# ABI-5366 and ABI-1179, Two Potent, Long-Acting Helicase Primase Inhibitors for the Treatment of Recurrent Genital Herpes

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**49th International Herpesvirus Workshop, Berlin, Germany; July 26–30, 2025**

# Presenter Disclosures

- William Delaney is an employee and stockholder of Assembly Biosciences, Inc.

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# Genital herpes remains a serious condition that impacts millions

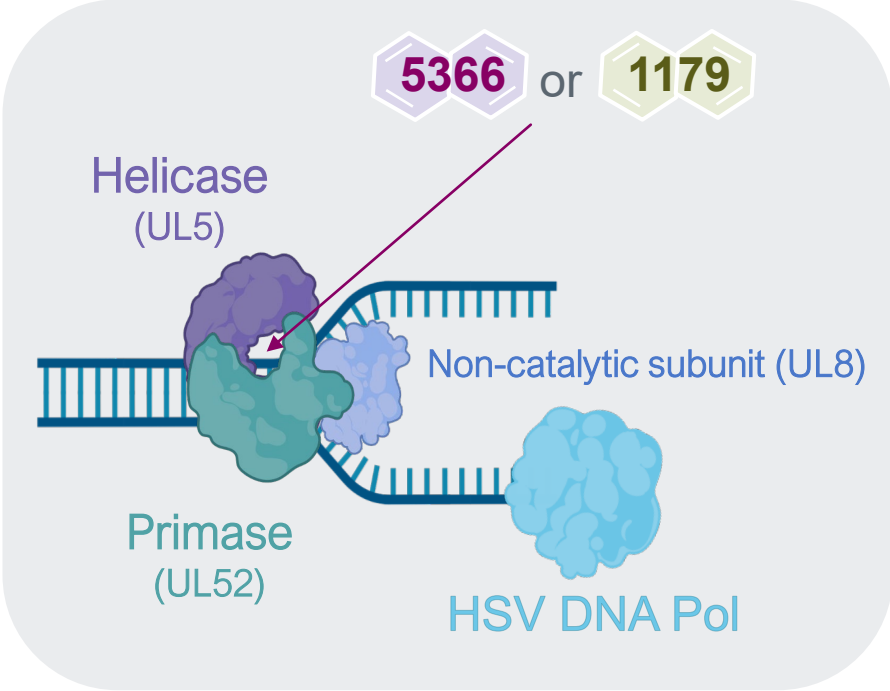
- Estimated 500 million people worldwide age 15 - 49 living with HSV-2
- >4 million have 3+ recurrences/year
- RGH → painful physical symptoms; significant psychosocial impact
- Nucleoside analogs partially effective; significant room for improvement

Goal: Develop a more effective, long-acting therapy for RGH

5366 and 1179: two novel, structurally-distinct HSV helicase primase inhibitors

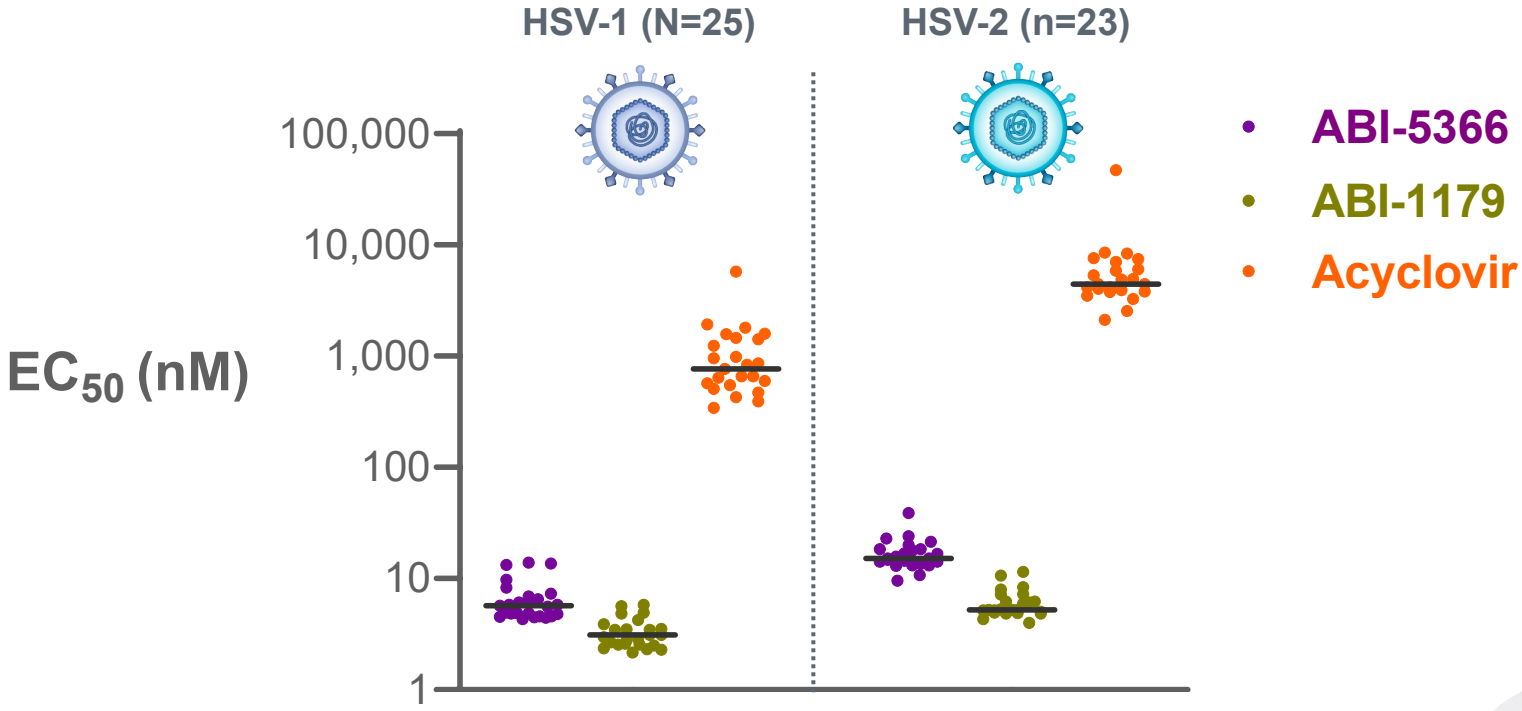

# HSV helicase primase is an attractive drug target

- Essential enzyme for HSV replication
- Amenable to design of inhibitors
- Potential for high selectivity
  - low homology to human enzymes
  - strong safety data in humans (amenamevir)[1]
- Clinically validated efficacy
  - pritelivir: greater reductions in shedding, less days with lesions vs. valacyclovir in clinical studies[2]



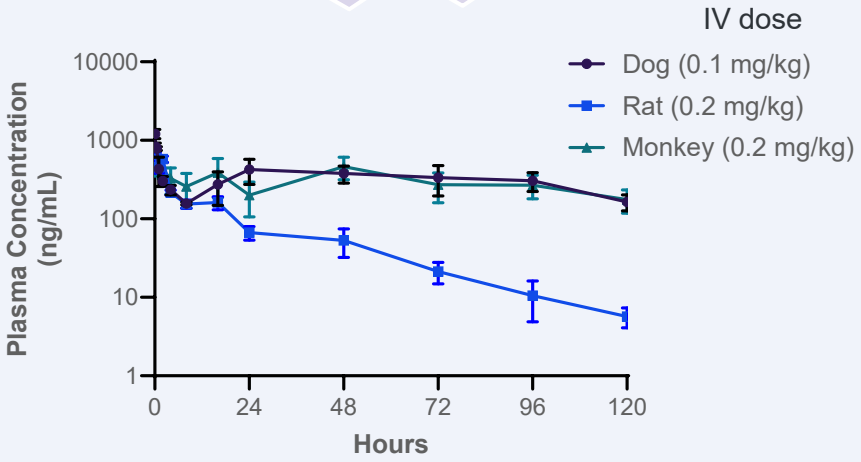

1. Shiraki et al. Viruses 2021; 2. Wald, et al. JAMA 2016

# ABI-5366 and ABI-1179: potent and broad in vitro activity against HSV-1/2

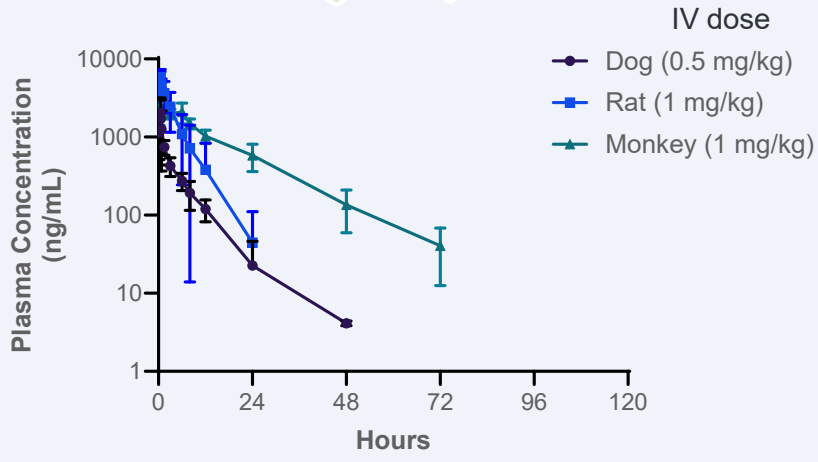


# ABI-5366 and ABI-1179 preclinical PK profiles predict long human $T_{½}$

## 5366



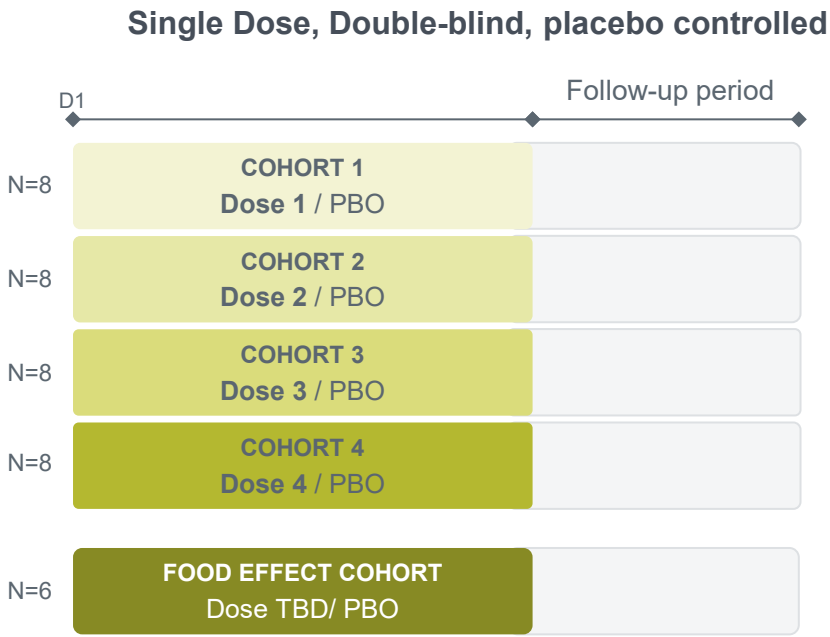

## 1179



# ABI-5366 and ABI-1179 have favorable preclinical safety profiles

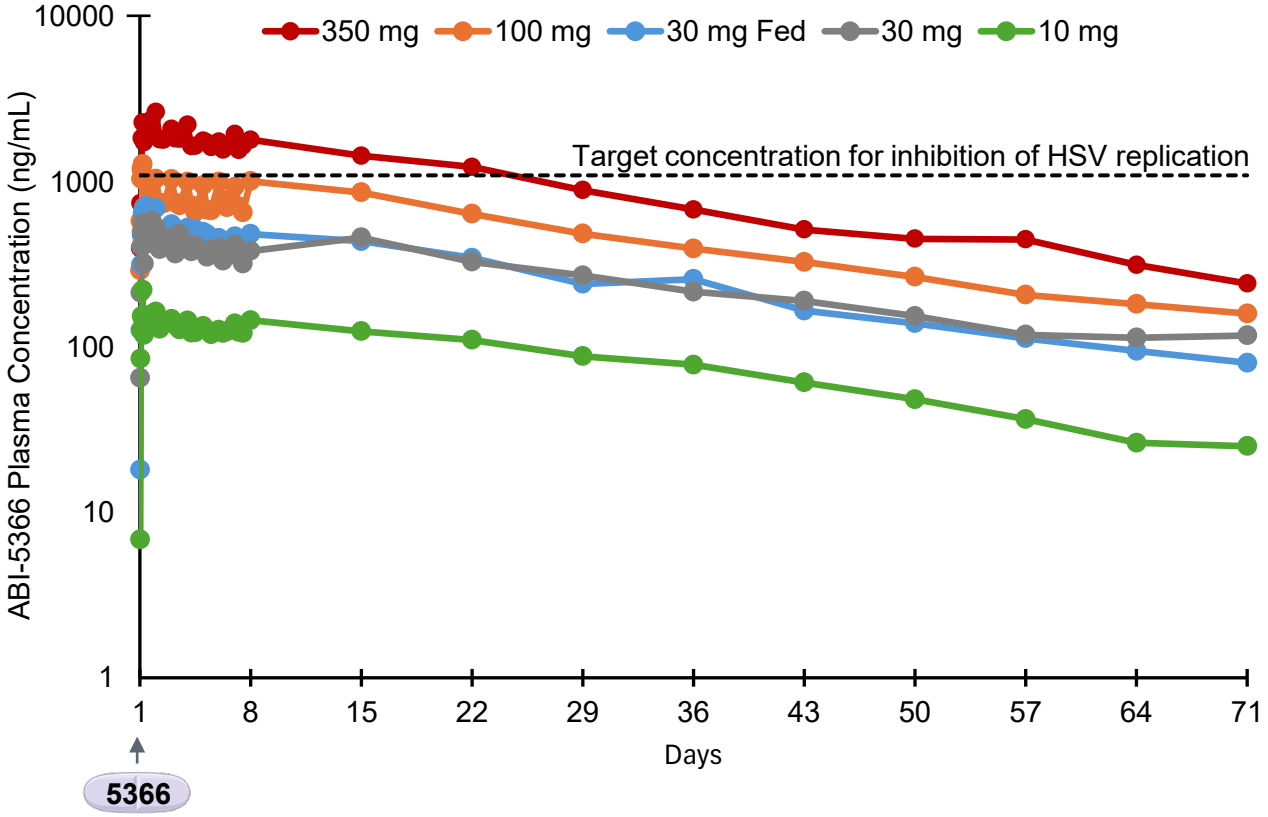
- Low potential for cytotoxicity, genotoxicity, and mitochondrial toxicity
- No significant inhibition of carbonic anhydrases
- No significant inhibition in broad panel of human receptors
- No findings in preclinical respiratory or cardiac studies
- Favorable safety profiles in 28-day oral toxicity studies
  - high safety margins relative to predicted human dose

# ABI-5366 & ABI-1179 Phase 1a study design

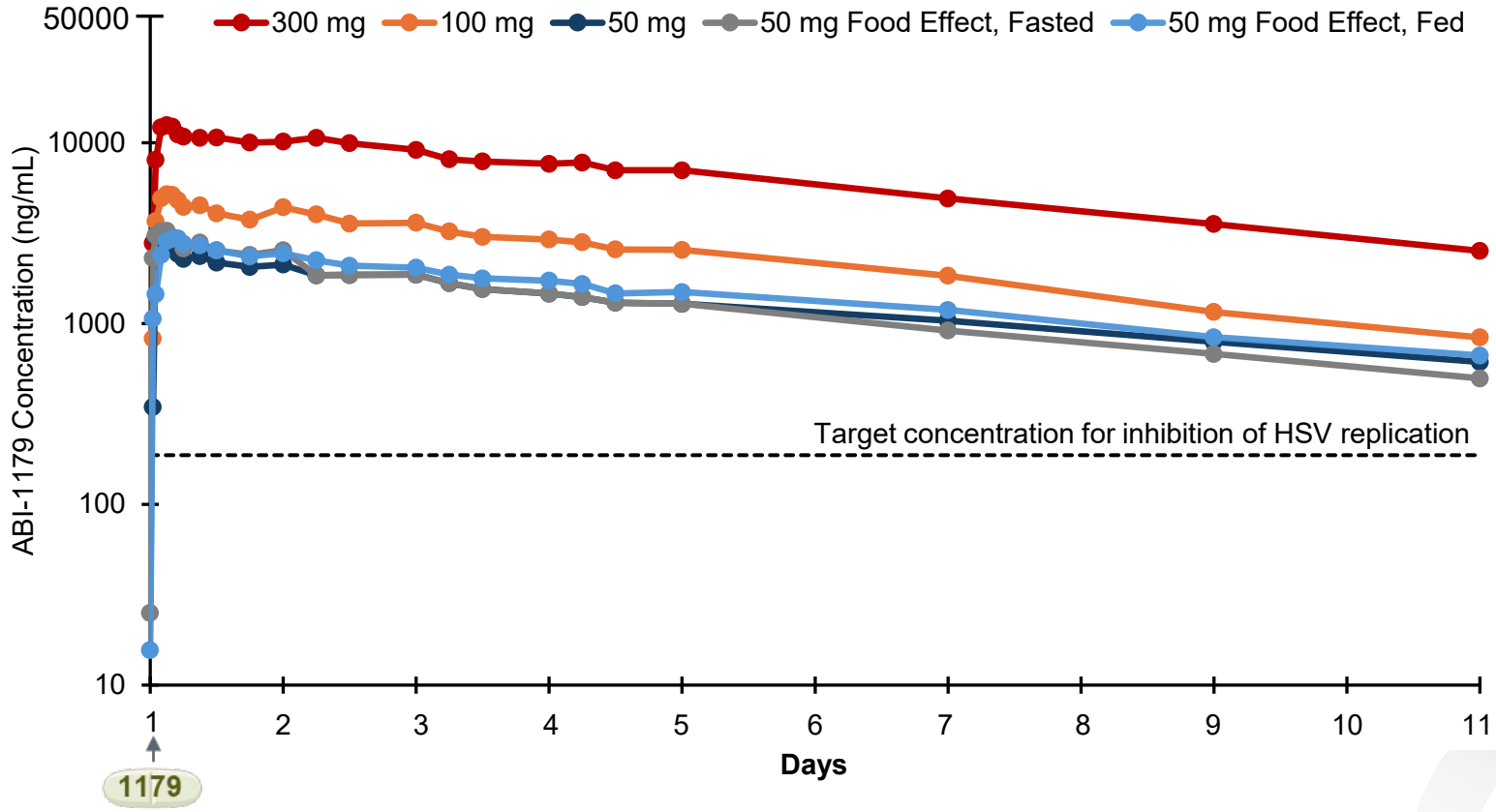



- Key parameters measured:
  - Safety: ECG, physical examination, AE, & lab abnormalities
  - PK: $T_{1/2}$ and $C_{min}$
- Enrolled in New Zealand

# ABI-5366 single dose PK achieves projected therapeutic levels with 20 day $T_{½}$



# ABI-1179 single dose PK achieves projected therapeutic levels with 4 day $T_{½}$

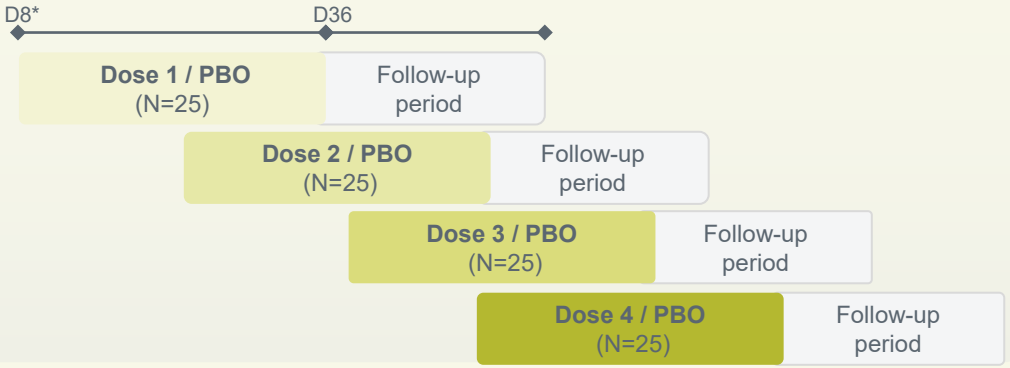


# ABI-5366 & ABI-1179 had favorable safety profiles in Phase 1a

| | ABI-5366 | ABI-1179 |
|---|---|---|
| Dose range tested (mg) | 10, 30, 100, 350 mg | 50, 100, 300 mg |
| Participants (n) | 38 | 30 |
| Follow up (days) | between 70-98 days | up to 10 days |
| Safety summary | • No grade 3 or 4 and no serious adverse events<br>• No significant treatment-related lab abnormalities noted<br>• No study discontinuations | • No grade 3 or 4 and no serious adverse events<br>• No significant treatment-related lab abnormalities noted<br>  • One self-limited grade 2 ALT observed at the highest dose (300 mg), and one self-limited grade 3 lipase elevation observed in the fed state cohort (50 mg)<br>• No study discontinuations |

# ABI-5366-101 and ABI-1179-101 Phase 1b study design

Double-blind, sequential cohorts
Participants positive for HSV-2 w/ recurrent genital herpes




## Key efficacy assessments

**Anogenital swabs (Day 8-36)**

- e.g., viral shedding rate

**Daily diary of symptoms**

- e.g., days with lesions

**INTERIM PHASE 1B DATA** from both studies expected in fall 2025

* Dosing begins on Day 1 with swab and diary evaluations beginning on Day 8

# Conclusions

- ABI-5366 & ABI-1179: novel inhibitors of HSV helicase-primase
  - low nM potency against HSV
  - preclinical PK predicted long human $T_{½}$
  - favorable preclinical safety
- Phase 1a demonstrated favorable safety and PK
  - ABI-5366: 20 day $T_{½}$
  - ABI-1179: 4 day $T_{½}$

→ Supports potential for long-acting oral administration

Phase 1b ongoing in recurrent genital herpes patients for both molecules
Data expected in Fall 2025