Population pharmacokinetic/pharmacodynamic (PK/PD) Model for BIIB059, a Monoclonal Antibody (mAb) for the Treatment of Systemic and Cutaneous Lupus Erythematosus

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Objectives: BIIB059 (anti-blood dendritic cell antigen 2 [anti-BDCA2]) is a humanized immunoglobulin G1 (IgG1) mAb currently under development for treatment of Systemic (SLE) and Cutaneous Lupus Erythematosus (CLE). The objective of this work was to develop a population PK/PD model for BIIB059.

Methods: Phase 1 PK and PD data of adult healthy volunteers (HV, n=87) and SLE patients (n=22) were utilized for the development of the popPK/PD model. The data included single and multiple dosing of intravenous and subcutaneous BIIB059. BDCA2 (PD marker) levels on the surface of pDCs from all patients were used for the development of the popPD model. Different models, including indirect response (IDR) and target mediated drug disposition models were tested to describe the PD effect of BIIB059. Parameter estimation was conducted in NONMEM® 7.3.

Robustness and predictive ability of the PK/PD model was evaluated using a bootstrap analysis and Visual Predictive Checks (VPCs).

Results: A two-compartment popPK model with linear plus non-linear elimination was found to best describe the BIIB059 PK data. BDCA2 levels were best captured using an IDR model with stimulation of Kout (rate of elimination of BDCA2 on pDCs). CL/F in SLE subject was 25% higher compared to HV (6.87 vs 5.52 mL/hr). Weight was identified as the only other covariate to have statistically significant effect on CL/F and V/F of central compartment. The estimate of EC50 and Emax were 0.386 μg/mL and 10.2, respectively. No difference in EC50 and Emax was observed between SLE and HV. The popPK/PD model described the data accurately as evaluated using VPCs (n=500) and bootstraps (n=1000).

Conclusions: A popPK/PD model based on Phase 1 trial data was developed that describes the PK/PD profile of BIIB059 in HV and SLE patients well. The model will be utilized for dose selection for Phase 2 studies.