ALKS 8700 is a prodrug of monomethyl fumarate (MMF), which is being developed as an oral disease-modifying treatment for relapsing forms of MS. In Phase 3 studies of DMF, gastrointestinal (GI) adverse events (AEs) have been among the most commonly reported AEs and were the lead reason for treatment interruption or discontinuation due to GI events, perhaps reflective of real-world patient experience.

The incidence of GI AEs with ALKS 8700 was lower than with DMF. In a Phase 1 crossover study in healthy subjects (N=12), indicating the active metabolite of DMF (Figure 1), ALKS 8700 has physiochemical properties that are distinct from DMF.

Fewer subjects reported GI AEs with ALKS 8700 420 mg (8.3%) compared to DMF 300 mg (10%) (p=0.454). The GI AEs of ALKS 8700 420 mg were predominantly GI distress (22.2%) and dyspepsia (11.1%). In the DMF capsule is over-encapsulated to create a blinded study drug.

In the ALKS 8700 treatment group, study drug includes ALKS 8700 462 mg twice daily with DMF 240 mg twice daily in approximately 420 patients with relapsing forms of MS. The DMF capsule is over-encapsulated to create a blinded study drug.

Study Objectives:
- Compare the GI tolerability of ALKS 8700 and DMF in adult patients with RRMS using the IGISIS and IGISIS symptom scales.
- The planned primary endpoint is the number of days with IGISIS symptom scores relative to exposure days.
- The planned secondary endpoints are:
  - Area under the curve for the total IGISIS symptom intensity score relative to exposure days.
  - Number of days with IGISIS symptom scores relative to exposure days.
  - Evaluation of the safety and tolerability of ALKS 8700 in adult patients with RRMS.

Eligibility Criteria:
- Patients aged 18–65 years
- Neurologically stable with no relapse over the previous 24 hours while taking study drug
- Baseline Expanded Disability Status Scale (EDSS) score of 0–5.5
- On a stable dose of fingolimod or dimethyl fumarate for ≥12 months
- Able to provide written informed consent

Study Treatment:
- In the ALKS 8700 treatment group, study drug includes ALKS 8700 462 mg administered as one capsule daily in a randomized, double-blind, placebo-controlled study.
- In the DMF treatment group, study drug includes commercially available DMF (Tecfidera®) administered as either one 120-mg capsule once daily or one 240-mg capsule once daily.

Table 1: Study Assessments

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<th>Safety and tolerability</th>
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