Clinical Efficacy, Safety, and Pharmacokinetic Profile of Bosakitug (BSI-045B), an Anti-Thymic Stromal Lymphopoietin (TSLP) mAb in a Phase 2 Study of Moderate and Severe Atopic Dermatitis Subjects

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Introduction/Background: Bosakitug (BSI-045B) is a humanized monoclonal antibody targeting thymic stromal lymphopoietin (TSLP) which is a master regulator of type 2 (Th2) immune responses at the barrier surfaces of skin and the respiratory/gastrointestinal tract. The expression of TSLP is elevated in individuals with atopic diseases such as atopic dermatitis (AD). Herein, we describe the clinical efficacy, safety, and pharmacokinetic results of bosakitug from a phase 2a study in moderate to severe AD subjects (ADAMANT).

Objectives: To evaluate the safety, clinical efficacy, pharmacokinetic characteristics, and immunogenicity (ADA) of monotherapy bosakitug injection in AD subjects.

Methods: Each enrolled AD subject received 300 mg of bosakitug subcutaneous injection weekly for 4 weeks and then every 2 weeks thereafter through 23 weeks of treatment. Following the treatment phase, subjects are followed for 12 weeks. Eczema Area and Severity Index (EASI), Investigator’s Global Assessment (IGA), and Peak Pruritus Numerical Rating Scale
(PPNRS) score were measured at baseline and at each study visit to assess clinical efficacy.

Pharmacokinetic, pharmacodynamic, and ADA samples were collected at pre-dose, at each study visit and, if necessary, at the time of early withdrawal of study drug.

**Results:** Twenty-two subjects with moderate and severe disease were enrolled into the trial. Baseline mean scores for the cohort were EASI of 17.5, IGA of 3.05, and PP-NRS of 6.5. At week 23, with 18 evaluable participants completing the dosing phase of the study, 79% of the AD subjects achieved an IGA 0/1, 89% achieved an EASI-75, 44% achieved an EASI-90 and 28% achieved an EASI-100. The mean PP-NRS score decreased by ~3 points through the end of the dosing period. The mean percentage change from baseline in EASI score showed continual improvement beyond week 23. By week 31, the five subjects who had reached eight weeks following their last dose, exhibited an EASI score reduction of 93% from baseline. One subject became pregnant after 7 doses at which time drug treatment was discontinued. The individual had already attained a 98% response in EASI score at that time. After 6 months post treatment the individual continues to maintain bosakitug exposure and an EASI response of 82%. A summary of the safety profile of bosakitug includes 19 AEs in 9 subjects during study treatment, all were of grade 1 except one of vertigo (grade 2); 16 subjects reported injection site reactions; and headache was the most common AE (4 cases in 4 subjects). No SAEs occurred. None of the 22 subjects exhibited a positive ADA response.

**Conclusions:** The efficacy profile exhibited by bosakitug, with 79% of AD subjects achieving an IGA 0 or 1 and almost 90% of subjects showing 75% skin clearance is quite striking, especially as monotherapy. The 44 and 28% of subjects that achieved EASI-90 and EASI-100, respectively, also shows the high efficacious potential of bosakitug. In this phase 2a proof-of-
concept study the dosing regimen was chosen to mimic the dupilumab dosing regimen in AD subjects to be able to compare efficacy and safety directly. Bosakitug’s substantially higher efficacy, as exhibited by 78% of subjects achieving an IGA 0/1, underscore its competitiveness to dupilumab and its potential as a first-in-class treatment for AD. The sustained concentration of bosakitug, due to its long half-life, and the continued efficacy after the last dose provides a good possibility that bosakitug could be administered at extended dosing intervals. Bosakitug’s impressive efficacy and safety profile, in conjunction with the opportunity for much longer dosing intervals than established therapies support further clinical development of bosakitug in a phase 2b, randomized, blinded, dose-finding trial in moderate to severe AD subjects.

**Keywords:** TSLP, EASI-75, IGA 0/1, Atopic Dermatitis, ADAMANT, NCT05932654