LONG-TERM SAFETY, EFFICACY, AND QUALITY OF LIFE (QOL) OF NAVENIBART IN HEREDITARY ANGIOEDEMA (HAE): INITIAL RESULTS FROM ALPHA-SOLAR

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SUMMARY

1 THE INITIAL COHORT OF 16 PARTICIPANTS FROM ALPHA-STAR ENROLLED INTO THE ONGOING ALPHA-SOLAR EXTENSION, PROVIDING A COMBINED MEAN FOLLOW-UP OF ~17 MONTHS, NAVENIBART WAS WELL TOLERATED AND THE SAFETY PROFILE WAS FAVORABLE.

2 IN ALPHA-SOLAR, NAVENIBART SHOWED AN OVERALL MONTHLY REDUCTION OF 92% IN MEAN HAE ATTACK RATE AFTER A MEAN FOLLOW-UP OF 10.1 MONTHS.

3 NAVENIBART CONTINUES TO DEMONSTRATE FAVORABLE SAFETY AND DURABLE EFFICACY FOR PATIENTS WITH HAE. Q3M AND Q6M REGIMENS ARE BEING EVALUATED IN AN ONGOING PIVOTAL PHASE 3 TRIAL, ALPHA-ORBIT (NCT06842823).

4 IN ALPHA-SOLAR, CLINICALLY MEANINGFUL IMPROVEMENTS IN AE-QoL SCORES WERE OBSERVED ACROSS ALL DOMAINS, WITH MEAN REDUCTIONS EXCEEDING THE 6-POINT MCID THRESHOLD, REFLECTING IMPROVED DAILY FUNCTIONING AND WELL-BEING.

OBJECTIVE

To evaluate the long-term safety and effectiveness of navenibart in patients with hereditary angioedema (HAE) across the Phase 1b/2 ALPHA-STAR trial and its long-term extension, ALPHA-SOLAR.

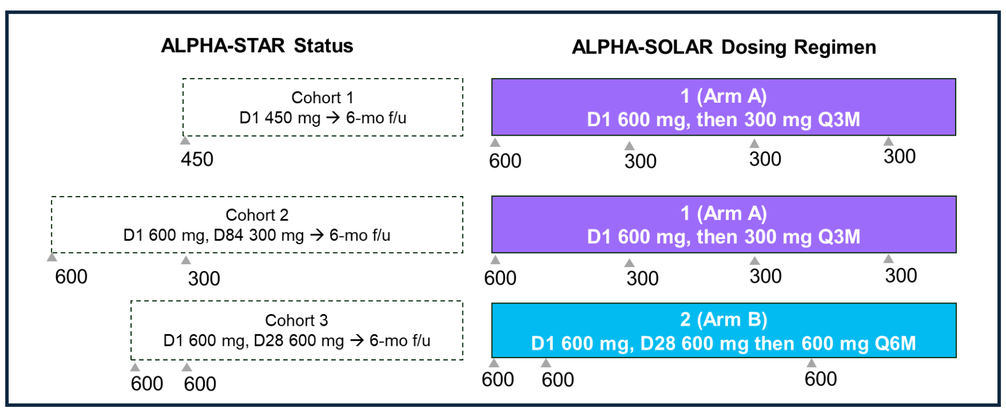
INTRODUCTION

- HAE is a rare, autosomal dominant disease associated with dysregulation of the kallikrein-kinin system with unpredictable and debilitating attacks of angioedema.
- Navenibart is a novel investigational therapeutic monoclonal antibody inhibitor of plasma kallikrein with extended half-life.
- Here, we report the initial results from ALPHA-SOLAR, an ongoing Phase 2 long-term open-label trial (NCT06007677), combined with ALPHA-STAR, a Phase 1b/2 trial (NCT05695248), with navenibart in participants with HAE.

METHODS

- ALPHA-SOLAR is a long-term open-label extension trial for participants who completed the ALPHA-STAR Phase 1b/2 trial (**Figure 1**). The current analysis includes data from rollover participants from ALPHA-STAR who continued treatment in ALPHA-SOLAR.
- The primary endpoint was the incidence of treatment-emergent adverse events (TEAEs) evaluated in the combined ALPHA-STAR and ALPHA-SOLAR population.
- Secondary endpoints included efficacy assessments evaluated in ALPHA-SOLAR.
- This initial analysis was performed once participants had achieved approximately 12-18 months of follow-up since the start of ALPHA-STAR and 6-12 months since the start of ALPHA-SOLAR. Participation in ALPHA-SOLAR may continue for up to 5 years.

Figure 1. ALPHA-SOLAR Clinical Trial Design



RESULTS

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

- All 16 participants in the initial cohort completed ALPHA-STAR and enrolled in ALPHA-SOLAR.
- The overall mean (SD) age was 46 (20) years, and 9 (56%) were female (**Table 1**).
- The mean (median) duration of follow-up is 17.4 (17.1) months across ALPHA-STAR and ALPHA-SOLAR, and 10.1 (9.1) months on ALPHA-SOLAR alone.

Table 1. Baseline Demographics and Disease Characteristics in Combined ALPHA-STAR and ALPHA-SOLAR

	Arm A (600/300 Q3M) (n=10)	Arm B (600/600/600 Q6M) (n=6)	Total (n=16)
Age (Years), Mean (SD)	44 (17)	49 (24)	46 (20)
Sex, n (%)			
Female	7 (70)	2 (33)	9 (56)
Race, n (%)			
White	9 (90)	5 (83)	14 (88)
Black or African-American	2 (20)	1 (17)	3 (19)
HAE-C1INH type, n (%)			
Type 1	9 (90)	5 (83)	14 (88)
Type 2	1 (10)	1 (17)	2 (13)
Age at the onset of first HAE symptoms (years), Mean (SD)	13 (9)	12 (6)	13 (8)
Baseline (run-in) monthly attack rate, Mean (SD)	2.5 (1.4)	1.8 (0.6)	2.2 (1.2)

RESULTS

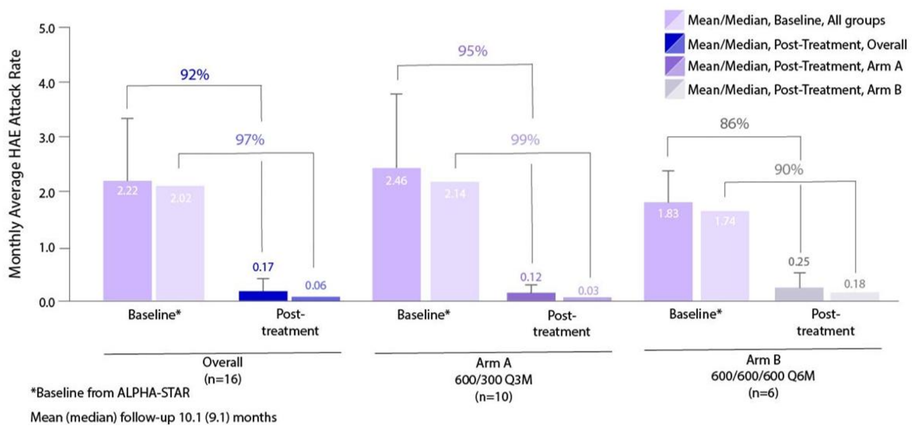
Table 2. Safety in Combined ALPHA-STAR and ALPHA-SOLAR

	Arm A (600/300 Q3M) (n=10)	Arm B (600/600/ 600 Q6M) (n=6)	Total* (n=16)
Participants with at least 1 Treatment-Emergent Adverse Event (TEAE)	10	6	16
TEAEs occurring in ≥2 participants			
Nasopharyngitis	3	2	5
Sinusitis	2	1	3
Urinary tract infection	2	1	3
Skin Laceration	2	1	3
Nasal congestion	1	1	2
Headache	2	-	2
Participants with ≥1 related TEAE	1	3	4
Injection site reaction[1]	-	1	1
Injection site erythema[2]	-	1	1
Injection site pruritus[2]	-	1	1
Injection site rash[3]	-	1	1
Dizziness[4]	1	-	1

1. One participant experienced 2 injection site reactions starting 0-1 day after the first and second doses in STAR-0215-202 Arm B (tenderness and pruritus lasting <1 day; erythema and pruritus lasting 5 days).
2. One participant experienced 2 injection site reactions: injection site erythema and injection site pruritus occurring 1 day after the second dose in STAR-0215-201 Cohort 3 and lasting <1 day.
3. One participant experienced injection site rash occurring 5 days after the second dose in STAR-0215-201 Cohort 3 and lasting < 1 day.
4. One participant experienced mild dizziness occurring 6 days after the first dose in STAR-0215-201 Cohort 2 and lasting < 1 day.

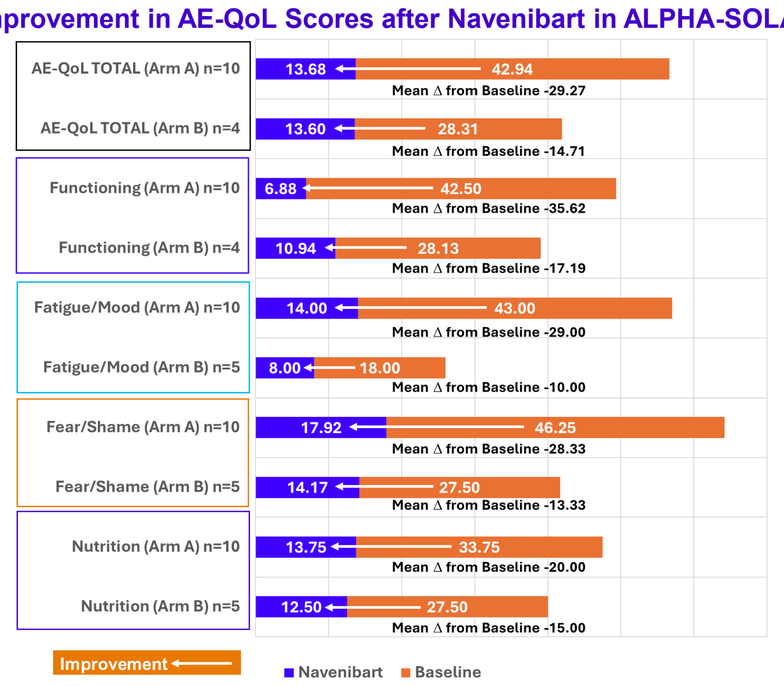
*Mean (Median) follow-up: 17.4 (17.1) months
Abbreviations: n, number of participants; Q3M, every 3 months; Q6M, every 6 months; SD, standard deviations.

Figure 2. Reduction in Monthly HAE Attack Rates in ALPHA-SOLAR



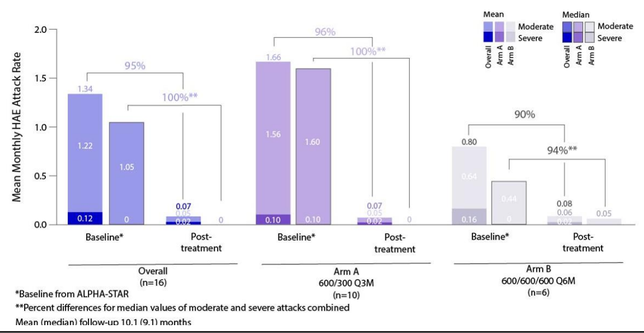
- **Navenibart substantially reduced mean monthly HAE attack rates**, with overall reductions of 92–99% from baseline across treatment arms.
- **Durable efficacy was maintained over a mean follow-up of ~10 months**, with most participants experiencing minimal or no attacks during treatment.
- **Navenibart markedly reduced monthly HAE attack rates requiring rescue medication by 92–98%** from baseline after ~10 months of treatment, with consistent reductions across both dosing regimens (Q3M and Q6M; Data not shown).

Figure 3. Improvement in AE-QoL Scores after Navenibart in ALPHA-SOLAR (interim analysis)



- **Clinically meaningful improvements (Hawkins et al., 2017) were observed across all AE-QoL domains** (functioning, fatigue/mood, fear/shame, and nutrition) in both dosing arms.
- **Mean total AE-QoL scores improved by 15–29 points from baseline**, exceeding the 6-point MCID threshold, indicating substantial enhancement in overall quality of life.
- **Improvement across all domains, functioning and fatigue/mood in particular,** reflects better daily activity and emotional well-being following navenibart treatment.

Figure 4. Durable Reduction in Moderate or Severe Monthly HAE Attack Rates in ALPHA-SOLAR



- **Navenibart markedly reduced moderate and severe HAE attack rate**, with overall mean monthly attack rates decreasing by ≥90–100% from baseline across both dosing regimens.
- **Most participants experienced no moderate or severe attack during follow-up** (~10 months), demonstrating durable attack prevention.

CONCLUSIONS

- Navenibart demonstrated durable prevention of HAE attacks, with >90% reductions in mean monthly attack rates and minimal to no attacks reported over ~10 months of follow-up in ALPHA-SOLAR.
- Long-term safety profile was favorable, with no new or unexpected safety findings and a low incidence of treatment-emergent adverse events.
- Clinically meaningful improvements in quality of life were observed across AE-QoL domains, reflecting sustained benefits in daily functioning, emotional well-being, and overall disease control.
- Navenibart, every 3 and 6 months, is being evaluated in the ongoing global Phase 3 pivotal trial, ALPHA-ORBIT (NCT06842823).

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