

Expanded Safety Analysis of the Deuterated Psilocin Analog HLP003 From a Phase 1/2a Study of Adult Participants With Major Depressive Disorder

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OBJECTIVE

An expanded safety analysis was conducted from this phase 1/2a trial to characterize acute and extended changes in clinical vital signs following one or two administrations of 16 mg HLP003 or placebo in participants with MDD

CONCLUSIONS

- Administration of 16 mg HLP003 was associated with transient increases in cardiovascular measures
- No persistent changes in vital signs or weight were observed through Day 56
- These results support the continued development of HLP003 to further characterize the overall safety profile and increase understanding of efficacy and duration of the clinical experience

References

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Disclosures

All authors are employees of Helus Pharma and may hold Helus Pharma stock.

INTRODUCTION

- The deuterated psilocin analog HLP003 is a novel serotonergic agonist with binding and functional activity at multiple 5-hydroxytryptamine (5-HT) receptors, including 5-HT_{2A}¹
 - HLP003 is being evaluated as an adjunctive treatment for major depressive disorder (MDD)¹
 - See **Poster #121** for a description of the HLP003 clinical development program
- HLP003 was well tolerated in a phase 1/2a, randomized, double-blind study (NCT05385783) of healthy volunteers (2 cohorts) and patients with moderate-to-severe MDD (4 cohorts)²
 - Reported adverse events were predominantly mild to moderate in severity and generally limited to the day of treatment

METHODS

Study Design

- These analyses included a subset of participants with MDD (Cohort 6) enrolled in a phase 1/2a trial randomized to receive a single dose of 16 mg HLP003 on Days 1 and 22 (n=9) or placebo on Day 1 followed by 16 mg HLP003 on Day 22 (n=3) (**Figure 1**)
 - All participants received psychological support based on the EMBARK framework³
 - Efficacy and safety assessments were conducted from Days 1 to 21 (16 mg HLP003 or placebo administration) and from Days 22 to 42 (first or second 16 mg HLP003 administration), on non-administration Day 56, and during the 12-week follow-up period

Assessments

- Systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse, respiratory rate, and body temperature were recorded at baseline (Day –1), predose (Day 22 only), on Days 1 and 22 post dose, on non-administration Day 56, and at regular intervals 0.5 to 12 hours post dose
- Weight and body mass index (BMI) were recorded at baseline, Day 2, and Day 56
- Descriptive data are summarized by means, ranges, and mean changes from baseline
- Adverse events were assessed

RESULTS

Table 1. Baseline Demographics and Clinical Characteristics Were Comparable Across Both Treatment Groups

Characteristic	16 mg HLP003/ 16 mg HLP003* (n=9)	Placebo/16 mg HLP003† (n=3)
Age, median (range), y	34.0 (25–53)	39.0 (26–49)
Sex, n (%)		
Male	6 (66.7)	1 (33.3)
Female	3 (33.3)	2 (66.7)
Race, n (%)		
White	4 (44.5)	2 (66.7)
Black or African American	5 (55.6)	1 (33.3)
Hispanic/Latino, n (%)	0	1 (33.3)
MADRS total score, mean (SD)	31.4 (4.0)	28.0 (4.6)
Vital measurement at baseline, mean (range)		
SBP, mmHg	121.2 (101–138)	126.7 (108–140)
DBP, mmHg	75.4 (62–86)	78.7 (74–86)
Pulse, bpm	70.8 (60–85)	65.7 (61–68)
RR, breaths per minute	15.1 (12–17)	13.3 (12–14)
Body temperature, °C	36.7 (36.6–37.0)	36.7 (36.6–36.9)
Weight, kg	77.1 (65.9–92.1)	72.1 (60.1–82.9)
BMI, kg/m ²	24.8 (20.9–28.7)	26.1 (23.2–27.8)

*Administration of 16 mg HLP003 on Days 1 and 22.

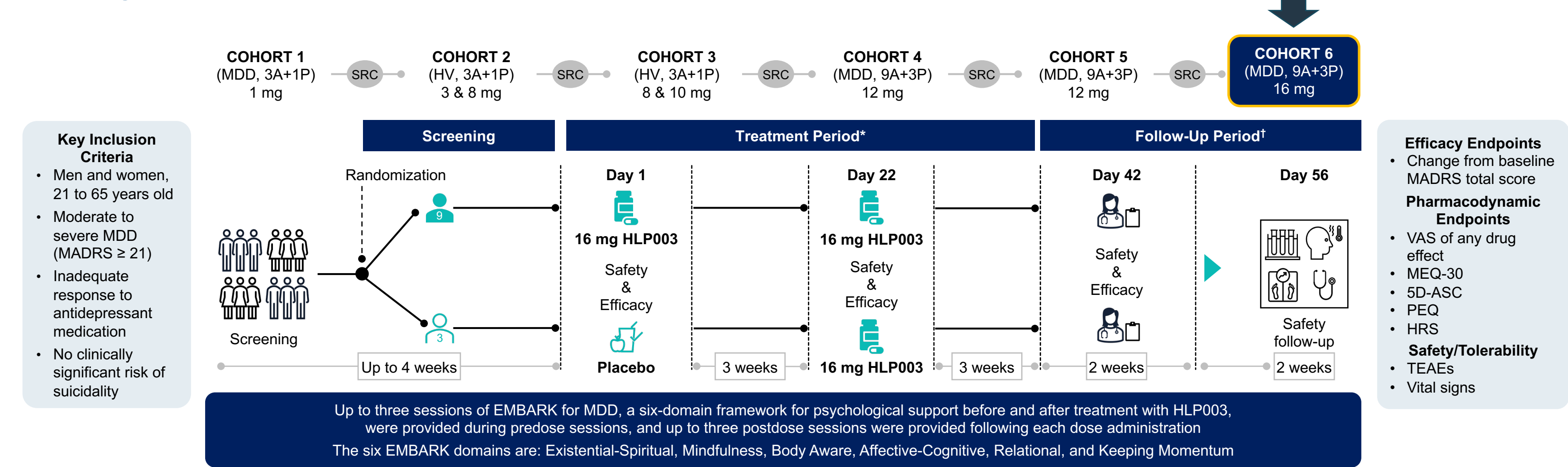
†Administration of placebo on Day 1 and 16 mg HLP003 on Day 22.

BMI, body mass index; bpm, beats per minute; DBP, diastolic blood pressure; MADRS, Montgomery-Åsberg Depression Rating Scale; RR, respiratory rate; SBP, systolic blood pressure. SD, standard deviation.

Vital Sign Measures on HLP003 Administration Days

- Peak effects on cardiovascular measures generally occurred within 0.5 to 2 hours post dose and resolved toward baseline levels within 8 to 12 hours post dose (**Figure 2**; **Table 2**)
- Peak changes in body temperature and respiratory rate were minimal
- Peak changes in vital signs with repeated administration of 16 mg HLP003 on Days 1 and 22 post dose were generally similar
- Participants who initially received placebo followed by 16 mg HLP003 generally showed changes in vital signs on Day 22 similar to changes in those who received 16 mg HLP003 on Days 1 and 22

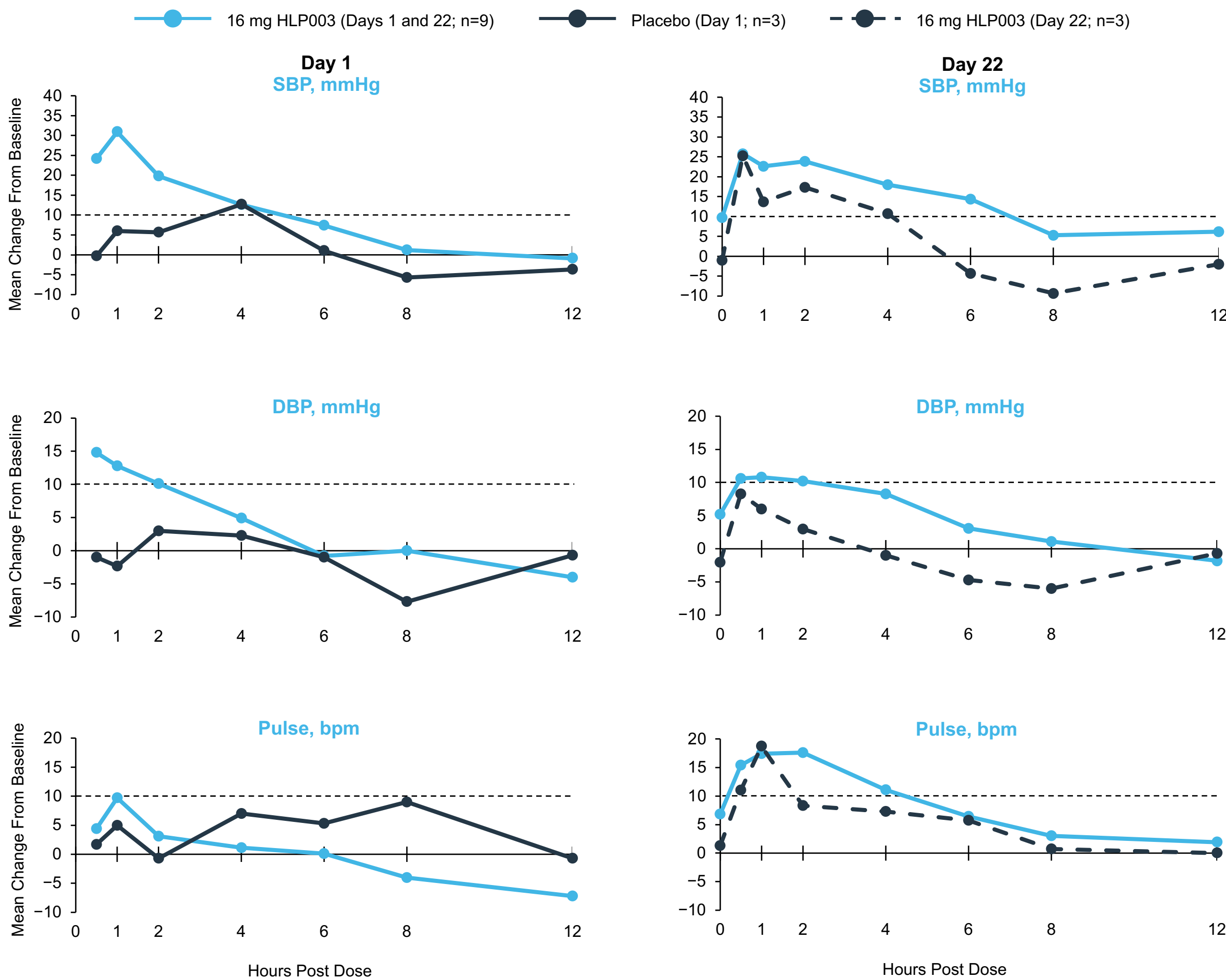
Figure 1. Phase 1/2a Trial Evaluating Safety, Tolerability, Pharmacokinetics, Psychedelic Effects, and Treatment Efficacy of Ascending Doses of HLP003



*Primary efficacy assessed at Day 21. †Follow-up 12 weeks after Day 42 to assess durability of effects.

5D-ASC, 5-Dimensional Altered States of Consciousness Rating Scale; A, active HLP003; HV, healthy volunteers; HRS, Hallucinogen Rating Scale; MADRS, Montgomery-Åsberg Depression Rating Scale; MDD, major depressive disorder; MEQ-30, Revised Mystical Experience Questionnaire; P, placebo; PEQ, Persisting Effects Questionnaire; SRC, Safety Review Committee; TEAE, treatment-emergent adverse event.

Figure 2. Mean Changes From Baseline in Cardiovascular Measures Were Transient and Normalized by 12 Hours on Days 1 and 22 Following Administration of 16 mg HLP003 or Placebo



Dotted lines indicate effect thresholds of 10 mmHg (SBP and DBP), and 10 bpm (pulse). bpm, beats per minute; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 2. Peak Changes in Vital Signs Were Generally Similar With Single and Repeated Administrations of 16 mg HLP003

	16 mg HLP003/16 mg HLP003* (n=9)	Placebo/16 mg HLP003† (n=3)
Day 1, mean change (range)		
SBP, mmHg	32.9 (19–54)	16.7 (10–24)
DBP, mmHg	18.8 (10–32)	5.3 (0–10)
Pulse, bpm	12.6 (4–33)	12.7 (8–19)
RR, breaths per minute	3.0 (0–8)	3.3 (3–4)
Body temperature, °C	0.9 (0.2–1.4)	0.4 (0.0–0.9)
Day 22, mean change (range)		
SBP, mmHg	32.7 (10–57)	27.0 (15–43)
DBP, mmHg	17.0 (4–28)	10.0 (1–15)
Pulse, bpm	24.7 (9–49)	20.0 (17–26)
RR, breaths per minute	2.9 (1–6)	4.3 (3–6)
Body temperature, °C	0.6 (0.2–1.3)	1.3 (0.7–1.8)

*Administrations of 16 mg HLP003 on Days 1 and 22.

†Administration of placebo on Day 1 and 16 mg HLP003 on Day 22.

bpm, beats per minute; DBP, diastolic blood pressure; RR, respiratory rate; SBP, systolic blood pressure.

Safety Follow-Up

- Elevations in pulse, SBP, and DBP seen on Day 22 following the first and second administrations of 16 mg HLP003 returned to baseline levels within 12 hours
- No clinically meaningful changes from baseline in vital sign parameters were observed at Day 56 in either group following the last dose on Day 22 (**Table 3**)
- HLP003 was well tolerated; all adverse events were mild to moderate in severity and limited to the day of treatment²

Table 3. Minimal Changes From Baseline in Vital Measurements Were Observed at Day 56 Following the Last Dose on Day 22

Change in Vital Measurement From Baseline at Day 56, Mean (Range)	16 mg HLP003/16 mg HLP003* (n=9)	Placebo/16 mg HLP00† (n=3)
SBP, mmHg	2.2 (–18 to 20)	–3.7 (–8 to 0)
DBP, mmHg	5.0 (–7 to 19)	–2.3 (–5 to 2)
Pulse, bpm	4.2 (–15 to 19)	10.0 (6 to 15)
Respiratory rate, breaths per minute	0.4 (–3 to 2)	2.0 (0 to 4)
Body temperature, °C	0.2 (0.0 to 0.5)	–0.1 (–0.4 to 0.2)
Weight, kg	–0.7 (–4.4 to 0.3)	–0.5 (–2.3 to 0.5)
BMI, kg/m²	–0.2 (–1.4 to 0.1)	–0.2 (–0.8 to 0.2)

*Administrations of 16 mg HLP003 on Days 1 and 22.

†Administration of placebo on Day 1 and 16 mg HLP003 on Day 22.

BMI, body mass index; bpm, beats per minute; DBP, diastolic blood pressure; RR, respiratory rate; SBP, systolic blood pressure.