Use of epigenetic cell counting to determine the effect of ozanimod on circulating leukocyte subtypes in patients with relapsing multiple sclerosis

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Introduction: Ozanimod, a sphingosine 1-phosphate (S1P) receptor modulator that binds with high affinity selectively to S1P receptor subtypes 1 and 5, causes lymphocyte retention in lymphoid tissues. Epigenetic cell counting evaluated the effect of ozanimod on circulating leukocyte subtypes in patients with relapsing multiple sclerosis (RMS).

Methods: A phase 1 pharmacokinetic/pharmacodynamic study randomised 24 patients with RMS to oral ozanimod HCl 0.5 mg (n=13) or 1 mg/d (n=11) [equivalent to ozanimod 0.46 or 0.92 mg] for ~12 weeks following an initial 7-day dose escalation (0.25 mg/d x 4 d + 0.5 mg/d x 3 d). Epigenetic cell counting was performed by Epiontis/Precision for Medicine. Results were expressed as geometric mean (95% confidence interval) for the percentage of baseline cells/μL at day 85.

Results: Dose-dependent decreases were observed for total circulating leukocytes and all subtypes tested, including total B cells and T cells, cytotoxic T cells, T helper cells, regulatory T cells (Tregs), Th17 cells, naive CD8+ cells, and PD1+ cells. Decreases were greatest for total T cells, Th17 and naive CD8+ cells (11%-13% of baseline with

ozanimod 1 mg), and less for Tregs and PD1+ cells (34%-35% of baseline with ozanimod 1 mg).

Conclusion: Epigenetic cell counting results were consistent with previously reported flow cytometry for all leukocyte subsets tested in both analyses, including decreases in total B cells and T cells as well as cytotoxic T cells, T helper cells, and naive CD8+ cells. Epigenetic cell counting also provided data on previously untested Th17, Treg, and PD1+ cells, further clarifying the differential effects of ozanimod on specific leukocyte subtypes in patients with RMS, which may have implications for the risk-benefit profile of ozanimod.