment options: Only 1 approved drug for HDV in Europe*

*Bulevirtide received conditional approval from EMA in 2020.

1. Prevalence of HBV 296M per WHO (2021); 2. Stockdale, J Hep 2020.

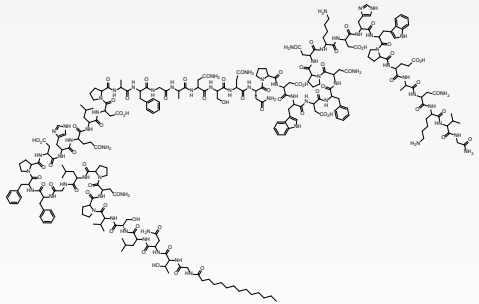
A potent, once-daily, oral pan-genotypic HBV/HDV entry inhibitor could provide significant innovation over current standard of care

- Viral entry is a validated antiviral target for intervention in the HDV replication cycle
- Multiple chemically differentiated leads with single digit nanomolar potency
- Potential to be used for antiviral intensification for HBV as well as to treat HDV



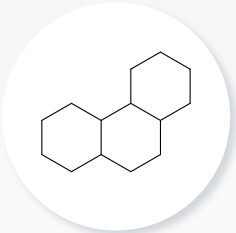
Development candidate nomination expected in 2023

Opportunity to disrupt HBV and HDV replication via viral entry inhibition while addressing disadvantages of current standard of care



BULEVIRTIDE HAS SHOWN SAFETY AND EFFICACY IN CLINICAL TRIALS BUT:

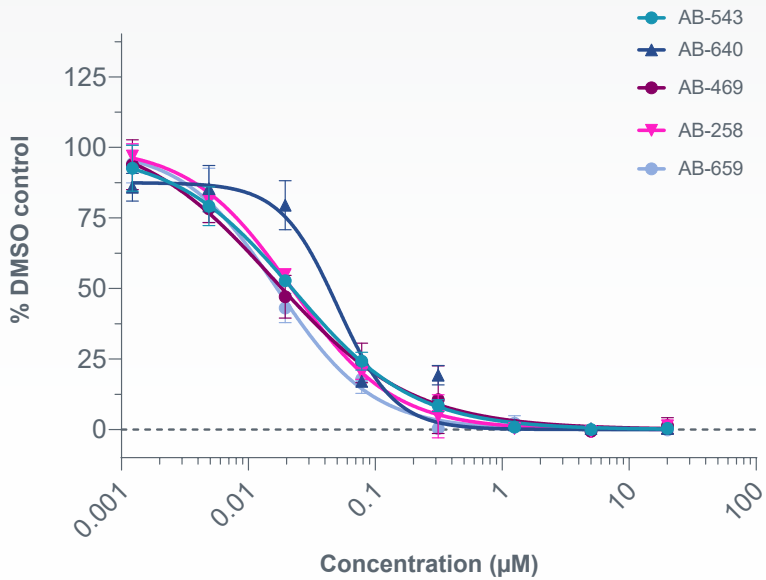
- Is a very large, complex molecule
- Requires daily injections

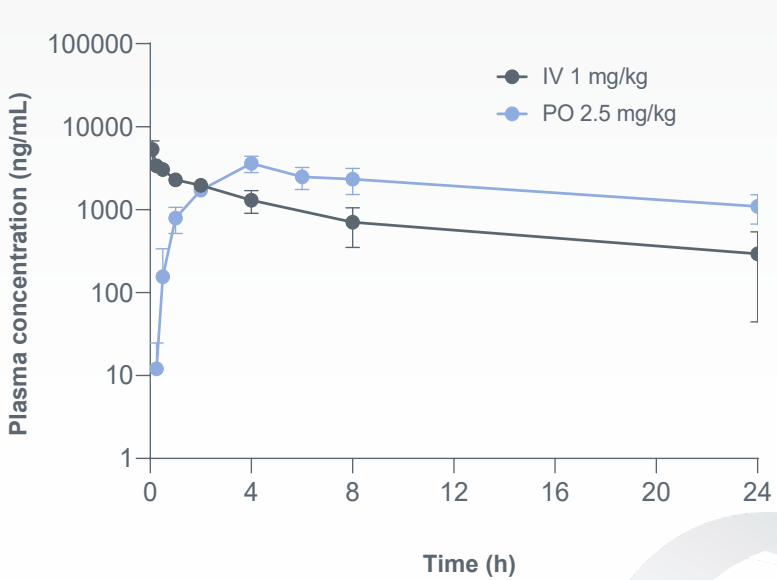


OPPORTUNITY TO DEVELOP A SAFE AND EFFECTIVE ORAL SMALL MOLECULE

- Improved convenience
- Potential for enhanced treatment uptake and diagnosis rates

Novel HBV/HDV entry inhibitors have desirable potency and oral PK profiles

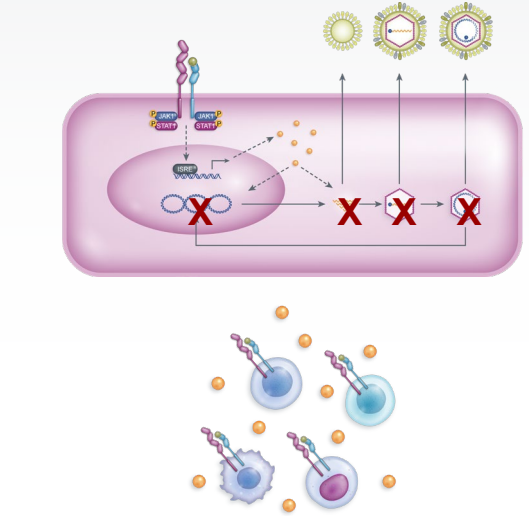




Oral, liver-focused IFNAR agonist for hepatitis B

A small-molecule liver-focused IFNAR agonist could provide significant innovation over current standard of care

- IFN-α is an approved drug for HBV associated with functional cure in some patients, but tolerability profile has significantly limited its use
- Agonists identified which closely mimic IFN-α by activating IFN signaling via the JAK–STAT pathway, leading to ISG induction *in vitro* and *in vivo*
- Targeting selective activation of the IFN-α pathway in the liver vs systemically to improve tolerability; PK data indicate desirable liver exposure and oral absorption

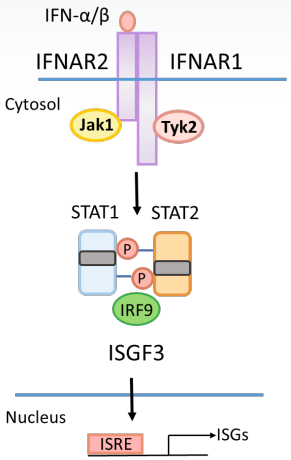


Lead optimization of multiple IFN-α receptor agonists in progress; aiming to advance compounds into preclinical safety assessments in 2023

Small molecule IFNAR agonist mimics biologic IFN-α *in vitro* and *in vivo*

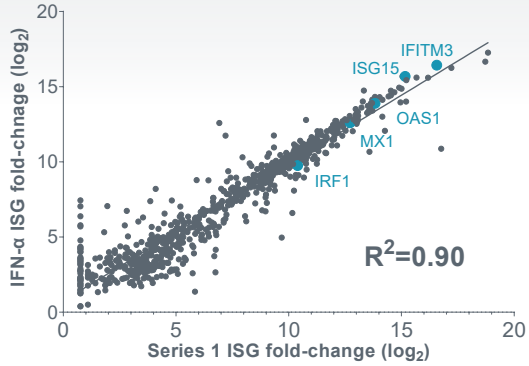
INTERFERON-α SIGNALING PATHWAY

Signaling through JAK/STAT; ISG induction

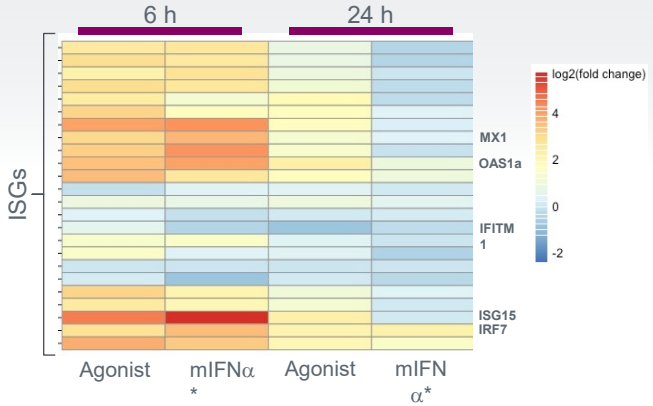


IN VITRO CORRELATION OF ISG EXPRESSION SMALL MOLECULE AGONIST VS IFN-α

IFNα vs Series 1 ISG

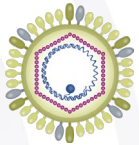


IN VIVO ISG EXPRESSION SMALL MOLECULE AGONIST & IFN-α



*Murine Interferon alpha (mIFNa)

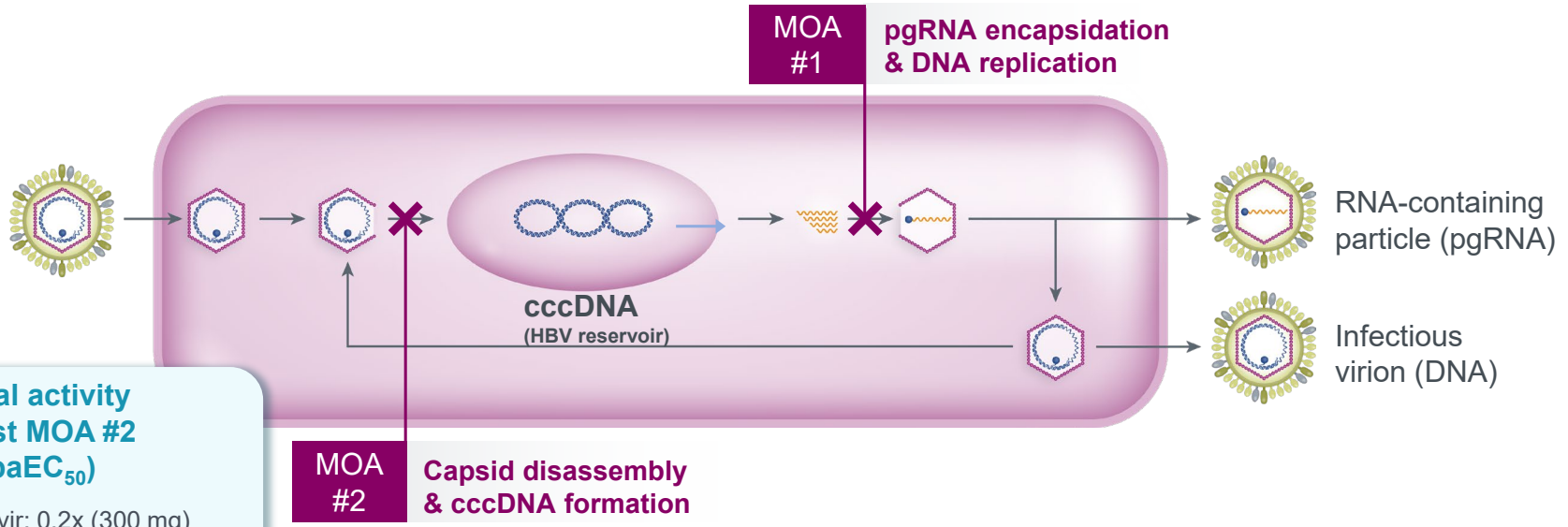
ISG, Interferon Stimulated Gene.



ABI-H3733 and ABI-4334: Potent clinical-stage core inhibitors (CIs) for hepatitis B

Under partnering evaluation

Next-generation CIs are differentiated from first-generation CIs by significantly greater activity against both MOAs including against cccDNA formation



Clinical activity against MOA #2 (C_{min}/$paEC_{50}$)

Vebicorvir: 0.2x (300 mg)
ABI-H3733: >10x* (200 mg)
ABI-4334: >30x* (200 mg)
50-150 x 1st gen activity

cccDNA, covalently closed circular DNA; $paEC_{50}$, protein-adjusted concentration of a drug that gives half-maximal response; pgRNA, pregenomic RNA.

*Projected from PK data. Comparison between projected 200 mg doses provided for illustrative purposes; doses have not been selected for ABI-H3733 or ABI-4334; ABI-H3733 Phase 1b study did not dose up to 200mg.

ABI-H3733 and ABI-4334 are highly potent clinical-stage core inhibitors in evaluation for partnering

	ABI-H3733 (PHASE 1b COMPLETE)	ABI-4334 (PHASE 1a COMPLETE)
STATUS	Completed 28-day Phase 1b (predominantly HBeAg-negative patients)	Completed Phase 1a in healthy volunteers (single-dose cohorts 30–400 mg; 100 and 200 mg multiple-dose cohorts and food effect cohort at 200 mg)
EFFICACY	All HBeAg-negative patients in 100 mg cohort reached <LLOQ within 21 days, with 57% (4/7) target not detected	Not yet available
PROJECTED $C_{min}/paEC_{50}$ VS. MOA#2*	>10 fold	>30 fold
SAFETY	• No SAEs or patterns of AEs or lab abnormalities • Chronic tox finding in one species; would likely require additional nonclinical studies to move into longer-term dosing	• TEAEs and lab abnormalities all mild to moderate; majority mild • No patterns of AEs or lab abnormalities; no SAEs or clinically significant ECG abnormalities
PK	Exposure supports QD dosing	Exposure supports QD dosing

Evaluating partnering options prior to further clinical development.

cccDNA, covalently closed circular DNA; LLOQ – lower limit of quantification; $paEC_{50}$, protein-adjusted concentration of a drug that gives half-maximal response.

*Projected from PK data for 200 mg doses. Comparison between projected 200 mg doses provided for illustrative purposes; doses have not been selected for ABI-H3733 or ABI-4334; ABI-H3733 Phase 1b study did not dose up to 200mg.

Key objectives and anticipated progress

2023

- [x] ABI-5366: Nomination of development candidate for HSV-2 program
- [x] Reported interim data for ABI-H3733 and ABI-4334
- [x] Announced evaluation of partnering options for core inhibitors and prioritization of expanded virology portfolio
- [ ] HBV/HDV entry inhibitor: Development candidate nomination

2024

- [ ] ABI-5366: Initiation of clinical studies 1H 2024
- [ ] ABI-5366: Report initial clinical data by the end of 2024
- [ ] HBV/HDV entry inhibitor: Initiation of clinical studies by the end of 2024

Nasdaq: ASMB