ABI-5366-101: A Phase 1b Study of a Novel, Oral, Long-Acting, Investigational HSV Helicase-Primase Inhibitor in Recurrent Genital Herpes

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Introduction

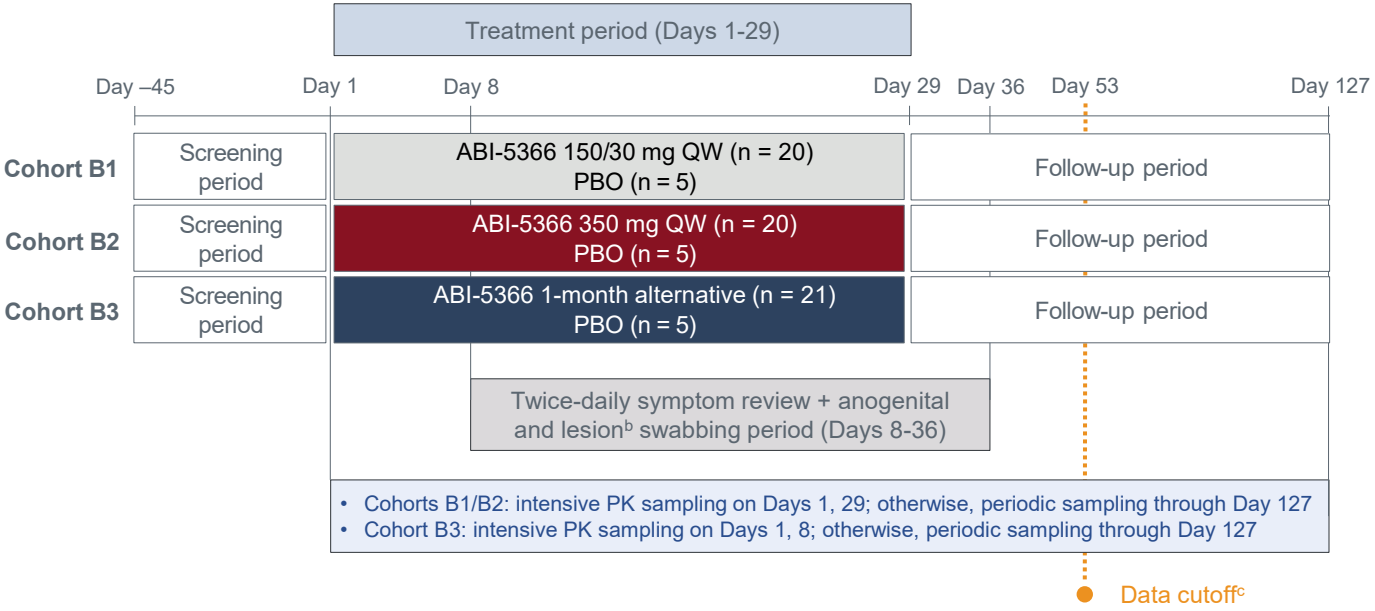
- An estimated ~520 million people between the ages of 15 and 49 years worldwide are infected with HSV-2, the primary cause of RGH[1,2]
- Standard-of-care therapy with nucleoside analogues requires daily administration and is suboptimal for suppression of disease recurrence and viral transmission[3,4]
- There is an unmet medical need for longer-acting novel therapeutic agents that are safe and well tolerated, provide improved efficacy, and are conveniently administered
- ABI-5366 is a novel, orally administered, long-acting inhibitor of the HSV helicase-primase complex in development for suppression of RGH
- Here we report interim results following weekly oral doses of ABI-5366[a] and a 1-month alternative in participants seropositive for HSV-2 with RGH from a Phase 1b study (ClinicalTrials.gov Identifier: NCT06385327)

[a]In December 2025, Gilead Sciences, Inc. exercised its combined option to exclusively license Assembly Bioscience's HSV helicase-primase inhibitor programs, including long-acting investigational candidate ABI-5366 for RGH.
HSV, herpes simplex virus; **HSV-2**, herpes simplex virus type 2; **RGH**, recurrent genital herpes.

1. World Health Organization. Herpes simplex virus. Accessed 19 February 2026. https://www.who.int/news-room/fact-sheets/detail/herpes-simplex-virus. 2. Gupta R, et al. *Lancet*. 2007:370:2127-37.
3. VALTREX (valacyclovir) tablets, for oral use [package insert]. GSK; 2022. 4. Birkmann A, Zimmermann H. *Curr Opin Virol*. 2016;18:9-13.

Methods: Study Design

- ABI-5366-101 is a randomised, observer-blinded,[a] placebo-controlled, Phase 1b study
- Three sequential cohorts were enrolled to evaluate multiple-dose regimens of ABI-5366 or PBO

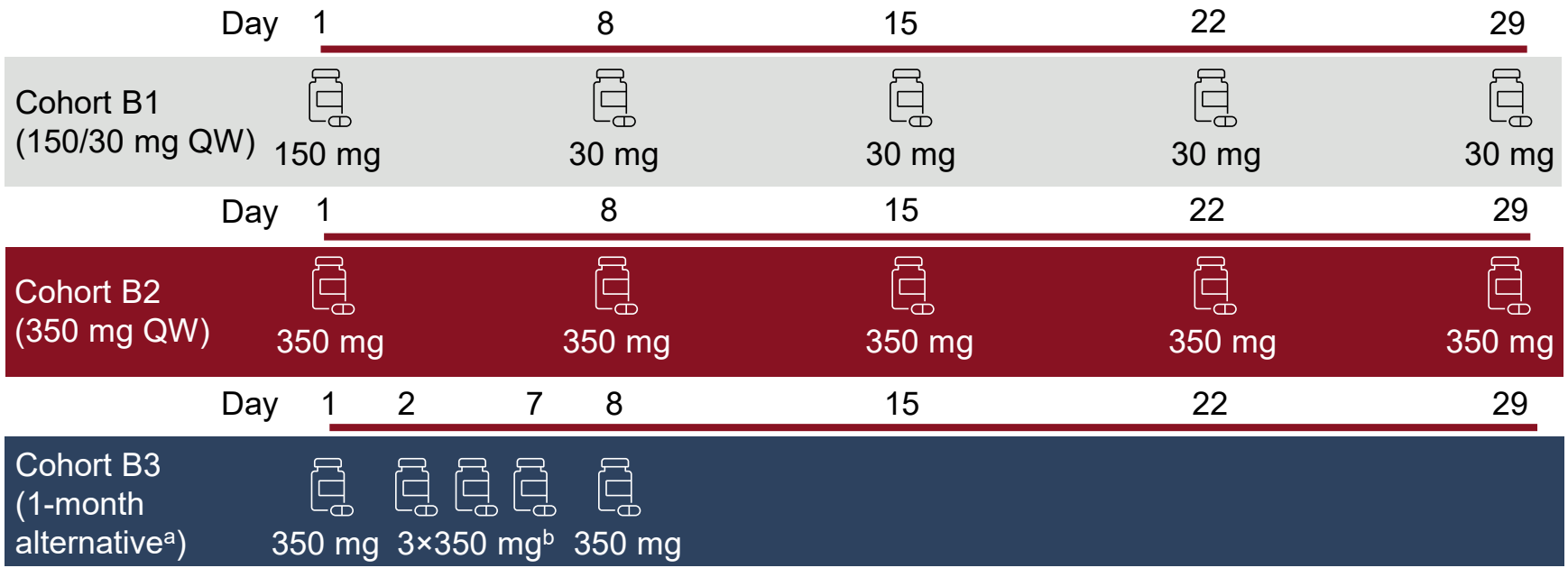


- **Primary end points** were safety and tolerability assessed via physical exams, AEs, and laboratory parameters
- **Secondary end points** included HSV-2 DNA shedding rates and genital lesion rates

[a]Blinded to everyone except the data review committee, as specified in the protocol. [b]Collected in the case of lesion occurrence until lesion resolution during the swabbing period. In the event of lesion occurrence, an unscheduled visit was performed within 48 hours if possible. Assessments included: visual assessment of anogenital area, documentation of morphology and characteristics of lesions, onset and end dates of the recurrence, and swab collection from the lesion site(s) in addition to those collected by the participant. [c]Available data through 25 November 2025 were included in this analysis. At this time, all participants had completed through at least Day 53.
AE, adverse event; **HSV-2**, herpes simplex virus type 2; **PBO**, placebo; **QW**, once weekly.

Methods: Study Design

- Three cohorts completed through at least Day 53 as of the data cutoff of 25 November 2025:



[a]This combination of doses was designed to maintain the target minimum concentration of ABI-5366 over a month, representing a 1-month dose. The goal was to generate PK data to evaluate the feasibility of once-monthly dosing in the future.
[b]Three doses were administered over Days 2 to 7.
PBO, placebo; **PK**, pharmacokinetic; **QW**, once weekly.

Results: Baseline Characteristics

Characteristic	PBO (n = 15)	ABI-5366 150/30 mg QW (n = 20)	ABI-5366 350 mg QW (n = 20)	ABI-5366 1-Month Alternative (n = 21)
Age, years, mean (SD)	41.2 (9.2)	39.3 (8.8)	41.7 (10.0)	38.8 (10.1)
Sex at birth, n (%)				
Male	7 (47)	10 (50)	13 (65)	6 (29)
Female	8 (53)	10 (50)	7 (35)	15 (71)
White race, n (%)	13 (87)	16 (80)	16 (80)	21 (100)
BMI, kg/m^2, median (range)	25.0 (20.3-27.8)	26.4 (21.4-31.4)	28.3 (20.8-32.6)	25.8 (18.1-29.7)
Years since genital herpes diagnosis, mean (SD)	11.6 (10.8)	11.4 (8.2)	12.7 (11.4)	13.1 (8.6)
Number of genital herpes lesion occurrences in past 12 months or prior to suppressive therapy, median (range)	6.0 (4-9)	5.8 (4-9)	5.0 (4-9)	6.0 (4-9)
HSV type, n (%)				
HSV-2 only	8 (53)	10 (50)	9 (45)	12 (57)
HSV-1 and HSV-2	7 (47)	10 (50)	11 (55)	9 (43)
Suppressive treatment at screening, n (%)	8 (53)	12 (60)	12 (60)	13 (62)

BMI, body mass index; **HSV**, herpes simplex virus; **HSV-1**, herpes simplex virus type 1; **HSV-2**, herpes simplex virus type 2; **PBO**, placebo; **QW**, once weekly.

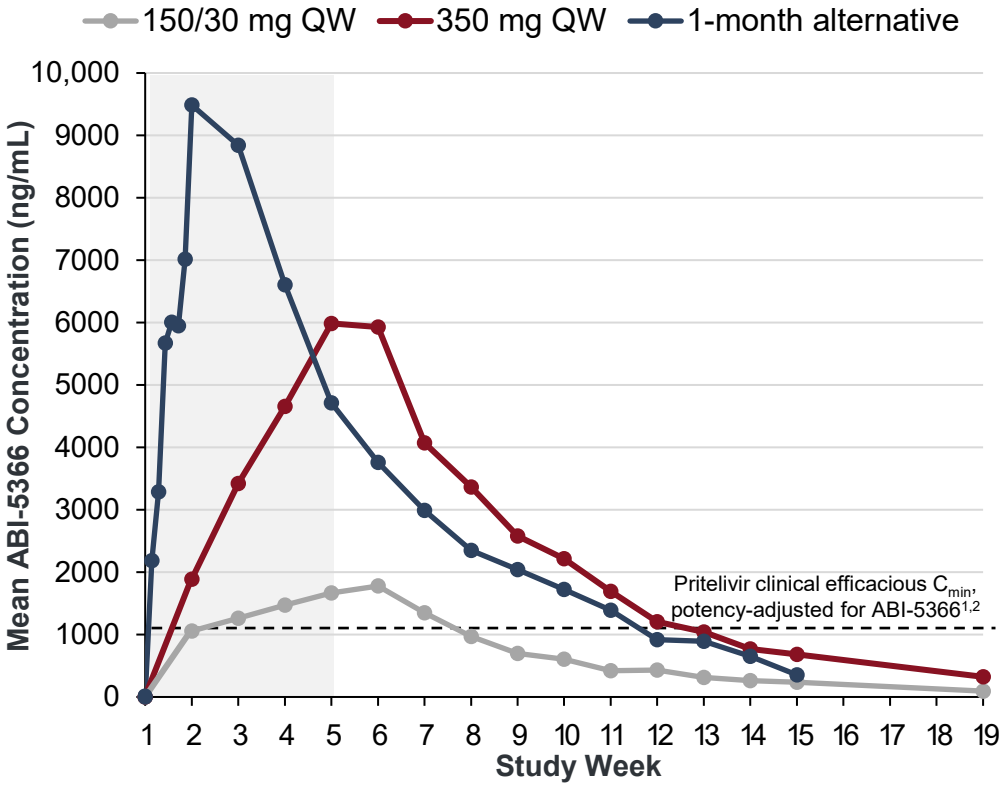
Results: Safety

Treatment-Emergent Adverse Event or Laboratory Abnormality, n (%)	PBO (n = 15)	ABI-5366 150/30 mg QW (n = 20)	ABI-5366 350 mg QW (n = 20)	ABI-5366 1-Month Alternative (n = 21)
Participants with any TEAE	14 (93)	18 (90)	19 (95)	21 (100)
Grade 1	12 (80)	17 (85)	17 (85)	19 (90)
Grade 2	8 (53)	6 (30)	9 (45)	10 (48)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
TEAE related to study drug	6 (40)	6 (30)	3 (15)	7 (33)
TEAE leading to study drug discontinuation	0	0	0	0
TESAE	0	0	0	0
Participants with TE laboratory abnormalities	10 (67)	14 (70)	15 (75)	13 (62)
Grade 1	8 (53)	12 (60)	12 (60)	13 (62)
Grade 2	3 (20)	3 (15)	5 (25)	2 (10)
Grade 3	1 (7)	1 (5)	1 (5)	0
Grade 4	0	0	0	0

- TEAEs reported in ≥5% of the overall population[a] were URTI, headache, viral URTI, arthralgia, back pain, diarrhoea, and fatigue

[a]In both ABI-5366 and PBO cohorts.
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: PK Profile and Parameters



The shaded box indicates Days 1 to 29.

PK Parameters	ABI-5366 150/30 mg QW; Day 29 (n = 20)	ABI-5366 350 mg QW; Day 29 (n = 20)	ABI-5366 1-Month Alternative; Day 8 (n = 19)
T_{max}, h, median (min-max)	4.0 (2.0-4.0)[a]	3.0 (1.0-5.0)[b]	4.0 (2.0-4.1)[c]
$t_{1/2}$, h	509.6 (18.3)[d]	478.8 (29.9)[b]	419.5 (26.2)[e]
C_{max}, ng/mL	2564 (35.3)[a]	8991 (36.1)[b]	14,970 (45.5)[c]
C_{tau}, ng/mL	1794 (41.9)[a]	5812 (41.9)[b]	4200 (64.5)[a]
AUC_{tau}, h·ng/mL	273,500 (32.7)[a]	989,000 (37.5)[b]	4,560,000 (47.9)[a]

PK parameters were assessed for those in the PK evaluable set, which consisted of all participants who received ≥1 dose of study drug and had sufficient PK profile to derive ≥1 PK parameter. All values are mean (CV%) unless otherwise stated. Tau was defined as 1 week for ABI-5366 150/30 mg QW and ABI-5366 350 mg QW and 4 weeks for the ABI-5366 1-month alternative. [a]n = 16. [b]n = 19. [c]n = 17. [d]n = 15. [e]n = 12.

- The mean $t_{1/2}$ ranged from 419.5 to 509.6 hours
- ABI-5366 350 mg QW C_{min} is in multifold excess of the pritelivir clinical efficacious C_{min} (potency-adjusted for ABI-5366)[1,2]

AUC_{tau}, area under the curve over tau; **C_{max}**, maximum concentration; **C_{min}**, minimum concentration; **C_{tau}**, concentration at the end of the dosing interval; **CV**, coefficient of variation; **HSV**, herpes simplex virus; **PK**, pharmacokinetics; **QW**, once weekly; **$t_{1/2}$**, terminal half-life; **T_{max}**, time to reach maximum concentration.

1. Schwab W, et al, inventors; AiCuris GmbH & Co. KG, assignee. N-[5-(aminosulfonyl)-4-methyl-1,3-thiazol-2-yl]-N-methyl-2-[4-(2-pyridinyl)phenyl]acetamide mesylate monohydrate having a specific particle size distribution range and a specific surface area range for use in pharmaceutical formulations. European patent EP2012/068958. April 4, 2013. 2. Kropeit D, et al. *Clin Pharmacol Drug Dev.* 2023;12:749-760.

Results: Viral Shedding and Genital Lesions

Outcome Measured	PBO (n = 15)	ABI-5366 150/30 mg QW (n = 20)	ABI-5366 350 mg QW (n = 20)	ABI-5366 1-Month Alternative (n = 20)[a]
HSV-2 shedding rate, %[b]	14.9	14.5	0.9	3.5
High viral load shedding rate, %[c]	11.8	9.4	0.2	2.2
Overall genital lesion rate, %[d]	18.3	11.5	1.1	6.5
Virologically confirmed HSV-2 genital lesion rate, %	16.2	11.5	0.5	2.0

Rate of Reduction for Each Outcome vs Placebo	Rate of Reduction 350 mg QW	*P* Value[e]	Rate of Reduction 1-Month Alternative	*P* Value[e]
Reduction in HSV-2 shedding rate, %[b]	94	<0.01	76	<0.01
Reduction in high viral load shedding rate, %[c]	98	<0.05	81	<0.01
Reduction in overall genital lesion rate, %[d]	94	<0.01	65	<0.05
Reduction in virologically confirmed HSV-2 genital lesion rate, %	97	<0.05	88	0.01

All outcomes measured over the evaluation period.

[a]One participant in the 1-month alternative cohort discontinued the study without any post-dose HSV DNA and diary data collected and was excluded from the efficacy analysis.

[b]HSV-2 shedding rate was calculated as the number of positive HSV-2 anogenital swabs divided by the total number of swabs collected.

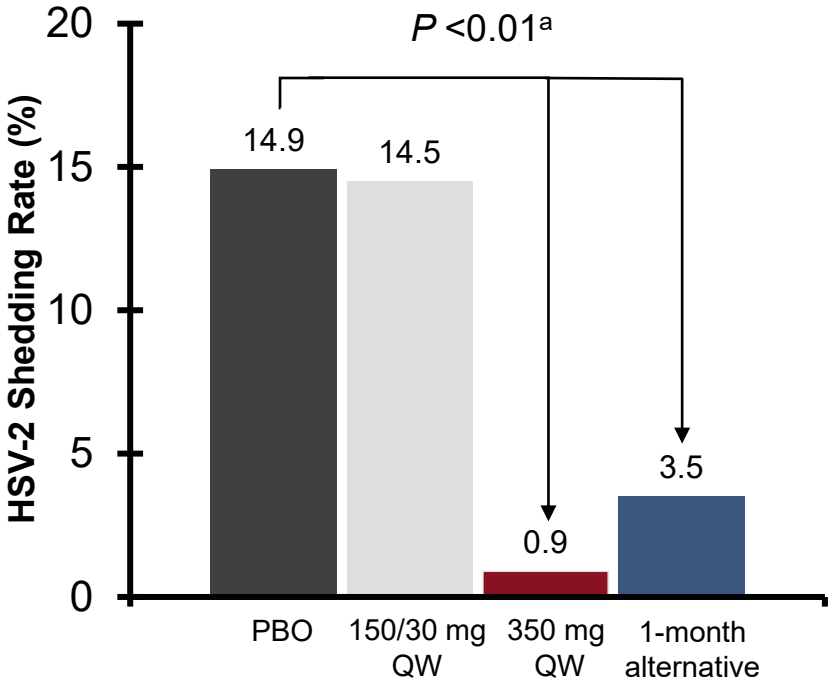
[c]High viral load shedding rate was calculated as the number of positive HSV-2 anogenital swabs with HSV-2 >10^4 copies/mL divided by the total number of swabs collected.

[d]Genital lesion rate was calculated as the number of days with genital lesions present divided by the total number of days assessed.

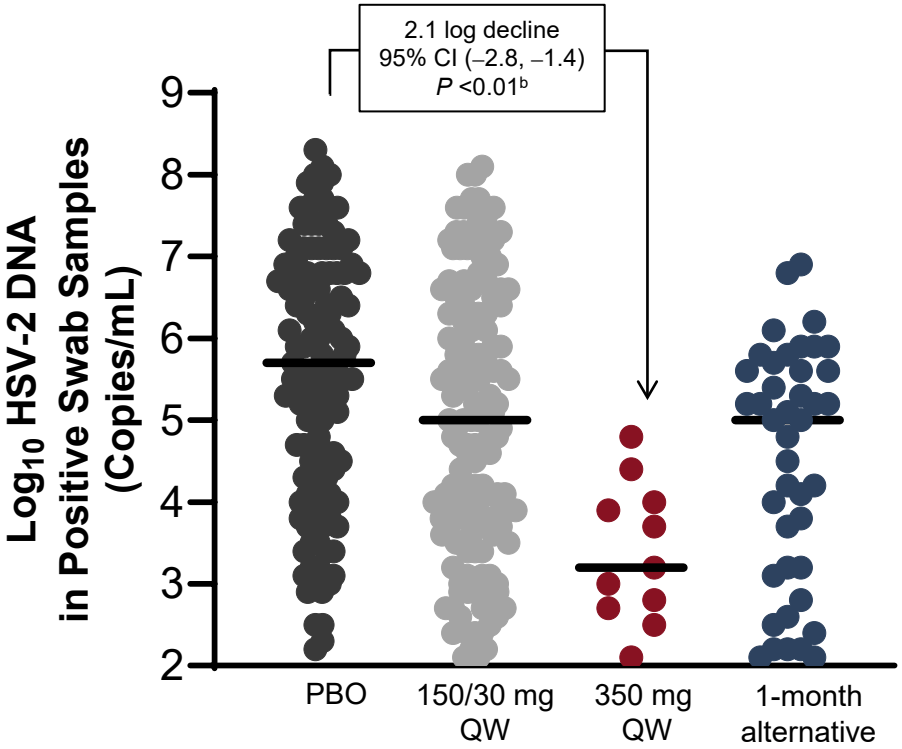
[e]Statistical analysis was conducted using Poisson regression models, and the corresponding *P* values were estimated accordingly.

HSV, herpes simplex virus; **HSV-2**, herpes simplex virus type 2; **PBO**, placebo; **QW**, once weekly.

Results: Reductions in HSV-2 Shedding and Viral Load



[a]Poisson regression analysis.



Horizontal bars indicate the median $\log_{10}$ HSV-2 DNA (copies/mL) in positive swab samples.
[b]Analysis by generalised estimating equations.

HSV-2, herpes simplex virus type 2; **PBO**, placebo; **QW**, once weekly.

Conclusions

- Treatment regimens were safe and well tolerated across all doses
- The observed long half-life of ABI-5366 across all cohorts supports QW oral dosing
- Highly potent antiviral activity was observed for the 350 mg QW regimen compared with PBO:
  - 94% reduction in HSV-2 shedding rate (*P* <0.01)
  - 98% reduction in the rate of samples with high viral load (ie, $>10^4$ copies/mL HSV-2 DNA; *P* <0.05)
  - 94% reduction in genital lesion rate (*P* <0.01)
  - 97% reduction in virologically confirmed HSV-2 genital lesion rate (*P* <0.05)
  - Significant reduction in mean HSV-2 DNA in positive swab samples (*P* <0.01)
- ABI-5366 has the potential to be a novel, long-acting, suppressive therapy for patients with RGH

HSV-2, herpes simplex virus type 2; **PBO**, placebo; **PK**, pharmacokinetic; **QW**, once weekly; **RGH**, recurrent genital herpes.

Acknowledgements

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  - Study investigators
    - Edward J Gane (University of Auckland, Auckland, New Zealand)
    - Cory Sellwood (New Zealand Clinical Research, Christchurch, New Zealand)
    - Andrew Edwards (Momentum Clinical Research, Waikanae, New Zealand)
    - Wayne Hayter (Momentum Clinical Research, Palmerston North, New Zealand)
    - Tess Tonkin (Canopy Clinical Research, Wollongong, NSW, Australia)
    - Karen Kaluhin (Canopy Clinical Research, Miranda, NSW, Australia)
    - Deon Smith (Canopy Clinical Research, Brookvale, NSW, Australia)
    - Joseph Sasadeusz (Royal Melbourne Hospital, Parkville, VIC, Australia)
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Additional HSV Presentations at ESCMID 2026

P0220 “Virologic Analyses Following Treatment With ABI-5366, a Novel, Oral, Long-Acting HSV Helicase-Primase Inhibitor in Participants Seropositive for HSV-2 With Recurrent Genital Herpes”

P0223 “The Safety and Tolerability of ABI-5366, a Novel, Oral, Long-Acting HSV Helicase-Primase Inhibitor in Participants With Recurrent Genital Herpes”

P5211 “The Efficacy, Safety, and Pharmacokinetics of ABI-1179, a Novel, Oral, Long-Acting HSV Helicase-Primase Inhibitor for Recurrent Genital Herpes: Interim Results From a Phase 1b Study”

To be presented 21 April, 12-1:30 pm in the Late Breakers Poster Session, 22. Clinical Trials