SAFETY, TOLERABILITY, PHARMACOKINETIC AND PHARMACODYNAMIC EFFECTS OF BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2 FOLLOWING INTRAVENOUS (IV) AND SUBCUTANEOUS (SC) SINGLE OR MULTIPLE DOSES ADMINISTRATION IN HEALTHY VOLUNTEERS (HV) AND SUBJECTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, upon activation, inhibits the inflammatory factors production by human pDCs, including IFN-α a major player in the pathogenesis of SLE. This 3-Part Phase 1 study evaluated the safety, tolerability, pharmaco-kinetis (PK), pharmacodynamics (PD) and clinical efficacy of single and multiple ascending doses (SAD-MAD) of BIIB059 in HV and SLE subjects (NCT02106897).

Objectives: To compare PK and PD parameters between HV and SLE following single and multiple dose administration of BIIB059

Methods: In the SAD Part 2, 12 subjects with active SLE were randomised 2:1 to receive either 2 or 3 SC administrations of Placebo or BIIB059 20, 50 or 150 mg Q4W or 3 SC 300 mg Q2W. Subjects with active SLE, received either 2 or 3 SC placebo or BIIB059 50 mg or 300 mg. The dose levels were selected based on emerging data from the Part 1 in HV and was not to exceed the maximum tolerated dose. Blood samples were obtained before and after each dose administration to characterise PK and PD (BDCA2 on pDC) relationship for BIIB059.

Results: Part 1 PK and PD results (SAD) in HV and Part 2 PD results have been previously presented. In Part 2 of the study, following IV administration, mean t½ in SLE subjects was 18.1 days, with a mean V of 5.41 L. Following SC administration, in Part 3a, mean t½ in HV subjects ranged from 13.3 to 19.5 days, mean CL/F ranged from 0.267 to 0.367 L/day and V/F ranged from 7.23 to 9.36 L. In Part 3b, mean t½ in SLE subjects ranged from 12.6 to 20.5 days with a mean CL/F of 0.455 to 0.485 L/day and a mean V/F of 5.93 and 12.8 L. Exposure (AUC and Cmax) for BIIB059 increased with dose in both HV and SLE subjects. However exposure in SLE subjects was approximately 40% lower compared to HV which could not be attributed to body weight differences. The observed mean accumulation ratio for AUC was slightly lower in SLE subjects (2.58) compared to HV (2.66) after BIIB059 SC administration. Complete BDCA2 internalisation was achieved at all dose levels, the duration of which was dose dependent, and similar for HV and SLE subjects. Reappearance of BDCA2 on circulating pDCs occurred when serum concentrations of BIIB059 dropped to <1 µg/mL. Single and multiple IV and SC doses of BIIB059 appeared to be well–tolerated in HV and SLE subjects.

Conclusions: BIIB059 was generally well tolerated. Exposure in SLE subjects was lower compared to HV while BDCA2 internalisation was similar. Based on the Phase 1 data, BIIB059 is currently evaluated in a Phase 2 trial (NCT02847598).

REFERENCES:
