Interim analysis results from a Proof-of-Concept study for ASLAN004 in adult moderate-to-severe atopic dermatitis: a double blind, randomized, placebo-controlled study

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Synopsis

- ASLAN004 is a fully human mAb with a novel mechanism of action that binds with high affinity to IL-13Rα1 and specifically inhibits both IL-4 and IL-13 signaling via the Type 2 cytokine receptor, an important biologic target in atopic dermatitis (AD).
- Results from a single-ascending dose study (SAD) helped elucidate the pharmacokinetic and pharmacodynamic profile of ASLAN004 and demonstrated that the molecule was well tolerated with no adverse events that led to study discontinuation in healthy male subjects.
- Here, we present an interim analysis of a ASLAN004-002, a multiple-ascending dose (MAD)/Proof-of-Concept study (NCT04090229).

Objective

- To evaluate the emerging safety, tolerability, and efficacy of ASLAN004 in a multiple-ascending dose escalation phase in patients with moderate-to-severe AD.

Methodology

- 25 adult patients with moderate-to-severe AD were recruited from the US, Australia and Singapore and randomized 3:1 in 3 cohorts to receive once weekly 200, 400 or 600 mg of subcutaneous ASLAN004 or matching placebo over 8 weeks, with a 12-week recovery period (Study design: Figure 1).
- An interim data readout was conducted after Cohorts 1–3 completed 8 weeks of treatment to evaluate various clinical endpoints in a limited number of patients before conducting an expansion cohort (Cohort 4, results reported elsewhere).
- Endpoints in the interim data readout include change from baseline in Eczema Area Severity Index (EASI) score at week 8 and safety assessments including local tolerability and incidence of adverse events (AEs). (NCT04090229)

Results

- Selected baseline demographics and disease characteristics at study entry are shown in Table 1, with details of the study recruitment illustrated in Figure 2.
- The mean ± SD (n=18) baseline scores were 32.5±11.8 for EASI and 44% had severe Investigator Global Assessment (IGA) scores.
- At week 8, mean reductions in EASI from baseline were 50%, 74% and 76% for the 200 mg (n=4), 400 mg (n=6) and 600 mg (n=3) ASLAN004 dose groups respectively, compared with 42% (n=5) for placebo (Figure 3a and 3b).
- Mean reductions of peak pruritus from baseline to week 8 were 34%, 48% and 39% for 200 mg (n=4), 400 mg (n=6) and 600 mg (n=2) ASLAN004 dose groups respectively, compared with 16% for placebo (n=5) (Figure 4a and 4b).
- Other secondary endpoints were also improved for ASLAN004 compared with placebo (EASI-50, EASI-75; reported elsewhere).
- The proportion of patients with AEs and treatment-emergent adverse events (TEAEs) were similar across ASLAN004 treatment and placebo arms (Table 2). There were no TEAEs leading to discontinuation in the ASLAN004 treatment groups.
- Only 1 severe adverse event was reported in the study (mild abdominal pain, 400 mg), considered unrelated to treatment.

Conclusion

- ASLAN004 was well tolerated, with 400mg and 600mg showing promising efficacy in adults with moderate-to-severe AD.

Acknowledgments

- ASLAN Pharmaceuticals Pte Ltd was the sponsor of this study and would like to acknowledge the investigators and patients who contributed.

Figure 1. ASLAN004-002 study design

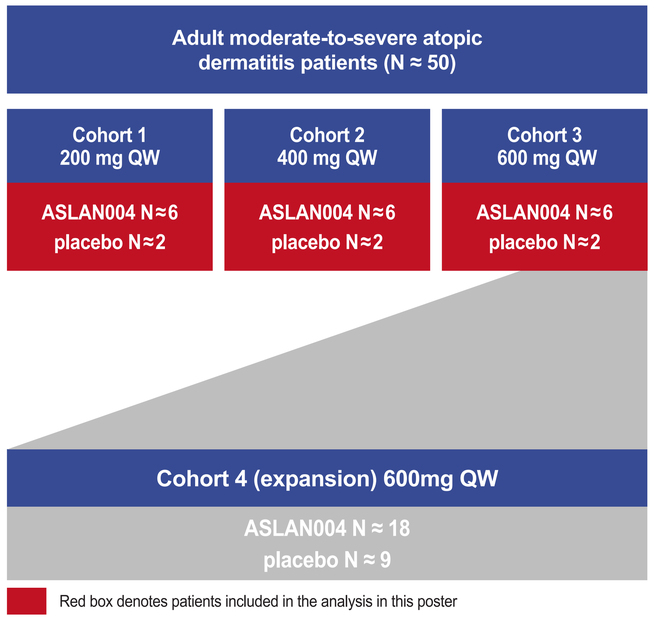
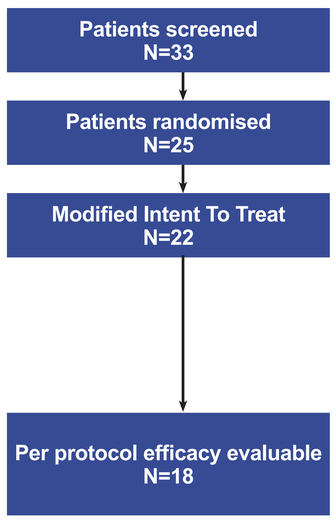


Figure 2. Study recruitment



3 patients discontinued study due to restrictions imposed in response to COVID-19

4 patients did not complete minimum 29 days treatment / assessment required to be evaluable

- 2 patients withdrew due to flare or lack of improvement of disease symptoms
- 1 patient had an SAE unlikely related to treatment (mild abdominal pain)
- 1 patient due to protocol deviation (did not meet recruitment eligibility criteria)

Criteria

- Chronic AD present for ≥3 years before screening visit
- EASI score ≥16 at screening and baseline
- IGA score ≥3 (scale of 0 to 4) at screening and baseline
- ≥10% body surface area (BSA) of AD involvement at screening and baseline

Table 1. Selected baseline demographics and disease characteristics

Per protocol efficacy evaluable (N=18)	200mg (N=4)	400mg (N=6)	600mg (N=3)	Placebo (N=5)
Age (years)	32.5 (±5.3)	28.3 (±4.3)	42.0 (±22.9)	33.8 (±15.8)
Mean EASI score	32.9 (±14.3)	30.9 (±13.4)	32.5 (±15.2)	33.9 (±9.5)
Mean BMI	25.8 (±2.9)	25.4 (5.6)	24.2 (±8.8)	25.4 (±6.6)
Patients with IGA 3 / IGA 4	50 / 50 %	83 / 17 %	33 / 67 %	40 / 60 %
Mean BSA	55.5 (±34.6) %	59.8 (±30.4) %	56.3 (±36.3) %	59.8 (±31.8) %
Mean peak pruritus NRS score	7.4 (±2.2)	7.3 (±1.3)	6.4*	7.4 (±1.4)

*N=2 as one subject did not have a baseline value

Table 2. TEAEs by category

Treatment Emergent Adverse Event (TEAE) by category	200mg (N=5)	400mg (N=8)	600mg (N=5)	All doses (N=18)	Placebo (N=7)
Any	5 (100%)	8 (100%)	3 (60%)	16 (88.9%)	5 (71.4%)
Related	5 (100%)	6 (75.0%)	2 (40.0%)	13 (72.2%)	5 (71.4%)
Moderate/Severe	2 (40.0%)	2 (25.0%)	1 (20.0%)	5 (27.8%)	3 (42.9%)
Serious adverse event (SAE)	0 (0%)	1 (12.5%)	0 (0%)	1 (5.6%)	0 (0%)
Drug-related AEs of Interest:					
Injection site reaction	1 (20.0%)	3 (37.5%)	0 (0%)	4 (22.2%)	2 (28.6%)
Conjunctivitis	0 (0%)	1 (12.5%)	1 (20.0%)	2 (11.1%)	0 (0%)

- There were no drug-related TEAEs that led to discontinuation.
- SAE was mild abdominal pain, classified as unlikely related.
- Conjunctivitis was classified as mild. Patients had prior history of allergy or allergic conjunctivitis.

Figure 3a. EASI mean change from baseline

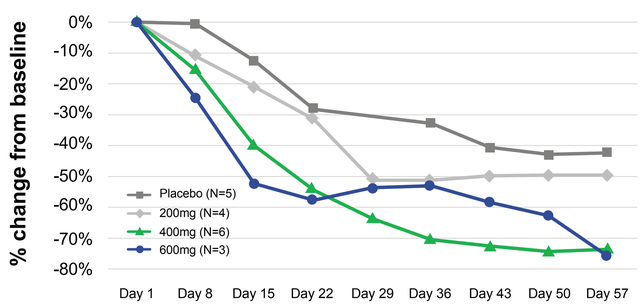


Figure 3b. EASI mean % change from baseline at week 8

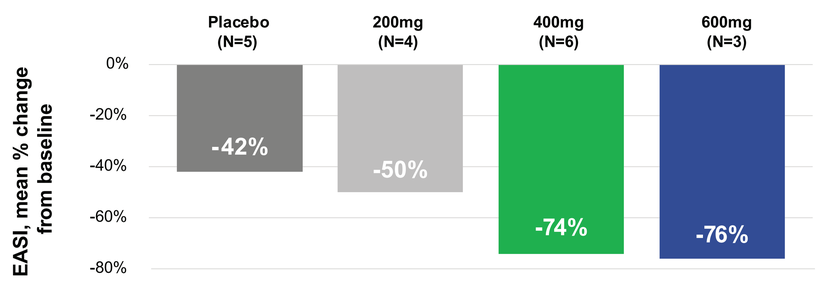


Figure 4a. Peak P-NRS % change from baseline

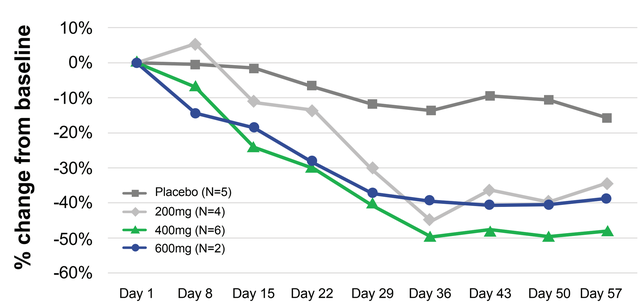
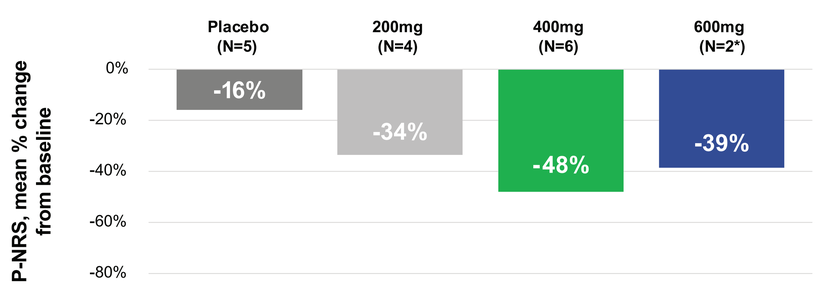


Figure 4b. Peak P-NRS % change from baseline at week 8



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