

Prifemilast, an Oral Phosphodiesterase 4B (PDE4B)-Selective Inhibitor, Demonstrates Rapid and Durable Efficacy With a Favorable Tolerability and Safety Profile in Moderate to Severe Plaque Psoriasis: Results From Phase 2 and 3 Trials

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SYNOPSIS

- Prifemilast (HPP737) is an oral phosphodiesterase 4B (PDE4B)-selective inhibitor in development for the treatment of immune-mediated inflammatory diseases (IMIDs; eg, psoriasis, inflammatory bowel disease)¹
- The structure of prifemilast limits central nervous system (CNS) penetration and slows absorption, features designed to reduce the risk of CNS-related adverse events (AEs; eg, headache and nausea)^{1,2}
- Prifemilast was well tolerated in pharmacokinetic studies, and its half-life supports once-daily dosing¹
- The placebo-controlled phase 2 and 3 trials described herein demonstrate that prifemilast provides rapid and durable efficacy with a favorable tolerability and safety profile for the treatment of moderate to severe plaque psoriasis

OBJECTIVE

- To determine the efficacy and safety of prifemilast in adults with moderate to severe plaque psoriasis

METHODS

PATIENTS

- Adults with a history of chronic plaque psoriasis for ≥6 months, moderate to severe in intensity (Psoriasis Area and Severity Index [PASI] score ≥12, static Physician's Global Assessment [sPGA] score ≥3, and body surface area [BSA] involvement ≥10%) were enrolled; both multicenter trials were conducted in China
- Study Design**
- Psor-201:** randomized, double-blind, placebo-controlled, dose-ranging, phase 2 trial (NCT07707141)
 - Participants were randomly assigned 1:1:1 to oral prifemilast 6 mg, 10 mg, or 20 mg, or placebo once daily for 12 weeks
- Psor-301:** randomized, double-blind, placebo-controlled, phase 3 trial (NCT07712705)
 - Participants were randomly assigned 1:1:1 to oral prifemilast 10 mg or 20 mg, or placebo once daily for 16 weeks
 - Patients who completed the 16-week treatment period were eligible to enter a 36-week extension period
 - Patients previously assigned to placebo were switched to prifemilast 20 mg once daily; those who had received prifemilast 10 mg or 20 mg continued the same dose

EFFICACY ENDPOINTS

- Primary endpoint: percentage of patients with ≥75% improvement from baseline in PASI score (PASI 75) at Week 12 (Psor-201) or Week 16 (Psor-301)
- Secondary/exploratory endpoints
 - PASI 75, PASI 90 (≥90% improvement from baseline), and PASI 100 (100% improvement) responses over time
 - sPGA response: score of 0 (clear) or 1 (almost clear) with a ≥2-point decrease from baseline over time
 - Change from baseline in Dermatology Life Quality Index (DLQI) score over time

REFERENCES:

1. Ye L, et al. *Drug Des Devel Ther.* 2026;20:598997. 2. Rabe KF. *Br J Pharmacol.* 2011;163(1):53–67.

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DISCLOSURES:

LC, KC, LL, LZ, HR, Yumei Li, LQ, LW, PQ, GZ, RX, Yuzhen Li, and JZ report being clinical trial investigators for Newsoara Biopharma Co., Ltd. Qinghua Zhu, Qian Zhu, and WZ are employees of Newsoara Biopharma Co., Ltd.

RESULTS

- Psor-201:** 123 patients were randomly assigned to treatment (**Table 1**), with completion rates higher in the prifemilast groups (83.9%-96.8%) versus placebo (76.7%)
- Psor-301:** 505 patients were randomly assigned to treatment and had ≥1 postbaseline efficacy assessment (**Table 1**), with 16-week completion rates higher in the prifemilast groups (90.5%-93.5%) versus placebo (83.7%)
 - 450 patients participated in the prifemilast treatment-extension period, with a 52-week completion rate of 85.8%
- Demographics and baseline characteristics were generally similar across treatment groups for each trial (**Table 1**)

Table 1. Demographics and Baseline Characteristics

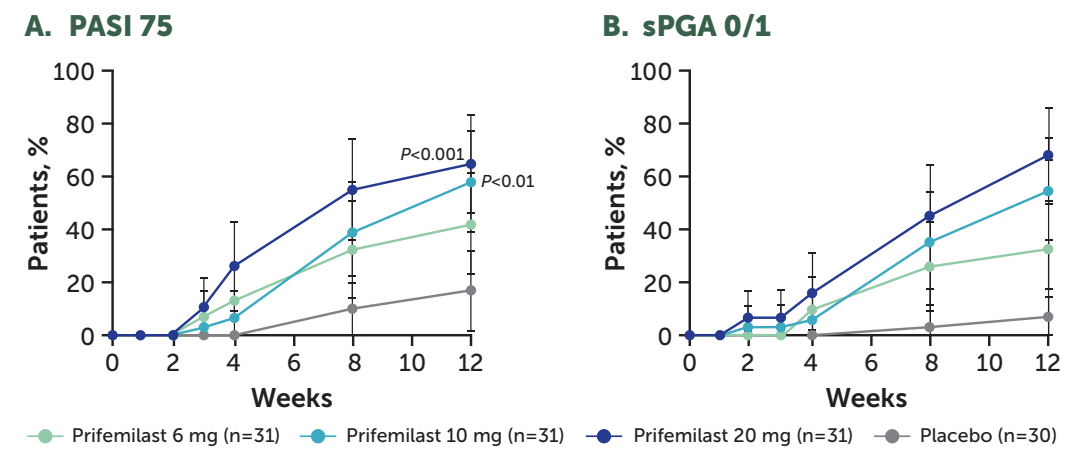
Parameter	Prifemilast			
	6 mg	10 mg	20 mg	Placebo
Psor-201 trial	n=31	n=31	n=31	n=30
Age, mean (SD), y	41.0 (12.2)	40.7 (12.5)	41.8 (14.0)	37.2 (11.6)
Male, n (%)	22 (71.0)	27 (87.1)	23 (74.2)	26 (86.7)
BMI, mean (SD), kg/m ²	26.3 (3.4)	25.8 (3.5)	25.8 (3.5)	25.6 (3.8)
History of psoriasis, n (%)				
Moderate	11 (35.5)	13 (41.9)	10 (32.3)	8 (26.7)
Severe	20 (64.5)	18 (58.1)	21 (67.7)	22 (73.3)
PASI score, mean (SD)	22.0 (7.6)	21.9 (9.3)	20.8 (7.7)	24.8 (10.8)
BSA involvement, mean (SD), %	29.0 (11.7)	34.3 (15.7)	31.0 (14.3)	38.1 (19.0)
DLQI score, mean (SD)	12.4 (6.4)	9.1 (6.2)	12.3 (7.1)	10.4 (6.1)
Psor-301 trial		n=170	n=169	n=166
Age, mean (SD), y	—	46.0 (12.8)	47.0 (13.2)	45.9 (12.8)
Male, n (%)	—	134 (78.8)	135 (79.9)	131 (78.9)
BMI, mean (SD), kg/m ^{2a}	—	25.1 (3.4)	25.3 (3.4)	25.5 (3.8)
History of psoriasis, n (%)	—			
Moderate	—	65 (38.2)	60 (35.5)	55 (33.1)
Severe	—	105 (61.8)	109 (64.5)	111 (66.9)
PASI score, mean (SD)	—	20.1 (8.1)	21.0 (8.9)	22.3 (9.5)
BSA involvement, mean (SD), %	—	28.8 (17.0)	31.0 (17.2)	32.1 (18.0)
DLQI score, mean (SD)	—	13.5 (7.4)	11.6 (7.4)	11.8 (7.2)

^aData missing for 1 patient each in the placebo and prifemilast 20-mg groups. BMI = body mass index; BSA = body surface area; DLQI = Dermatology Life Quality Index; PASI = Psoriasis Area and Severity Index.

EFFICACY

- Psor-201:** dose-dependent increases in PASI 75 (primary endpoint; **Figure 1A**) and PASI 90 responses at Week 12 were observed for prifemilast, with a significant difference versus placebo at the 2 highest doses, for both endpoints (P≤0.03 vs placebo)
 - PASI 100 response increased with prifemilast dose and time on treatment, whereas no patients who received placebo achieved PASI 100
 - sPGA 0/1 at Week 12 was markedly higher in the prifemilast groups (32.3% [6 mg], 54.8% [10 mg], and 67.7% [20 mg]) versus placebo (6.7%; **Figure 1B**)
- Psor-301:** a significantly greater percentage of patients treated with prifemilast 10 mg or 20 mg achieved PASI 75 at Week 16 (primary endpoint) versus placebo (P<0.0001 vs placebo; **Figure 2A**)
 - Onset of efficacy with prifemilast was rapid, with significant differences in PASI and sPGA responses versus placebo observed as early as Week 2 (**Figure 2A-C**)

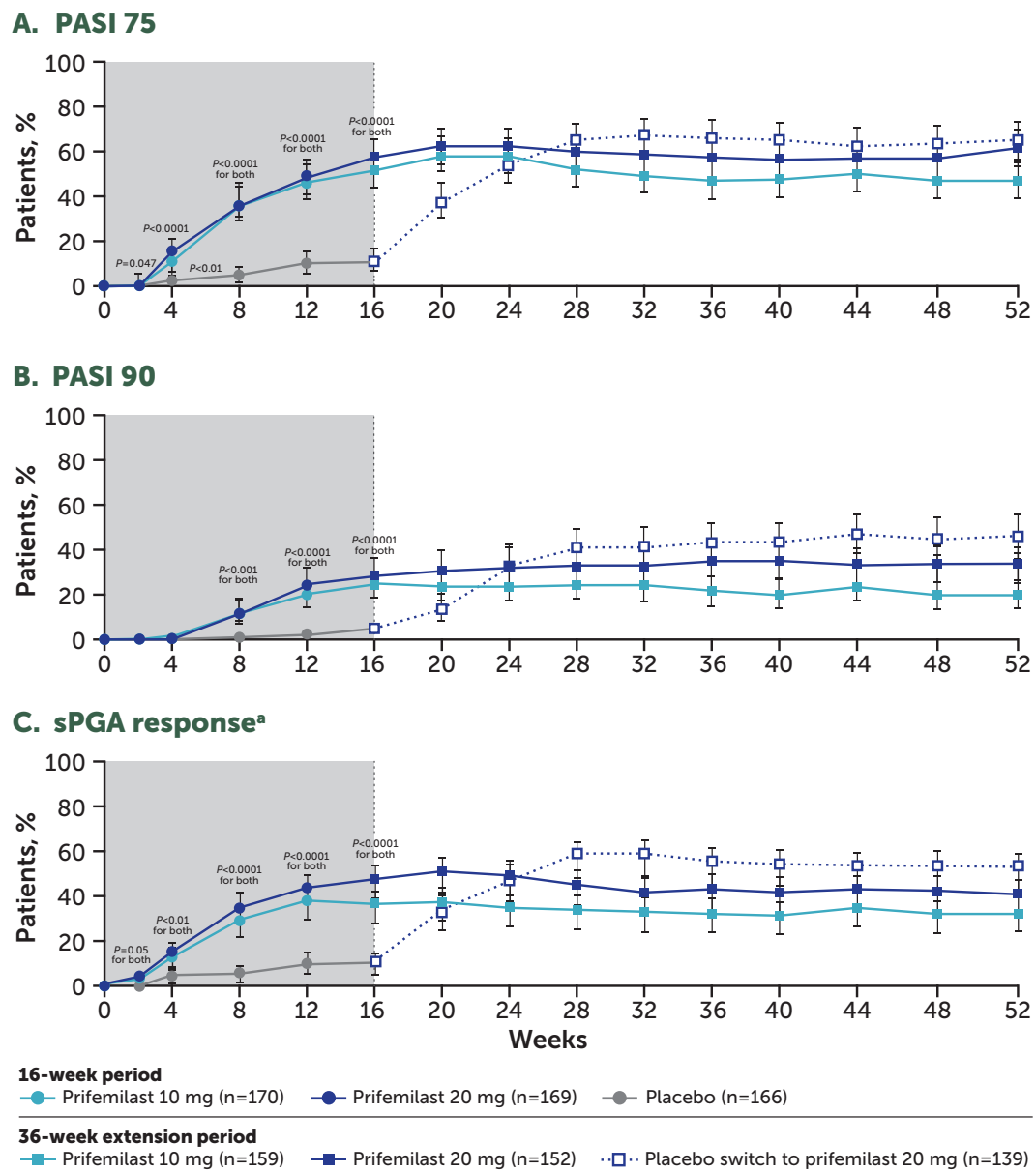
Figure 1. Percentage of Patients Achieving (A) PASI 75 and (B) sPGA 0/1 Over Time (Psor-201 Trial)^a



^aError bars represent 95% CI. Nonresponder imputation was applied for all measures. Prifemilast versus placebo statistical comparisons were only performed for PASI 75, at Week 12.

PASI = Psoriasis Area and Severity Index; sPGA = static Physician's Global Assessment.

Figure 2. Percentage of Patients Achieving (A) PASI 75, (B) PASI 90, and (C) sPGA Response^a Over Time (Psor-301 Trial)^b

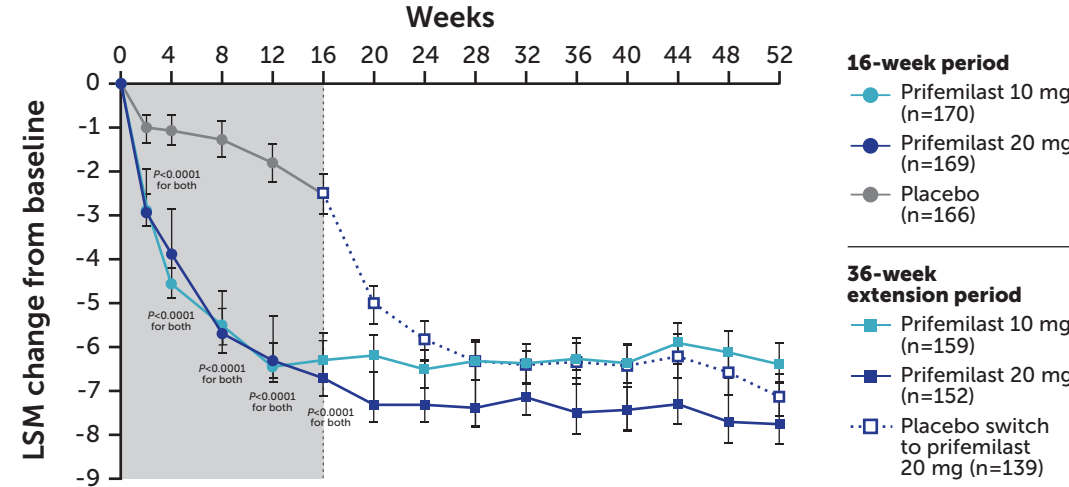


^aScore of 0 (clear) or 1 (almost clear) with a ≥2-point decrease from baseline. ^bError bars represent 95% CI. Nonresponder imputation was applied for all measures. Prifemilast versus placebo statistical comparisons were only performed through Week 16 (shaded area).

PASI = Psoriasis Area and Severity Index; sPGA = static Physician's Global Assessment.

- In both trials, improvements in DLQI scores were significantly greater with prifemilast versus placebo (P<0.05), with clinically meaningful changes from baseline observed by Week 8 in Psor-301 (**Figure 3**)
- In the Psor-301 extension period, PASI and sPGA responses, as well as DLQI scores, were maintained through Week 52 for those continuing prifemilast (**Figures 2A-C** and **3**)

Figure 3. Change in DLQI Score (Psor-301 Trial)^a



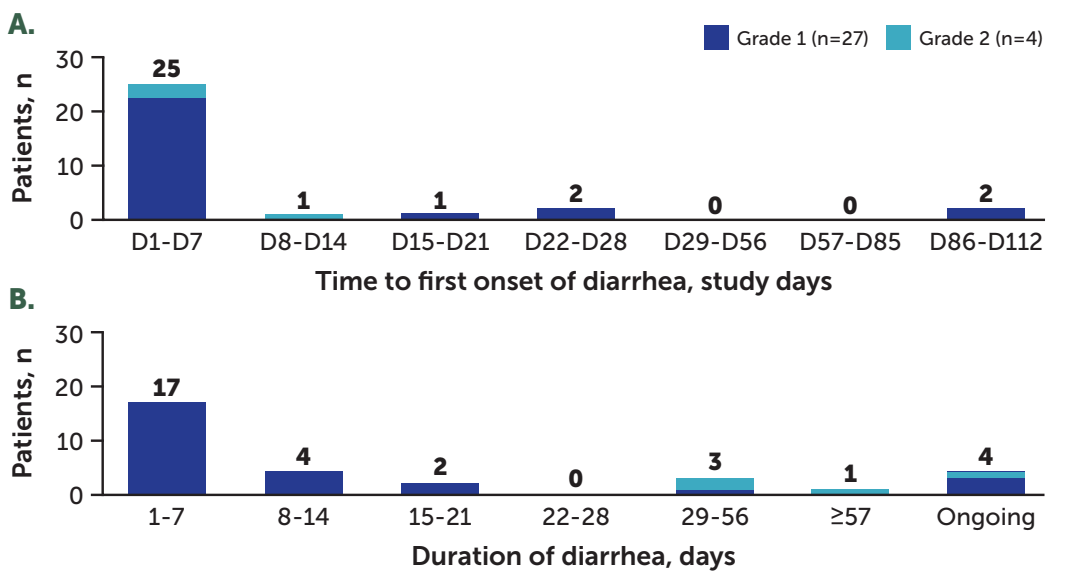
^aError bars represent SE. Prifemilast versus placebo statistical comparisons were only performed through Week 16 (shaded area).

DLQI = Dermatology Life Quality Index; LSM = least-squares mean.

SAFETY

- Prifemilast was generally well tolerated in both trials, with a safety profile consistent with that known for PDE4 inhibitors; most treatment-emergent AEs were grade 1 or 2, and there were low rates of discontinuations due to AEs (**Table 2**)
- In Psor-201, only diarrhea appeared to be a dose-dependent AE; in Psor-301, in the 20-mg group during the first 16 weeks, all diarrhea AEs were mild or moderate in intensity, occurred early, and most cases resolved within the first 2 weeks (**Figure 4A-B**)
- In Psor-301, all AEs of weight loss were mild or moderate over the 52-week duration (5% to <20% decrease from baseline)
- Two deaths occurred, during the phase 3 extension period, and both were considered unrelated to study treatment

Figure 4. Diarrhea (A) Time to First Onset and (B) Duration for the Prifemilast 20-mg Group During the First 16 Weeks (Psor-301 Trial)



D = study day; Ongoing = episode unresolved at data cutoff, total duration not calculable.

CONCLUSION

- Prifemilast provided rapid and durable improvements in the extent and severity of moderate to severe psoriasis with a favorable tolerability profile
- These findings support continued development of prifemilast as a potential oral treatment option for psoriasis and other IMIDs, including ulcerative colitis and Crohn's disease

Table 2. Summary of AEs

Patients with an AE, n (%)	Prifemilast			
	6 mg	10 mg	20 mg	Placebo
Psor-201 trial	n=31	n=31	n=31	n=30
Any AE	19 (61.3)	22 (71.0)	26 (83.9)	17 (56.7)
Treatment-related AEs	18 (58.1)	21 (67.7)	25 (80.6)	16 (53.3)
Grade ≥3 AEs	1 (3.2) ^a	0	0	0
Serious AEs	0	0	0	0
AEs leading to discontinuation	0	0	1 (3.2) ^b	0
Most frequent AEs^c				
Diarrhea	2 (6.5)	7 (22.6)	10 (32.3)	2 (6.7)
Dizziness	4 (12.9)	2 (6.5)	5 (16.1)	1 (3.3)
Headache	5 (16.1)	1 (3.2)	4 (12.9)	0
Muscular weakness	0	0	4 (12.9)	0
URTI	2 (6.5)	4 (12.9)	3 (9.7)	2 (6.7)

Psor-301 trial (16-week period)	10 mg	20 mg	Placebo
	n=171	n=172	n=171
Any AE	133 (77.8)	146 (84.9)	106 (62.0)
Treatment-related AEs	94 (55.0)	110 (64.0)	57 (33.3)
Grade ≥3 AEs	7 (4.1)	14 (8.1)	5 (2.9)
Serious AEs	4 (2.3) ^d	10 (5.8) ^d	5 (2.9) ^d
Deaths	0	0	0
AEs leading to discontinuation	3 (1.8)	3 (1.7)	3 (1.8)
Most frequent AEs^c			
Diarrhea	25 (14.6)	31 (18.0)	11 (6.4)
URTI	24 (14.0)	27 (15.7)	16 (9.4)
Psor-301 trial (36-week extension period)	10 mg	20 mg	Placebo/prifemilast 20 mg
	n=159	n=152	n=139
Any AE	134 (84.3)	132 (86.8)	123 (88.5)
Treatment-related AEs	94 (59.1)	102 (67.1)	89 (64.0)
Grade ≥3 AEs	16 (10.1)	15 (9.9)	6 (4.3)
Serious AEs	7 (4.4) ^e	9 (5.9) ^e	7 (5.0) ^e
Deaths	0	1 (0.7) ^f	1 (0.7) ^f
AEs leading to discontinuation	1 (0.6)	3 (2.0)	1 (0.7)
Most frequent AEs^c			
URTI	31 (19.5)	36 (23.7)	22 (15.8)
Decreased weight	7 (4.4)	17 (11.2)	15 (10.8)
Hypertriglyceridemia	20 (12.6)	15 (9.9)	12 (8.6)
Increased blood glucose	12 (7.5)	10 (6.6)	14 (10.1)
Diarrhea	3 (1.9)	8 (5.3)	17 (12.2)

^aHypertriglyceridemia considered by the investigator to be unrelated to study treatment. ^bDiscontinuation due to headache, diarrhea, muscular weakness, nausea, and vomiting on Day 1. ^c≥10.0% of patients in any treatment group. ^dNo serious AE was reported in >1 patient in any treatment group. ^eTwo patients experienced drug-related serious AEs: infectious pneumonia (prifemilast 10 mg [n=1]) and headache (placebo/prifemilast 20 mg [n=1]). ^fOne patient in the prifemilast 20-mg group had cardiopulmonary arrest, pericardial effusion, and severe closed craniocerebral injury and died during the extension period; 1 patient in the placebo/prifemilast 20-mg group died from cerebral hemorrhage >14 days after the last prifemilast dose. All events leading to the 2 deaths were considered by the investigator to be unrelated to study treatment.

AE = adverse event; URTI = upper respiratory tract infection.