Safety, Pharmacokinetics (PK) and Pharmacodynamics (PD) of Briquilimab after Single Subcutaneous (SC) Administration to Healthy Male and Female Participants

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Background: Briquilimab is an aglycosylated monoclonal antibody that binds to the cell-surface receptor c-Kit, also known as CD117, thereby inhibiting binding of stem cell factor and signaling through the receptor. Safety, PK and PD of briquilimab was evaluated in a double-blind, placebo-controlled study after single SC administration to healthy subjects.

Methods: Subjects received briqulimab at doses ranging from 0.2 mg to 280 mg SC or 5 mg IV. Blood samples were collected for PK and immunogenicity assessments. At dose levels ≥ 10 mg, pre- and post-dose punch biopsy was performed for determination of skin mast cell count. Safety assessments were based on laboratory tests and adverse events (AE).

Results: A total of 96 subjects (briquilimab (71), placebo (25)) were treated. Briquilimab serum exposure increased in a more-than dose proportional manner in the dose range evaluated. At dose levels ≥ 84 mg, consistent decrease in skin mast cell count was observed on Day 7 with further drop on Day 29 at higher dose levels; PD effect appeared to correlate with briquilimab exposure. Anti-briquilimab antibodies were observed in 10 subjects and 6 of these subjects were positive for neutralizing antibodies without any apparent effect on mast cell count. No deaths or serious AEs were reported. All AEs were mild or moderate. Nausea, upper respiratory tract infection, dizziness, back pain and lethargy were reported by ≥ 10% of subjects receiving briquilimab without a clear association with dose. Escalation to 420 mg was not implemented due to dysgeusia and apparent maximal PD effect at 280 mg.

Conclusion: Briquilimab was well tolerated, exhibited a favorable pharmacokinetic profile and a single SC dose was found to result in sustained inhibition of mast cell recruitment in a cutaneous wound model in healthy subjects. PK and PD profiles were used to support dose selection for clinical trials in CSU and CIndU.