**Prolonged half-life and sustained inhibition of key inflammatory biomarkers: a phase 1 study of APG777, a high-affinity humanized IgG1 monoclonal antibody targeting IL-13**

Xiu Qin Lim¹, Erica Winter², Kristine Nograles², Sai Thankamony², Lukas Dillinger², Carl Dambkowski²

¹CMAX Clinical Research, Adelaide, SA, Australia; ²Apogee Therapeutics, Inc., Waltham, MA, USA

**Introduction:**
APG777 is a high-affinity humanized anti-IL-13 IgG1 monoclonal antibody (mAb) that blocks formation of the IL-13/IL-13Rα1/IL-4Rα complex, preventing receptor heterodimerization and downstream signaling. APG777 contains a triple amino acid modification, YTE, in the Fc region that extends half-life ($t_{1/2}$) by increasing binding to neonatal Fc receptor.

**Objectives:**
This is a report of initial results of the first study of APG777 in humans, including safety, pharmacokinetics (PK), and pharmacodynamics (PD).

**Methods:**
This first-in-human, randomized, double-blind, placebo (PBO)-controlled trial evaluated safety, tolerability, PK, and PD of APG777 in healthy participants. The study was conducted in Australia and consisted of single ascending dose (SAD) and multiple dose (MD) cohorts. Participants received single subcutaneous (SC) doses up to 1200 mg in the SAD and repeat doses of 300 mg SC in the MD. Each cohort consisted of 8 participants randomized 6:2 to APG777 or PBO. Safety assessments were conducted throughout the study and blood draws for PK and PD were obtained at multiple timepoints.

**Results:**
Forty participants were enrolled. To date, adverse events (AEs) were mild and generally unrelated to study drug. There were no serious AEs or dose-dependent trends. APG777 pharmacokinetics were dose proportional, with $t_{1/2}$ of approximately 75 days (Figure 1). Single doses of APG777 resulted in sustained inhibition of pSTAT6 and TARC for 12 weeks, the longest available follow-up.
Figure 1. APG777 single dose concentration-time profile

Conclusions: APG777 was well-tolerated at doses up to 1200 mg, similar to other IL-13-targeted mAbs. The t_{1/2} of APG777, due to its YTE modification, is approximately 3 times longer than currently available mAbs and PD assessments confirm sustained inhibition of key biomarkers of atopic dermatitis. The favorable safety profile and optimized PK of APG777 support the initiation of a phase 2 study in adults with moderate-to-severe atopic dermatitis where every 3- to 6-month maintenance dosing will be evaluated.

Keywords: APG777, biologic, therapy

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