Ozanimod demonstrates efficacy and safety in a phase 3 trial of relapsing multiple sclerosis (SUNBEAM)

Short Title: Safety and efficacy of ozanimod (SUNBEAM)

G. Comi[1], L. Kappos[2], K.W. Selmaj[3], A. Bar-Or[4], D.L. Arnold[5], L. Steinman[6], H.-P. Hartung[7], X. Montalbán[8], E. K. Havrdová[9], B.A.C. Cree[10], J.K. Sheffield[11], K. Raghupathi[11], J.A. Cohen[12], on behalf of the SUNBEAM investigators

[1]Department of Neurology, San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milano, Italy; [2]Department of Neurology, University Hospital Basel, Basel, Switzerland; [3]Department of Neurology, Medical University of Łódź, Łódź, Poland; [4]Center for Neuroinflammation and Therapeutics, and Multiple Sclerosis Division, University of Pennsylvania, Philadelphia, Pennsylvania, United States; [5]NeuroRx Research and Montréal Neurological Institute, McGill University, Montréal, Quebec, Canada; [6]Beckman Center for Molecular Medicine, Stanford, California, United States; [7]Department of Neurology Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany; [8]University of Toronto, St. Michael's Hospital Toronto, Canada, and Cemcat Vall d'Hebron Hospital, Universitat Autonoma Barcelona, Barcelona, Spain; [9]Department of Neurology and Center for Clinical Neuroscience, First Medical Faculty, Charles University, Prague, Czech Republic, [10]UCSF Weill Institute for Neuroscience, Department of Neurology, University of California San Francisco, San Francisco, California, Unites States; [11]Receptos, a wholly owned subsidiary of Celgene, San Diego, California, United States; [12]Mellen Center for MS Treatment and Research, Cleveland Clinic, Cleveland, Ohio, United States

Background: Ozanimod is an oral, once daily immunomodulator selectively targeting sphingosine 1-phosphate 1 and 5 receptors. SUNBEAM, the first of two phase 3 studies, evaluated efficacy and safety of ozanimod vs interferon β-1a (IFN) in relapsing multiple sclerosis (RMS).

Methods: This multicenter, randomized, double-blind, double-dummy, parallel-group, active-controlled study evaluated daily oral ozanimod 1 or 0.5 mg (initiated with 7-day dose escalation) for ≥1 year vs weekly intramuscular IFN 30 µg. Primary endpoint was annualized relapse rate (ARR). Key secondary endpoints included new/enlarging T2 lesions through month 12 and gadolinium enhancing (GdE) T1 lesions at month 12. Disability progression was pre-specified to be pooled and evaluated with a second phase 3 study.

Results: 1346 RMS patients were enrolled; baseline characteristics were similar across treatment groups (mean age 36 years, 66% female, mean EDSS 2.6, mean relapses in the prior year 1.3, 47% with GdE lesions, 31% previously treated with disease-modifying therapy). Mean treatment duration was 13.6 months. Ozanimod 1 and 0.5 mg reduced ARR (0.181 [p<0.0001] and 0.241 [p=0.0013]) vs IFN (0.350). Adjusted mean new/enlarging T2 lesions per scan over 12 months was reduced 48% and 25%, respectively, for ozanimod 1 mg (1.465; p<0.0001) and 0.5 mg (2.139; p=0.0032) vs IFN (2.836). Adjusted mean GdE lesions at 12 months was reduced 63% and 34% for ozanimod 1 mg (0.160; p<0.0001) and 0.5 mg (0.287; p=0.0182) vs IFN (0.433). Most treatment-emergent adverse events (AEs) were mild, with

low incidence of serious AEs, and similar across groups. Rate of discontinuation due to AEs was low and similar across groups. No first-dose, clinically relevant bradycardia or 2nd degree or higher atrioventricular block were reported.

Conclusion: Both ozanimod doses demonstrated superiority to IFN on relapse and MRI endpoints. This, coupled with the safety and tolerability results, demonstrates a favorable benefit-risk profile for ozanimod in RMS.