Abstract Title: Evidence of Remyelination with the Anti-LINGO-1 Monoclonal Antibody BIIB033 After Acute Optic Neuritis

Press Release Title: Experimental Drug That May Repair Nerve Damage in MS Moves Forward

Objective: To determine the efficacy of the anti-LINGO-1 antibody BIIB033 for CNS remyelination.

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Background: BIIB033, a fully human anti-LINGO-1 monoclonal antibody, showed efficacy in preclinical models of remyelination and was well tolerated in Phase 1 studies.

Design/Methods: RENEW (NCT01721161) was a randomized, double-blind, placebo-controlled, parallel-group study in subjects with first unilateral acute optic neuritis episode. Subjects (18 to 50 years) completed treatment with high-dose steroids and were then randomized 1:1 to 100 mg/kg BIIB033 IV or placebo once every four weeks (wks; six doses total) and followed up to Week 32. Remyelination was evaluated by recovery of optic nerve conduction latency using full-field visual evoked potential (FF-VEP) compared with the unaffected fellow eye at baseline. Neuroprotection was studied by measuring the thickness of the retinal nerve fiber layer and ganglion cell layer using spectral-domain optical coherence tomography (SD-OCT), and change in low-contrast letter acuity (LCLA). Between-treatment comparisons were evaluated by ANCOVA and MMRM in the per-protocol (PP) and intent-to-treat (ITT) populations. Safety/tolerability were also evaluated.

Results: Eighty-two subjects received BIIB033 (ITT N=41; PP N=33) or placebo (ITT N=41; PP N=36). In the PP population BIIB033-treated patients showed a significantly improved average difference in latency recovery vs placebo: 7.55 msec at 24wks (ANCOVA p=0.05) and 9.13 msec (MMRM p=0.01) at 32wks. Corresponding differences in the ITT population were 3.48 msec (p=0.33) at 24wks and 6.06 msec (p=0.07) at 32wks. During this period, no differences were observed in SD-OCT and LCLA. Overall incidence and severity of adverse events (AEs) were comparable across treatment arms. Treatment-related serious AEs were infusion-related hypersensitivity reactions (N=2) and asymptomatic transient elevation in liver transaminases (N=1).

Conclusions: RENEW is the first clinical trial reporting on the efficacy of BIIB033. The observed shortening of the FF-VEP provides evidence of proof of biology for remyelination.

Study Supported by: Biogen.