**Introduction**

- Dimethyl Fumarate (DMF) is a fumaric acid ester (FAE) approved in Germany for the treatment of moderate to severe chronic plaque psoriasis. Monomethyl fumarate (MMF) is the active moiety of DMF.
- XP-23839 is an extended release FAE that is being developed for the treatment of moderate to severe plaque psoriasis.
- Here, we examine a phase 2 study to evaluate the safety and efficacy of 3 doses and 2 dosing regimens at 12 weeks.

**Methods**

- Randomized, double-blind, placebo-controlled, dose-finding efficacy and safety study in 33 US sites.
- Patients with chronic plaque psoriasis > 6 months, PASI (Psoriasis Area and Severity Index) ≥ 12, sPGA (static Physician Global assessment) ≥ 3, and psoriasis BSA (Body Surface Area) ≥ 10%.
- 200 subjects randomized in a 1:1:1:1 ratio into 4 arms: 400 mg QD, 400 mg BID, 800 mg QD, Placebo.
- A 3-week titration phase was followed by 9 weeks of treatment.
- The primary endpoint was the percentage change in PASI score from baseline to the end of week 12.

**Results**

- Primary efficacy analysis (mITT population) included 194 subjects: 400 mg QD (48), 800 mg QD (53), 400 mg BID (46), and placebo (47).
- Least squares mean percent change from baseline was statistically significant compared with placebo for the 800 mg QD group (-48.2% vs -25.0%, P < .001) and the 400 mg BID group (-50.7% vs -25.0%, P < .001); the difference between 400 mg QD and placebo did not reach statistical significance (-38.1% vs -25.0%, P = .066) (Table 1).
- Diarrhea was the most common TEAE, reported in 22.4%, 40.0%, 39.6%, and 14.6% of subjects in the XP-23829 400 mg QD, 800 mg QD, 400 mg BID, and placebo groups, respectively. Most cases of diarrhea were mild to moderate in severity (Table 2).
- Nausea and abdominal pain were reported in more than 10% of the overall XP-23829 population (Table 2).
- Flushing was reported in 5.9% of XP-23829 subjects and 6.3% of placebo subjects (Table 2).
- No subject demonstrated grade 3 or 4 lymphopenia (Table 2).
- No new or unexpected adverse events related to XP-23829 were reported compared to what is known for the FAE class (Table 2).

**Conclusions**

- In this study XP-23829 in 400 mg BID and 800 mg QD doses demonstrated significant efficacy over 12-week of treatment and efficacy did not appear to have plateaued at the end of the study.
- Efficacy and safety is being further assessed in a 24-week phase 2 study.