Safety, Tolerability, and PK of SM17 in Healthy Volunteers, a Novel IL-17 Receptor B Targeting Antibody in Phase I Development for the Treatment of Asthma

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BACKGROUND:

- SM17 is a novel humanized monoclonal antibody against the alarmin cytokine receptor, IL-17RB, being developed for the treatment of asthma.
- In an animal model of asthma, SM17 demonstrated beneficial effects in improving allergic asthma (Xu et al.), which supported the clinical development of SM17.

METHODS:

- A randomized, double-blinded, placebo-controlled, dose-escalation study evaluated the safety, PK, and immunogenicity of IV doses of SM17 in healthy volunteers (HVs).
- In Part A, HVs (n=53) received a single IV dose of SM17 (2, 20, 70, 200, 400, 600, 1200 mg) or placebo.
- In Part B, HVs (n=24) received multiple IV doses of SM17 (200, 400, 600 mg) or placebo every 2 weeks (Q2W) for a total of 3 doses.

RESULTS:

- ***Part A PK:*** Total exposure ($AUC_{0\text{-}inf}$) increased by ~180-fold across 20 mg to 1200 mg SM17.
- ***Part B PK:*** Over 4 weeks (3 x Q2W), AUC_T increased by ~3-fold across 200 mg to 600 mg SM17, in a dose-proportional manner. Mean accumulation ratios over 200-600 mg were 1.5 to 2.1, which confirms moderate accumulation of SM17.
- ***Safety:*** The most frequently reported treatment-emergent adverse event (AE) was headache and there were no drug-related serious AEs observed.
- ***Immunogenicity:*** Anti-drug antibodies (ADAs) for SM17 were detected in 8 and 3 participants receiving SM17 in Part A and Part B, respectively. No trends in positive ADA response was observed.

SM17, a *first-in-class* IL-17RB-targeting monoclonal antibody, in development to treat *asthma*, was well tolerated following single and multiple IV doses in a first-in-human healthy volunteer study

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Xu et al., 2024 Evaluation of the safety, tolerability, pharmacokinetics and pharmacodynamics of SM17 in healthy volunteers: results from pre-clinical models and a first-in-human, randomized, double blinded clinical trial. Front. Immunol. 15:1495540

Figure 1. Proposed SM17 Mechanism

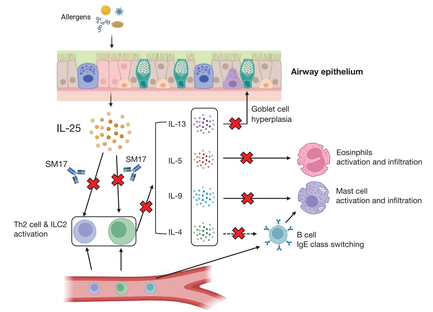
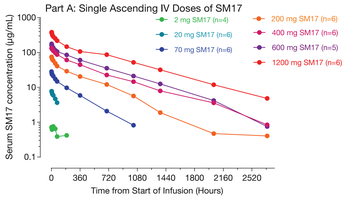
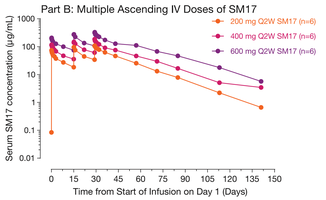


Figure 2. Semi-Log Serum SM17 vs. Time





CONCLUSION:

- After single doses, $AUC_{0\text{-}inf}$ increased in a greater than dose-proportional manner from 2-1200 mg SM17.
- After 3 x Q2W doses, AUC_T increased dose-proportionally from 200-600 mg SM17.
- A Phase Ib clinical trial investigating SM17 for moderate-to-severe atopic dermatitis in Chinese patients is currently ongoing with topline results expected to be disclosed in Q2 2025.

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