Development of a Non-Human Primate PK/PD Model of a Monoclonal Antibody for the Treatment of Systemic Lupus Erythematosus

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Objectives: Systemic Lupus Erythematosus (SLE) constitutes an auto-immune disease that affects approximately 1 in 2,000 individuals [1]. Although SLE is a widespread disease, only one new treatment has been approved by FDA since 1955 and therefore new, more targeted and effective therapies are needed. The objective of this work was to develop a nonhuman primate (NHP) pharmacokinetic/pharmacodynamic (PK/PD) model for a novel humanized monoclonal antibody (mAb), BIIB059, that targets the blood dendritic cell antigen 2 (BDCA2) on plasmacytoid dendritic cells and is currently under development for SLE treatment [2].

Methods: PK data from 19 cynomolgus monkeys were utilized for the development of the NHP PK model. These data were obtained from 3 different studies including single or multiple dosing, with BIIB059 administered intravenously or subcutaneously. BDAC2 receptor (PD marker) levels from 6 cynomolgus monkeys were used for the development of the NHP PD model, wherein both direct and indirect response models were evaluated. Parameter estimation was conducted in NONMEM 7.3.

Results: A two-compartment PK model with first order elimination was found to best describe the NHP BIIB059 data. BDCA2 levels were best captured using an indirect PD model with stimulation of the dissipation of the response. Despite the limited data availability, the PK/PD model described the data with reasonable accuracy.

Conclusions: A PK/PD model was built that describes the PK/PD profile of BIIB059 in NHP. Various approaches are now being tested [3,4] for scaling the NHP model to humans and will be validated against available PK/PD data from healthy subjects and SLE patients.

References: