Safety, Pharmacokinetics and Antiviral Activity of ABI-5366, a Novel, Oral, Long-Acting HSV Helicase-Primase Inhibitor in Subjects with Recurrent Genital Herpes: Interim Analysis from a Phase 1b Study

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Disclosures

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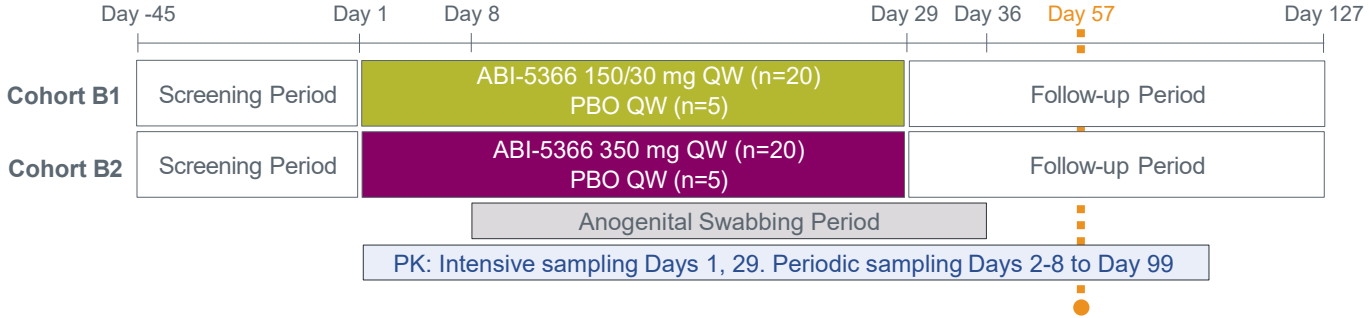
Introduction

- Approximately 520 million people aged 15-49 years worldwide are infected with herpes simplex virus type 2 (HSV-2), the primary cause of genital herpes [1,2]
- Nucleoside analogue therapy requires daily administration and is suboptimal for suppression of viral transmission and disease recurrence[3,4]
- There is an unmet medical need for longer acting novel therapeutic agents that are safe, provide improved efficacy and are conveniently administered
- ABI-5366 (5366) is a novel, orally administered, long-acting inhibitor of the HSV helicase-primase enzyme complex in development for suppression of recurrent genital herpes (RGH)
- Here we report interim results following weekly, oral doses of ABI-5366 in subjects seropositive for HSV-2 with RGH from an ongoing randomized, blinded, Phase 1b study (NCT06385327)

[1]World Health Organization Herpes Simplex Virus Factsheet 30 May 2025; [2]Gupta R, et al. Lancet, 2007:370(9605):2127-37; [3]Valtrex(valacyclovir). US package insert. GSK; revised 2022; [4]Birkmann A and Zimmermann H. Curr Opin Virol, 2016;18:9-13

Methods
Study Design

- ABI-5366-101 is a randomized, observer-blinded, placebo-controlled, Phase 1b viral shedding study
- Up to 4 sequential cohorts to be enrolled evaluating multiple-dose regimens of 5366 or PBO
  - Each cohort to enroll 25 participants, (20 5366, 5 PBO); 29 Days of treatment, with 98 Days of follow-up
  - Twice daily anogenital swabs collected from Days 8-36 for HSV-2 DNA quantification
- Safety assessments included physical exams, adverse events and lab parameters



- **Primary endpoints** were safety and tolerability
- **Secondary endpoints** included HSV-2 DNA shedding rates and genital lesion rates

- Two cohorts completed through at least Day 57 as of the data cut-off of 29 July 2025:
  - B1 (150/30 mg QW): Loading dose of 150 mg on Day 1, and 30 mg QW on Days 8, 15, 22, 29
  - B2 (350 mg QW): 350 mg on Days 1, 8, 15, 22, 29
- As follow-up is ongoing, combined 5366/PBO safety data are presented by cohort to retain study blinding

Results

Baseline Demographic and Disease Characteristics

Characteristics	Placebo QW (n=10)	ABI-5366 150/30 mg QW (n=20)	ABI-5366 350 mg QW (n=20)
Age, years; mean (SD)	43.1 (6.9)	39.3 (8.8)	41.7 (10.0)
Sex at birth, n (%)			
Male	5 (50.0)	10 (50.0)	13 (65.0)
Female	5 (50.0)	10 (50.0)	7 (35.0)
White Race; n (%)[a]	9 (90.0)	15 (75.0)	16 (80.0)
BMI, kg/m^2; mean (SD)	23.8 (2.5)	26.7 (3.1)	27.3 (3.2)
Years since genital herpes diagnosis; mean (SD)	10.7 (6.8)	11.4 (8.2)	12.7 (11.4)
Number genital herpes lesion occurrences in past 12 months or prior to suppressive therapy; mean (SD)	**5.9 (1.7)**	**5.9 (1.6)**	**5.6 (1.5)**
HSV Type; n (%)			
HSV-2 Only	6 (60.0)	10 (50.0)	9 (45.0)
HSV-1 and HSV-2	4 (40.0)	10 (50.0)	11 (55.0)
Suppressive Treatment at Screening; n (%)	**5 (50.0)**	**12 (60.0)**	**10 (50.0)**

Data shown are n (%) unless otherwise indicated.
[a]As the study is ongoing, to maintain study blinding, only the 'Race' category with the predominant number of participants is listed.

BMI, body mass index; HSV-1, herpes simplex virus type 1; HSV-2, herpes simplex virus type 2; QW, once weekly; SD, standard deviation.

Results

Treatment-Emergent Adverse Events and Lab Abnormalities

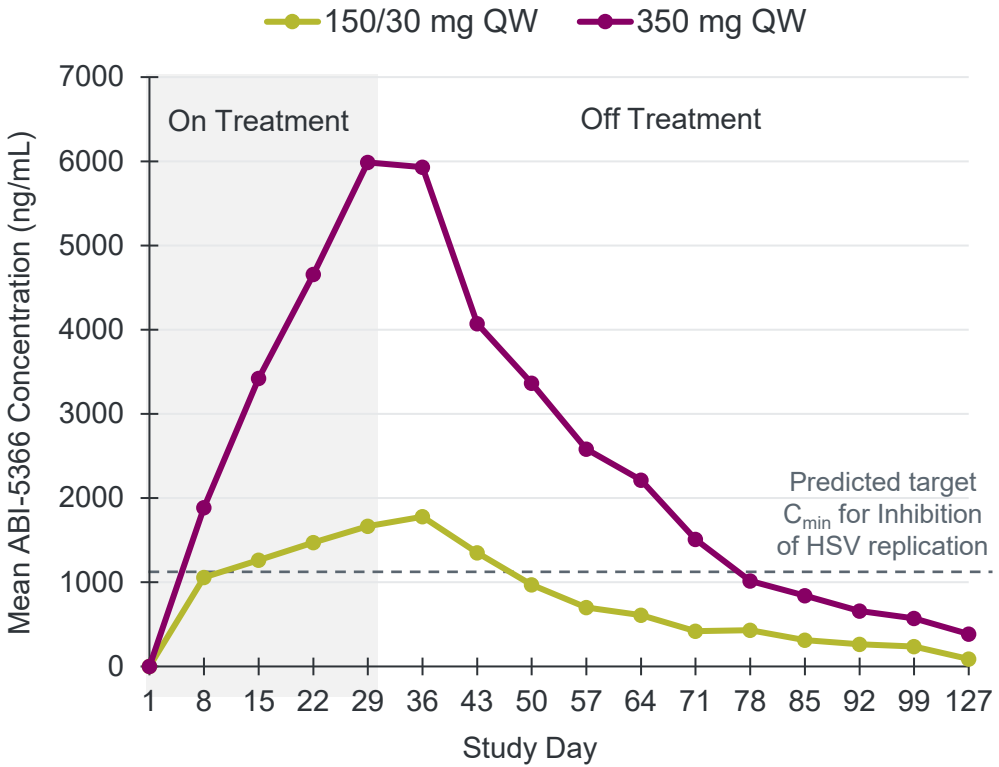
	ABI-5366 150/30 mg QW/PBO QW (n=25)	ABI-5366 350 mg QW/PBO QW (n=25)
Participants with any TEAE, n (%)	23 (92.0)	22 (88.0)
Subjects with any TEAE by grade, n (%)		
Grade 1	21 (84.0)	19 (76.0)
Grade 2	7 (28.0)	10 (40.0)
Grade 3	0	1 (4.0)
Grade 4	0	0
TEAE Related to ABI-5366 or PBO, n (%)	7 (28.0)	6 (24.0)
TEAE Leading to Study Drug Discontinuation, n (%)	0	0
TESAE	0	0
TE Lab Abnormalities, n (%)	18 (72.0)	18 (72.0)
Grade 1	14 (56.0)	15 (60.0)
Grade 2	6 (24.0)	5 (20.0)
Grade 3	1 (4.0)	2 (8.0)
Grade 4	0	0

- TEAEs reported ≥5% overall were URTI, headache, backpain, diarrhea and ligament sprain

PBO, placebo; QW, once weekly; TE, treatment emergent; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; URTI, upper respiratory tract infection

Results

Mean Plasma Pharmacokinetic Profile and Parameters



PK Parameters After Last Dose (Day 29)	ABI-5366 150/30 mg QW (n=20)	ABI-5366 350 mg QW (n=20)
T_{max}, hours, median	4.0	3.0
$t_{1/2}$, hours	501.1 (17.5)	443.7 (34.9)
C_{max}, ng/mL	2564 (35.3)	8991 (36.1)
C_{168h}, ng/mL	1778 (43.1)	5431 (51.5)
AUC_{tau}, h·ng/mL	272,200 (33.1)	965,600 (36.2)

All values are mean (CV%) unless otherwise stated

- ABI-5366 was rapidly absorbed with median T_{max} of 3 to 4 hours
- ABI-5366 exposures increased in a less than dose proportional manner between 150/30 mg QW and 350 mg QW
- ABI-5366 350 mg QW C_{min} is in multi-fold excess of the predicted target concentration for inhibition of HSV replication

AUC_{tau}, area under the curve from Day 29 to Day 36; C168h, concentration at 168 hours (Day 36) postdose; C_{max}, maximum concentration; CV, coefficient of variation; $t_{1/2}$; terminal half-life; T_{max}, time to reach C_{max}

Results
Viral Shedding and Genital Lesions

Outcome Measured	Placebo QW (n=10)	ABI-5366 150/30 mg QW (n=20)	ABI-5366 350 mg QW (n=20)
HSV-2 Shedding Rate,[a] %	14.6	14.5	0.9
High Viral Load Shedding Rate,[b] %	11.4	9.4	0.2
Genital Lesion Rate,[c] %	19.7	11.8	1.3
Duration of Viral Shedding; mean (SD) days	5.8 (4.1)	3.6 (2.7)	1.8 (0.8)
Duration of Genital Lesions; mean (SD) days	6.3 (4.3)	5.7 (4.3)	1.8 (1.0)

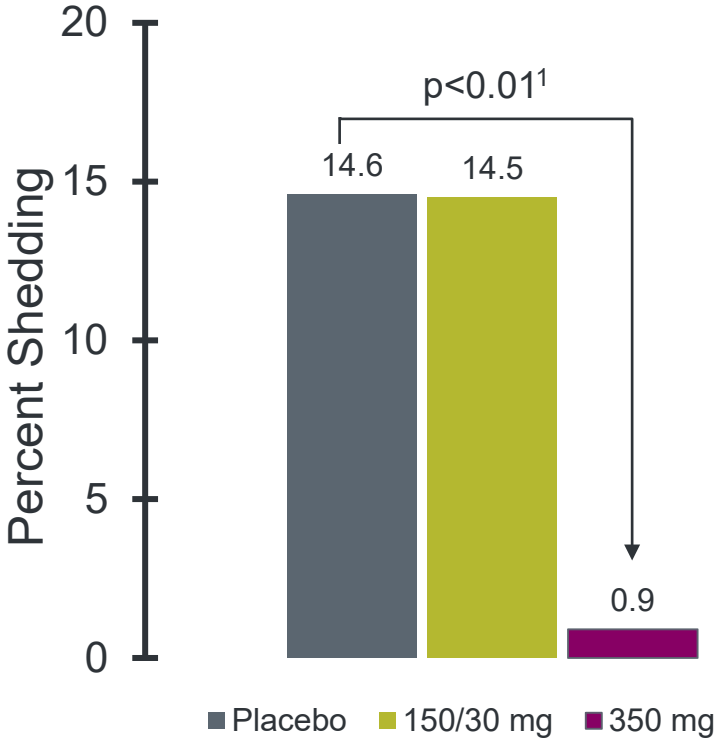
High viral load is defined as >10^4 HSV DNA copies/mL. All outcomes measured over the evaluation period.

Rate of Reduction for each outcome for 350 mg QW versus Placebo QW	Rate of Reduction	p-value[d]
Reduction in HSV-2 Shedding Rate %	94	p<0.01
Reduction in High Viral Load Shedding Rate %	98	p<0.05
Reduction in Genital Lesion Rate %	94	p<0.01

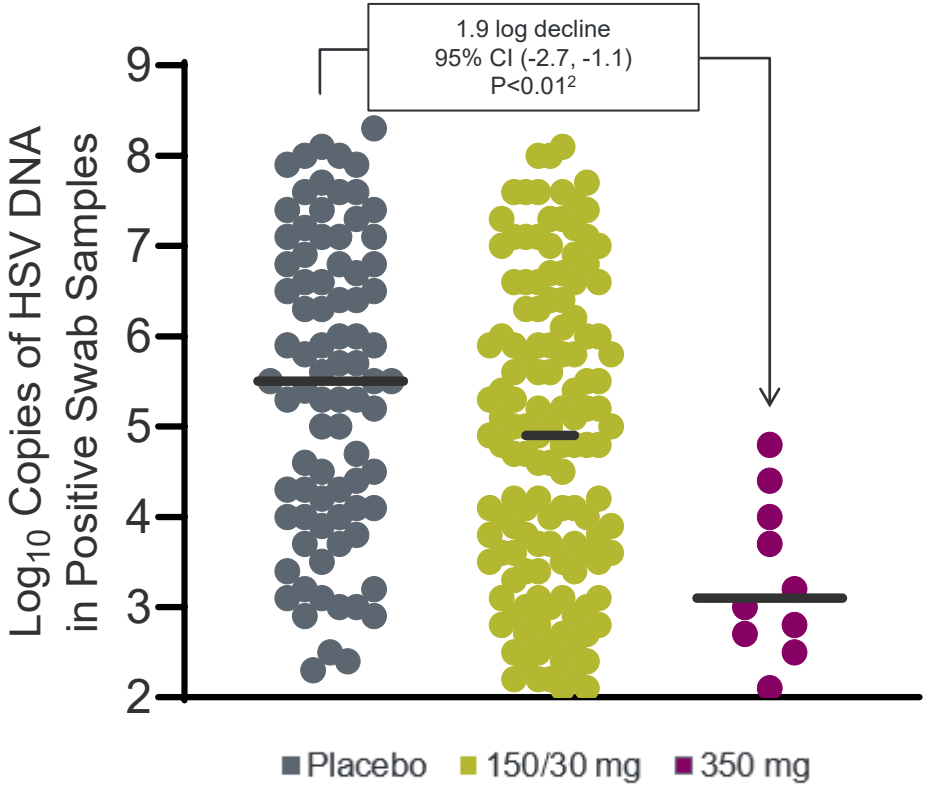
[a]HSV-2 shedding rate calculated as the number of positive HSV-2 anogenital swabs/the total number of swabs collected.
[b]High viral load shedding rate calculated as the number of positive HSV-2 anogenital swabs with HSV-2 >10^4 copies/mL/the total number of swabs collected.
[c]Genital lesion rate calculated as the number of days with genital lesions present/the total number of days assessed.
[d]Statistical analysis conducted using Poisson regression models and the corresponding p-values estimated accordingly.
HSV-2, herpes simplex virus type 2; QW, once weekly; SD, standard deviation.

Results

Reductions in HSV-2 Shedding and Viral Load in HSV-2 Positive Swabs



[1]Poisson regression analysis



[2]Analysis by generalized estimating equations

Conclusions

- Treatment regimens were safe and well tolerated when administered orally as 150/30 mg/PBO QW and 350 mg/PBO QW for 29 days
- The observed PK profile continues to support once-weekly dosing and the potential for once-monthly oral dosing regimens
- Highly potent antiviral activity was observed:
  - 94% reduction on HSV-2 shedding rate for 350 mg QW compared to placebo ($p<0.01$)
  - 98% reduction on the rate of samples with high viral load (i.e., $>10^4$ copies/mL HSV-2 DNA) for 350 mg QW compared to placebo ($p<0.05$)
  - 94% reduction in genital lesion rate for 350 mg QW compared to placebo ($p<0.01$)
  - Dose dependent reductions in both the duration of viral shedding and the duration of genital lesions were observed
- ABI-5366 has the potential to advance the management of patients with Recurrent Genital Herpes
- Planning for a longer-duration Phase 2 study is underway, which is expected to initiate in mid-2026

Acknowledgments

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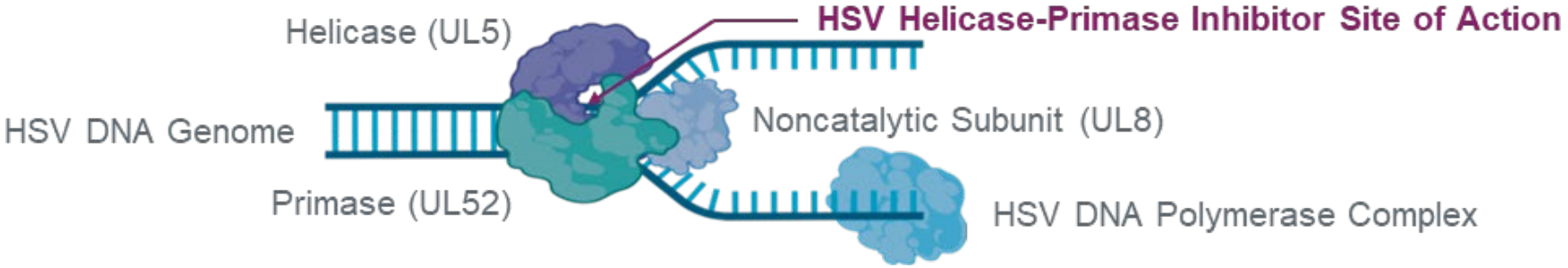
    - **Karen Kaluhin** (Canopy Clinical Sutherland, Miranda, NSW, Australia)
    - **Deon Smith** (Canopy Beaches Clinical Research, Brookvale, NSW, Australia)
    - **Joseph Sasadeusz (**Royal Melbourne Hospital, Parkville, VIC, Australia)
    - **Mark Bloch** (Momentum Clinical Research - Darlinghurst, Sydney, NSW, Australia and Kirby Institute, University of New South Wales, Sydney, Australia
- This study was sponsored by Assembly Biosciences, Inc.

Back-up Slides

Figure 1. The HSV Helicase-Primase Enzyme Complex



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HSV, herpes simplex virus (HSV)

Results

Treatment-Emergent Adverse Events, ≥5% in Either Cohort

	ABI-5366 150/30 mg QW/PBO QW (n=25)	ABI-5366 350 mg QW/PBO QW (n=25)
Subjects with any TEAE, n (%)	23 (92.0%)	22 (88.0%)
Upper Respiratory Tract Infection	9 (36.0%)	11 (44.0%)
Headache	4 (16.0%)	3 (12.0%)
Back Pain	1 (4.0%)	2 (8.0%)
Diarrhoea	0	3 (12.0%)
Ligament Sprain	2 (8.0%)	1 (4.0%)
Viral Upper Respiratory Tract Infection	0	3 (12.0%)
Arthropod Bite	2 (8.0%)	0
Depressed Mood	2 (8.0%)	0
Dermatitis	0	2 (8.0%)
Fatigue	2 (8.0%)	0
Nasal Congestion	2 (8.0%)	0
Nausea	2 (8.0%)	0

Data shown are n (%) unless otherwise indicated.
TEAE, treatment-emergent adverse event;

Results

Laboratory Abnormalities, ≥5% in Either Cohort

Laboratory Abnormalities	ABI-5366 150/30 mg QW/PBO QW (n=25)	ABI-5366 350 mg QW/PBO QW (n=25)
Number of Participants with postbaseline abnormalities	18 (72.0%)	18 (72.0%)
Grade 1	14 (56.0%)	15 (60.0%)
Grade 2	6 (24.0%)	5 (20.0%)
Grade 3	1 (4.0%)	2 (8.0%)
Laboratory abnormality		
Cholesterol (increased)	10 (40.0%)	8 (32.0%)
Grade 1	6 (24.0%)	4 (16.0%)
Grade 2	4 (16.0%)	3 (12.0%)
Grade 3	0	1 (4.0%)
Triglycerides (increased)	5 (20.0%)	2 (8.0%)
Grade 1	3 (12.0%)	1 (4.0%)
Grade 2	2 (8.0%)	1 (4.0%)
Bicarbonate (decreased)	2 (8.0%)	6 (24.0%)
Grade 1	2 (8.0%)	6 (24.0%)
Urate (increased)	1 (4.0%)	2 (8.0%)
Grade 1	1 (4.0%)	2 (8.0%)
Amylase (increased)	0	2 (8.0%)
Grade 1	0	1 (4.0%)
Grade 2	0	1 (4.0%)
Lipase (increased)	0	2 (8.0%)
Grade 1	0	2 (8.0%)
Leukocytes (decreased)	0	2 (8.0%)
Grade 1	0	2 (8.0%)

Data shown are n (%) unless otherwise indicated.