Title: (13 words/limit of 15 words)

Briquilimab Is Well-Tolerated And Effectively Depletes Tissue Resident Mast Cells in Non-Human Primates

Authors: (7 authors/limit of 8 authors)

Song Eun Lee[1,*], Christopher Banfield[3,#] Jane R. Parnes[3], Mang Yu[1], Edwin Tucker[1], Hye-Sook Kwon[1], Wendy W. Pang[1]

[1]Jasper Therapeutics, Inc., Redwood City, CA 94065, USA.

[2]Division of Allergy and Immunology, University of South Florida, Tampa, Florida, USA

[3]Early Development, Amgen, Thousand Oaks, Californica, USA

*Presenting author

[#]Present address: CB Pharma Consulting Services LLC, Woburn, Massachusetts, USA

Body (247 words/250 words limit)

Introduction: Mast cells (MCs) are key players in many allergic and other inflammatory diseases. Briquilimab is a monoclonal antibody that binds to c-Kit, and blocks SCF to prevent c-Kit activation and signaling, leading to MC apoptosis and depletion. We evaluated briquilimab pharmacokinetics (PK), pharmacodynamics (PD), and safety in non-human primates (NHPs).

Methods: African Green monkeys (AGMs) were administered subcutaneous (SC) single- (0.1 to 10 mg/kg) or repeat-dose (0.3 to 3 mg/kg, weekly for 4 weeks) of briquilimab for PK and PD assessments. GLP-compliant toxicology studies were evaluated in cynomolgus monkeys administered 1- and 6-month weekly (1 to 300 mg/kg/dose) briquilimab SC. Clinical changes and MC depletion were monitored.

Results: After single administration of briquilimab in AGMs, non-linear, dose-dependent clearance of briquilimab and dose-dependent reduction of MC numbers in the colon submucosa and MC recruitment adjacent to wounded skin were observed. Dose-dependent decreases in colon submucosal MCs, interstitial and peribronchial lung MCs, and dermal MCs migrating into adjacent wounded skin were also observed after repeat dosing of briquilimab in AGMs. **C**hronic, high dosing of briquilimab in cynomolgus monkeys was well-tolerated with no significant changes in body weight, clinical chemistry, ophthalmology, electrocardiography, respiratory or neurological function. Transient and reversible reductions in reticulocyte count, red cell mass, and testis and epididymis weights were observed, while no microscopic abnormalities were noted among the female reproductive tissues. Further, there were no correlative bone marrow cytologic findings.

Conclusion: Briquilimab was well-tolerated at weekly SC doses up to 300 mg/kg and significantly depleted tissue resident MCs in NHPs.