

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

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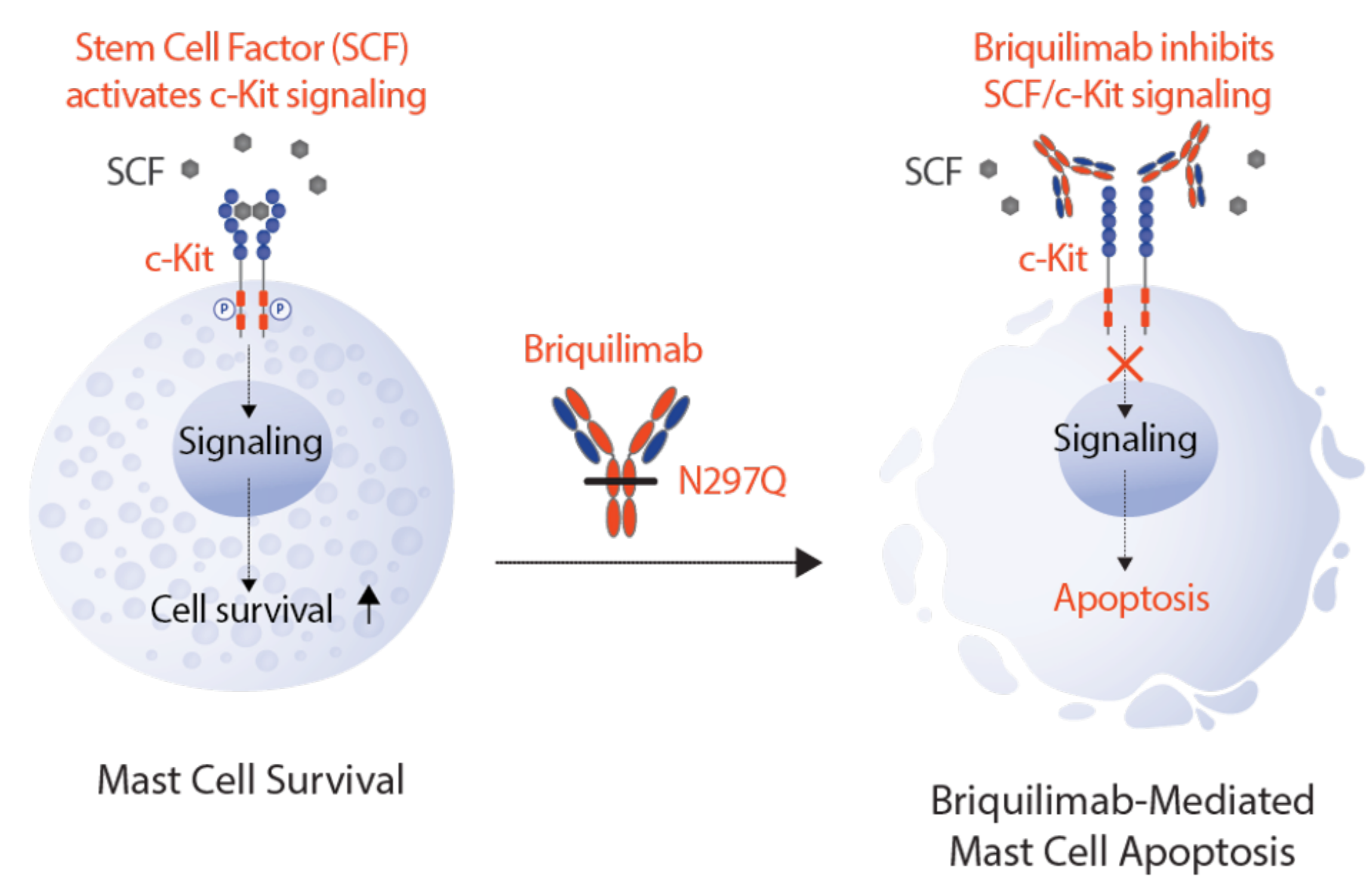
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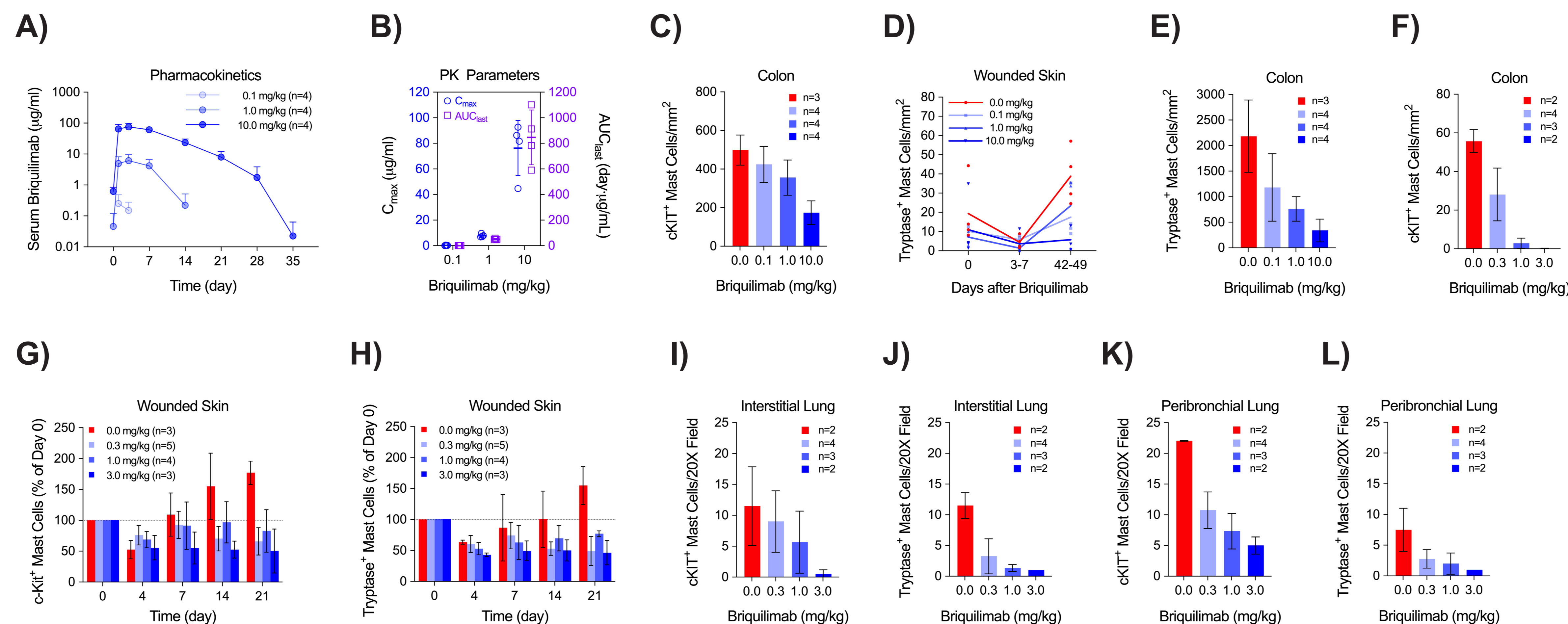
## INTRODUCTION

- Mast cells (MCs) are key players in many allergic and other inflammatory diseases
- Mast cell activation and survival relies on stem cell factor (SCF)/c-Kit signaling
- Briquilimab is a monoclonal antibody that binds to c-Kit and blocks SCF to inhibit 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)



**Figure 1. SCF/c-Kit signaling is essential for mast cell activation and survival.** Briquilimab blocks SCF ligand-binding to c-Kit, inhibits SCF/c-Kit signaling, and induces MC apoptosis.

## RESULTS



**Figure 2. Briquilimab depletes MCs in various tissues of NHPs.**

After single administration of 1 or 10 mg/kg briquilimab in AGMs, (A,B) non-linear, dose-dependent clearance of briquilimab, and (C-E) dose-dependent reduction of MC numbers in the colon submucosa (49 days post-briquilimab) and MC recruitment adjacent to wounded skin (42-49 days post-briquilimab) were observed, even after serum briquilimab has been cleared. After repeat dosing of briquilimab once weekly for 4 weeks (0.3, 1, or 3 mg/kg) in AGMs, (F-L) dose-dependent decreases in colon submucosal MCs, interstitial and peribronchial lung MCs, and dermal MCs migrating into adjacent wounded skin were also observed.

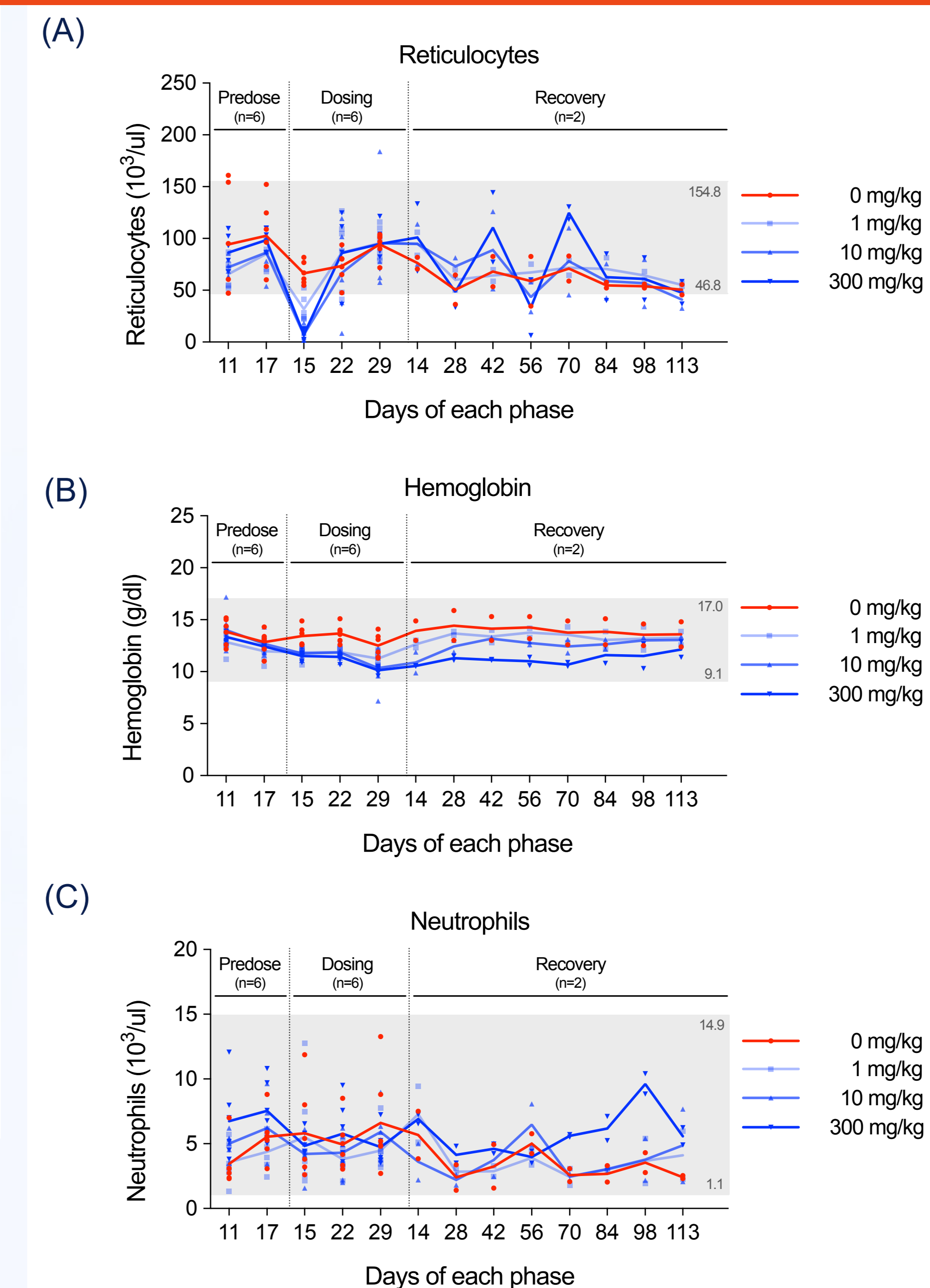
## METHODS

Briquilimab was evaluated in the following studies in NHPs:

- Non-GLP studies in African Green monkeys (AGMs)
  - Subcutaneous (SC) single-dose (0.1 to 10 mg/kg)
  - SC Repeat-dose (0.3 to 3 mg/kg, weekly for 4 weeks)
- GLP-compliant toxicology studies in cynomolgus monkeys
  - SC 1-month weekly (1 to 300 mg/kg/dose)
  - SC 6-month weekly (1 to 300 mg/kg/dose)

## CONCLUSION

- Briquilimab was well-tolerated at weekly SC doses up to 300 mg/kg for 6 months and significantly depleted tissue resident MCs in colon, lung, and wounded skin of NHPs
- In NHPs following initiation of weekly briquilimab dosing up to 300 mg/kg for 1 month, a decrease in peripheral blood reticulocytes was observed within a week, which recovered during the dosing period. Hemoglobin and neutrophils remained within the normal range during and after chronic briquilimab dosing
- Chronic high dosing of briquilimab in NHPs showed no significant changes in body weight, clinical chemistry, ophthalmology, electrocardiography, respiratory or neurological function. Transient and reversible reductions in 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. Additional studies may be warranted
- Jasper is actively enrolling participants in a phase 1b/2a trial evaluating briquilimab in patients with chronic spontaneous urticaria (BEACON trial, NCT06162728) and in patients with chronic inducible urticaria (SPOTLIGHT trial, NCT06353971), and will commence enrolling participants for the proof-of-concept Phase 1b/2a asthma challenge study evaluating briquilimab in asthma



**Figure 3. Briquilimab is generally well-tolerated in NHPs.**

(A) Administration of briquilimab SC once weekly to cynomolgus monkeys for 1 month at 1, 10, and 300 mg/kg/dose is well-tolerated in both sexes (female data shown). Briquilimab at all doses results in a transient decrease in absolute reticulocyte count at Day 15 of the dosing phase, which recovered during the dosing period. (B) A mild to moderate decrease (6 to 10% decrease from predose levels for 1 mg/kg/dose and 14 to 19% for 10 and 300 mg/kg/doses, respectively) in red cell mass (hemoglobin levels shown as representative data) were observed. (C) White blood cell (neutrophil) counts are also maintained within the normal hematological reference range of cynomolgus monkeys. Shaded gray area represents normal range.