SPOTLIGHT: A Phase 1b/2a, Dose Escalation Trial of Safety, Pharmacokinetic/Pharmacodynamic and Preliminary Clinical Activity of Briquilimab in Adult Patients with Chronic Inducible Urticaria (CIndU) Who Remain Symptomatic Despite Treatment with H1-Antihistamines

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Background: Chronic inducible urticaria (CIndU) is characterized by recurring itchy wheals and/or angioedema for longer than six weeks. Lesion development is driven by mast cell (MC) degranulation in response to specific and definite triggers such as cold, heat or pressure. The two most common forms of CIndU are symptomatic dermographism (SD) and cold contact urticaria (ColdU), the most severe urticaria disease, with systemic involvement leading to anaphylaxis in some cases.
The primary treatment for CIndU is avoidance of specific triggers. As this, in many cases, is not possible, symptom-directed drug therapy is often recommended. Treatment mainstay is second-generation antihistamines, at standard or higher doses, and is often not sufficient to control the symtoms of CIndU. There are no other approved treatments for CIndU and there is a clear and significant need for new treatment options.

Given the significant role of MCs in CIndU, the development of novel therapies that deplete skin MCs offers a new treatment modality. Briquilimab is an aglycosylated monoclonal antibody that binds to the MC-surface receptor c-Kit, also known as CD117, thereby inhibiting binding of stem cell factor and signaling through the receptor, initiating MC apoptosis. Therefore, briquilimab, has therapeutic potential for treatment-refractory CIndU.

Trial Design:

This is an open-label, single ascending dose Phase 1b/2a trial to assess safety, tolerability and preliminary efficacy of briquilimab, administered subcutaneously (SC), in adult participants with ColdU or SD, who remain symptomatic despite treatment with H1 antihistamines.

Endpoints:

Safety and tolerability: Review of laboratory data (hematology, clinical chemistry, urinalysis), physical examinations, vital signs, ECG, reports of treatment emergent adverse events (TEAEs)

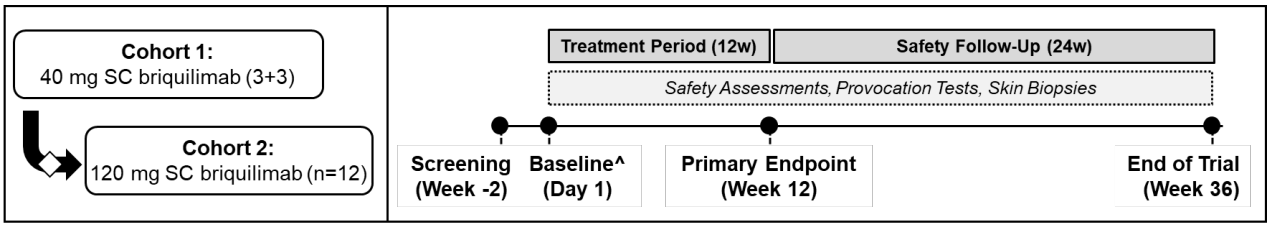
Pharmacokinetics: Cmax, tmax and AUClast

Preliminary Efficacy: Change from baseline to Week 12 in provocation testing scores (TempTest® for ColdU and FricTest® for SD) and Urticaria Control Test (UCT).

Pharmacodynamics: Serum tryptase

Conclusions: This single ascending dose trial will provide important information on the safety, tolerability and preliminary efficacy of briquilimab in treatment-refractory CIndU and inform potential future clinical trials on dosing and dosing schedules.

Figure 1: Trial Design



◇ DLT Assessment

^ Patient Dosing on Day 1