Interim safety results of amlitelimab (anti-OX40 ligand antibody) in participants with moderate-to-severe atopic dermatitis from the RIVER-AD Phase 2/3 ongoing open-label study

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Key Conclusions

1. This interim safety analysis of RIVER-AD included 249 participants who were previously enrolled in STREAM-AD with a cumulative exposure of 185.7 patient-years
2. Interim safety analysis of RIVER-AD showed amlitelimab was well tolerated, consistent with what was previously reported in the parent study, STREAM-AD
3. Ongoing trials, including the OCEANA Phase 3 trials and long-term extension studies (ATLANTIS and ESTUARY), will provide additional long-term safety data

Introduction

- Amlitelimab (SAR445229) is a fully human nondepleting anti-OX40 ligand monoclonal antibody[1,2]
- In the Phase 2b STREAM-AD (NCT05131477) study in participants with moderate-to-severe AD:[2]
  - The primary endpoint was met (percentage change in EASI score at Week 16); the efficacy and safety of amlitelimab was observed at Week 24 (Part 1)
  - The durability of response in clinical responders (defined as those achieving ≥75% reduction in EASI score [EASI-75] and/or IGA 0/1) and safety on and off therapy was observed at Week 52 (Part 2)
- Participants with moderate-to-severe AD from STREAM-AD[3] and other amlitelimab AD clinical trials are eligible to enter RIVER-AD[4]

Objective

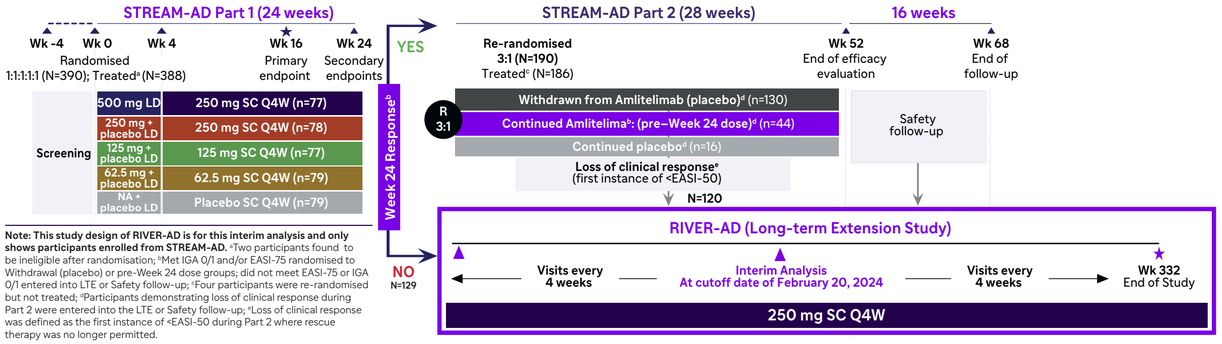
- To report the interim safety results of amlitelimab in RIVER-AD for participants previously enrolled in STREAM-AD, from the date the first participant enrolled, August 22, 2022, to the cutoff date of February 20, 2024

Methods

Study Design

- RIVER-AD (NCT05492578) is an ongoing Phase 2/3, open-label, 332-week extension study evaluating the long-term safety and efficacy of amlitelimab (**Figure 1**)
- This interim safety analysis with a cutoff date of February 20, 2024, **only includes participants** who previously enrolled in STREAM-AD and then entered RIVER-AD
- All participants received amlitelimab 250 mg SC Q4W in RIVER-AD

Figure 1. Study Design of STREAM-AD (NCT05131477) and RIVER-AD (NCT05492578)



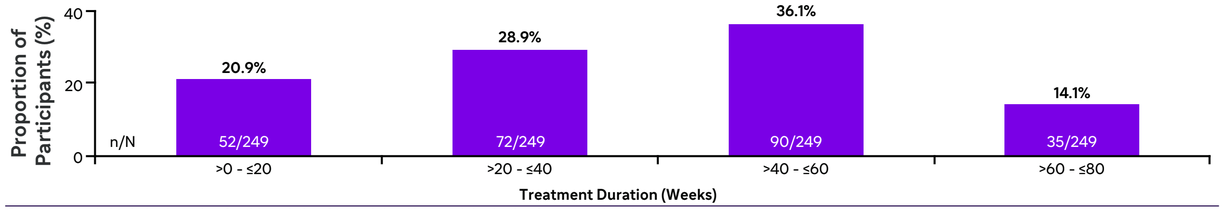
Note: This study design of RIVER-AD is for this interim analysis and only shows participants enrolled from STREAM-AD. [a]Two participants found to be ineligible after randomisation; [b]Met IGA 0/1 and/or EASI-75 randomised to Withdrawal (placebo) or pre-Week 24 dose groups; did not meet EASI-75 or IGA 0/1 entered into LTE or Safety follow-up; [c]Four participants were re-randomised but not treated; [d]Participants demonstrating loss of clinical response during Part 2 were entered into the LTE or Safety follow-up; [e]Loss of clinical response was defined as the first instance of <EASI-50 during Part 2 where rescue therapy was no longer permitted.

Results

Baseline Exposure

- This interim analysis of RIVER-AD included 249 participants previously enrolled in the STREAM-AD study (N=129, STREAM-AD Week 24 nonresponders; N=120, STREAM-AD Part 2 participants with loss of response or those who completed the study)
- The cumulative exposure was 185.7 patient-years
- The median treatment duration was 282.0 days (range: 28-548 days), with treatment duration by category shown in **Figure 2**

Figure 2. Duration of Study Treatment by Category[a]



[a]Percentages are calculated using the number of participants in the safety population with a non-missing duration of exposure as denominator.

Interim Safety Summary of RIVER-AD

	Participants with ≥1 event, n (%)	nP/PYR (nP/100 PYR)
TEAE	144 (57.8)	144/100.6 (143.1)
Treatment-emergent SAE[a]	4 (1.6)	4/178.6 (2.2)
TEAE leading to death	0	0/179.7
TEAE leading to discontinuation	4 (1.6)	4/178.5 (2.2)
AESI	6 (2.4)	6/176.9 (3.4)

Note: nP/100 PYR is the number of participants with at least one event per 100 patient-years at risk (PYR). PYR is calculated as the time from first dosing of amlitelimab to the initial occurrence of an event or end of follow-up/data cutoff (minimum of last IMP date +140 days, end of study date, cutoff date) for those without any event.
The cutoff date for this interim analysis was February 20, 2024. [a]SAEs included urinary tract infection, anaphylactic reaction (not related to amlitelimab administration, per Investigator), nasal septum deviation, and atopic dermatitis (n=1 each).

Most Commonly Reported TEAEs (Occurring in ≥5% of Participants)

	Participant with ≥1 event, n (%)	nP/PYR (nP/100 PYR)
Nasopharyngitis	28 (11.2)	28/167.6 (16.7)
Upper Respiratory Tract Infection	18 (7.2)	18/169.0 (10.6)
Dermatitis Atopic	25 (10.0)	25/166.1 (15.1)

Note: nP/100 PYR is the number of participants with at least one event per 100 patient-years at risk (PYR). PYR is calculated as the time from first dosing of amlitelimab to the initial occurrence of an event or end of follow-up/data cutoff (minimum of last IMP date +140 days, end of study date, cutoff date) for those without any event.
The cutoff date for this interim analysis was February 20, 2024.

References

1. Weidinger S, et al. *Br J Dermatol*. 2023;189(5):531-539; **2.** Weidinger S, et al. *J Allergy Clin Immunol*. 2025;155(4):1264-1275; **3.** ClinicalTrials.gov identifier: NCT05131477. Accessed August 20, 2025. clinicaltrials.gov/ct2/show/NCT05131477; **4.** ClinicalTrials.gov identifier: NCT05492578. Accessed August 20, 2025. clinicaltrials.gov/ct2/show/NCT05492578.

Abbreviations

AD, atopic dermatitis; AE, adverse event; AESI, adverse event of special interest; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; IMP, investigational medicinal product; LD, loading dose; LTE, long-term extension; NA, not applicable; nP/100 PYR, number of participants with ≥1 event per 100 patient-years at risk; Q4W, every 4 weeks; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event; Wk, week.

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Disclosures

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