ALPHA-STAR, a Phase 1b/2 Clinical Trial of Single and Multiple Doses of Navenibart (STAR-0215) in Patients with Hereditary Angioedema: Interim Safety and Efficacy Outcomes

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DISCLOSURES

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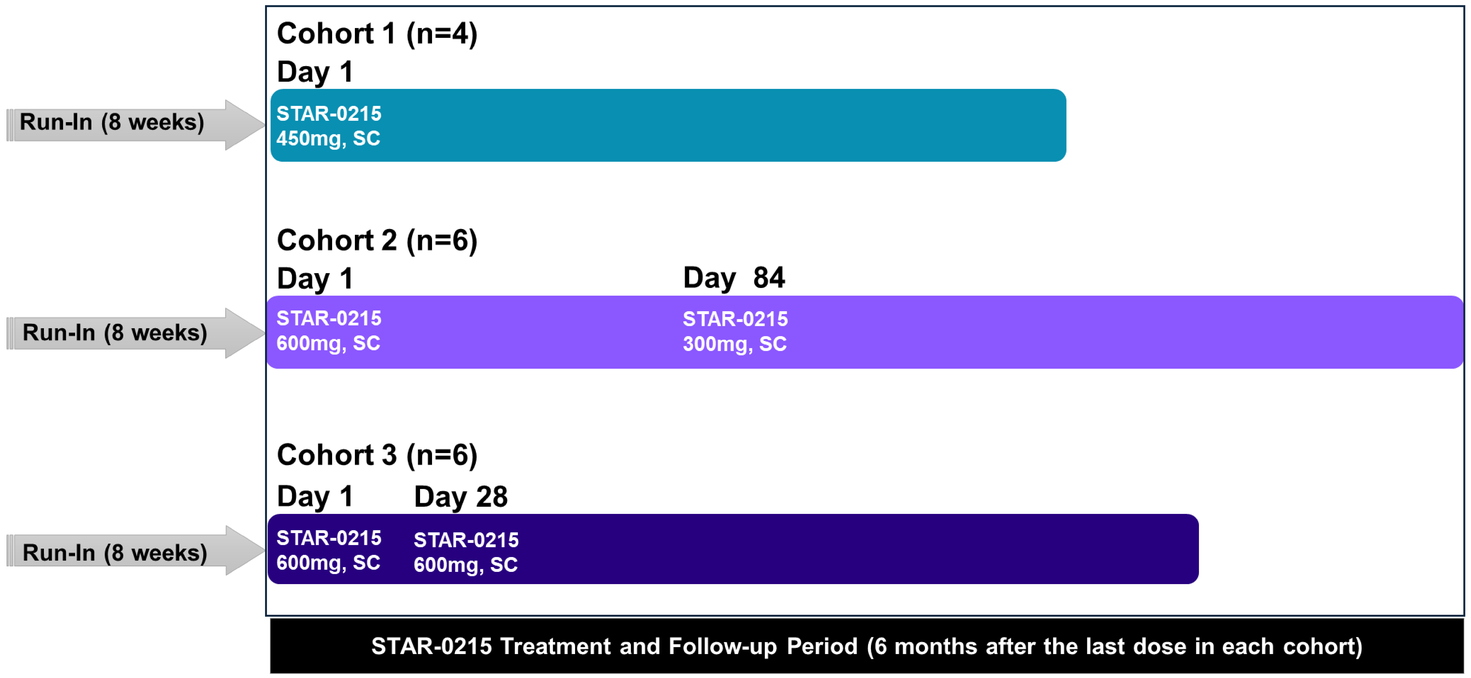
ALPHA-STAR Clinical Trial of Navenibart in Hereditary Angioedema (HAE)

- HAE is a rare, autosomal dominant disease associated with heterogeneous and recurrent clinical manifestations of angioedema with variable severity that can incur substantial morbidity, diminished quality of life, high economic burden, and increased mortality.
- Navenibart (STAR-0215) is an investigational, long-acting antibody of plasma kallikrein enabled by a YTE-modified Fc domain
- Adults with HAE-C1INH Type 1 and 2, reporting ≥ 2 HAE attacks during the 8-week run-in period, were sequentially assigned to receive navenibart subcutaneously.
- Participants were recruited into 3 dose cohorts; all cohorts were followed for 6 months after the last dose.



*ALPHA-STAR (NCT05695248) is a proof-of-concept, dose ranging clinical trial of navenibart (STAR-0215) in HAE

- Results reported here are from data cut-off performed on 13-Mar-2024. At the cut-off date, ALPHA-STAR participants accrued 6.5 years of exposure to navenibart.
- The mean age of study participants across all three cohorts was 46 years, 56% were female, and 88% had HAE-C1INH Type 1.
- The mean number of HAE attacks in the previous 12 months was 22.

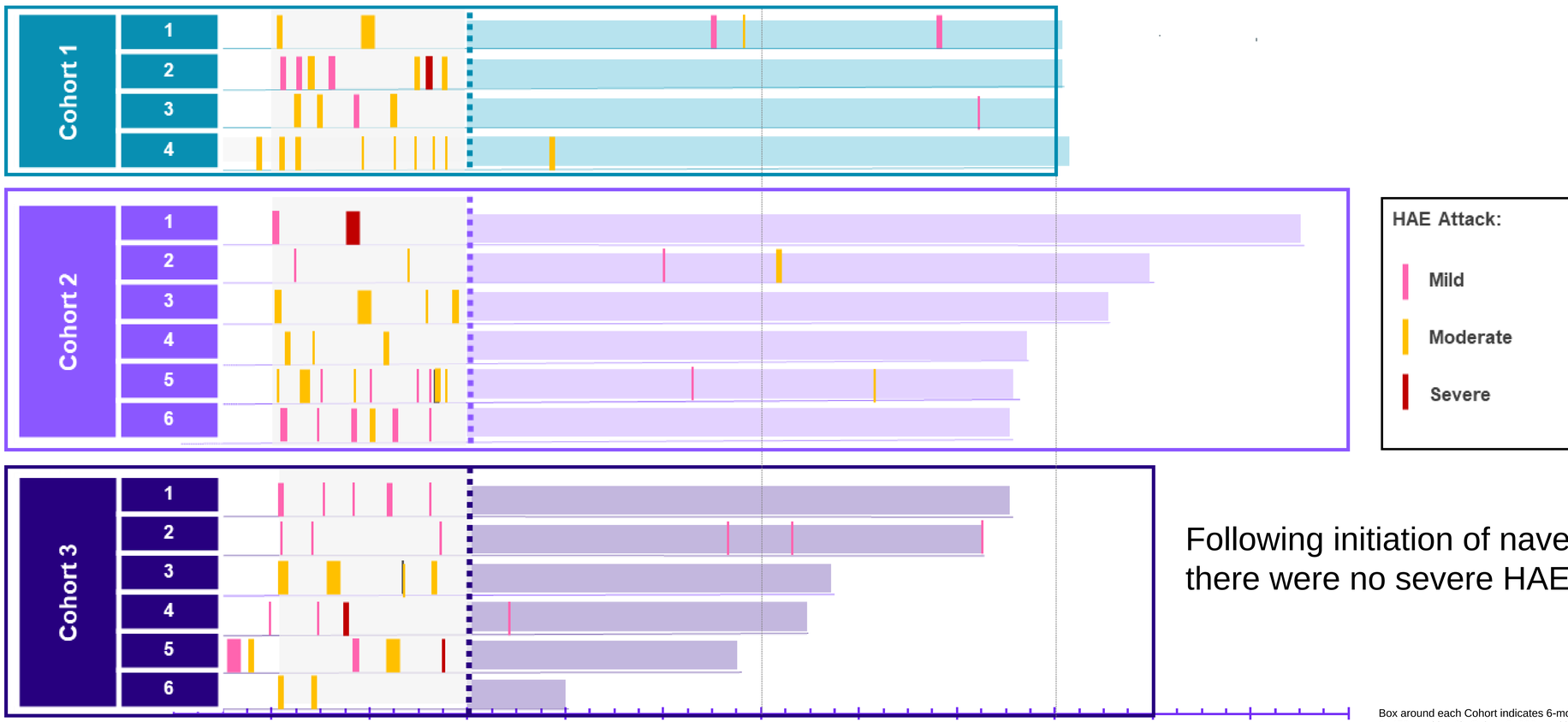
Cumulative Safety in ALPHA-STAR Participants

- The most common treatment emergent adverse events (TEAEs), occurring in 2 or more participants who received navenibart, included nasopharyngitis, contusion, and headache.
- No serious or severe TEAEs and no treatment discontinuations were reported.

	Navenibart 450 mg SC* (N = 4)	Navenibart 600/300(84d) mg SC* (N = 6)	Navenibart 600/600(28d) mg SC* (N = 6)	Navenibart Total (N = 16)
Number of subjects with at least 1 TEAE, n (%)	4 (100)	3 (50)	6 (100)	13 (81)
Subjects with a related TEAE n (%)	0	1 (16.6)	1 (16.6)	2 (12.5)
Subjects with a serious TEAE n (%)	0	0	0	0
Number of TEAEs	20	3	9	32
Number of related TEAEs	0	1[a]	1[b]	2
Number of serious TEAEs	0	0	0	0
Number of TEAEs leading to study discontinuation	0	0	0	0
TEAEs occurring in ≥2 participants (Preferred term)				
Nasopharyngitis n (%)	1 (25)	1 (16.6)	1 (16.6)	3 (18.75)
Contusion n (%)	2 (50)	0	0	2 (12.5)
Headache n (%)	2 (50)	0	0	2 (12.5)

*SC, subcutaneous; a One participant experienced mild dizziness on day 6 after the first dose in Cohort 2.
b One participant experienced an injection site reaction (rash) 5 days after the second dose in Cohort 3, lasting less than 1 day.

Cumulative HAE Attack Occurrences for Each ALPHA-STAR Participant (Interim Analysis)

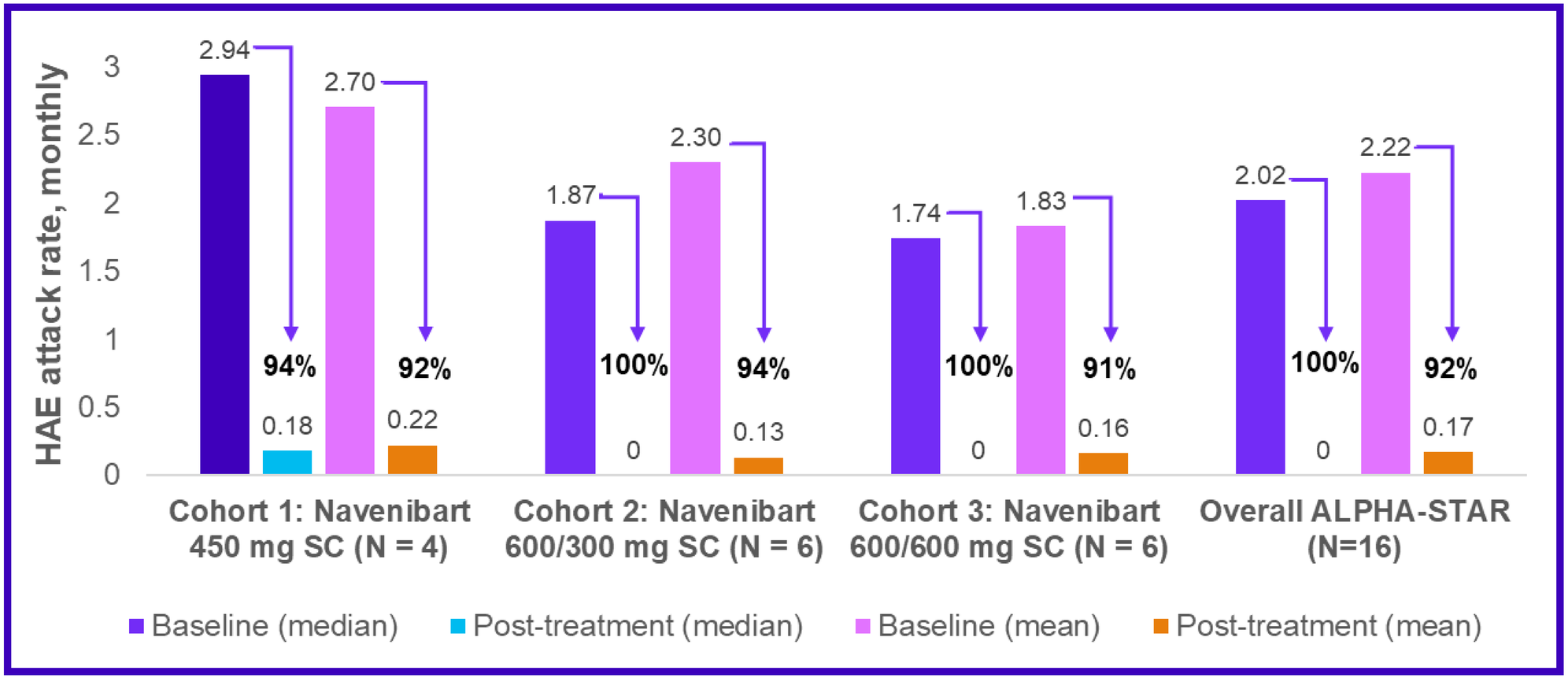


Box around each Cohort indicates 6-month period after the last injection; Cohort 1: 450 mg (day 1); Cohort 2: 600 mg (day 1), 300 mg (day 84); Cohort 3: 600 mg (day 1), 600 mg (day 28). Vertical lines indicate efficacy analyses at Day 84 (3 months) and Day 168 (6 months). Thickness of vertical bars indicate various duration of discrete HAE attacks.

For the first 3 months (84 days):

- 50%, 67%, and 50% of participants with available follow-up were HAE attack-free in Cohorts 1-3, respectively;
- baseline rates (mean) of mild/moderate/severe HAE attacks/month of 0.95/1.25/0.11 were reduced to 0.13/0.05/0.00;
- mean rates of HAE attacks/month requiring rescue medication were reduced from 1.86 at baseline to 0.16.

Overall Cumulative Change in HAE Attack Rate (Baseline to Post-Treatment)



Efficacy outcomes are based on 6.5 patient years (PY) of accumulated follow-up (individual follow-up at the time of data cut-off is shown in Figure 2). HAE attack rate (unique, non-overlapping, investigator-confirmed) was calculated as: (number of HAE attacks / duration of evaluation period in days) * 30.4375; where the run-in period started at the Screening visit until the day before first treatment, the treatment period started at first treatment date until the end of study date.

After treatment with navenibart, median (mean) percent reduction of the monthly HAE attack rate calculated for each participant was:

- In Cohort 1, from 2.94 (2.70) to 0.18 (0.22); after median follow-up of 6 months
- In Cohort 2, from 1.87 (2.30) to 0 (0.13); after median follow-up of 5 months
- In Cohort 3, from 1.74 (1.83) to 0 (0.16); after median follow-up of 2.8 months

SUMMARY & CONCLUSIONS

- Interim data from the ALPHA-STAR clinical trial indicate a favorable safety profile of navenibart for patients with HAE.
- Significant clinical benefit of HAE attack prevention was observed after the first navenibart dose and sustained for 3-6 months thereafter.
- These results suggest that navenibart may be administered 2 or 4 times a year as the first long-acting, long-term preventative treatment for HAE.
- The Phase 2 long-term open-label trial ALPHA-SOLAR is ongoing, with initial data expected mid-2025.
- Results show proof of concept and support proceeding to phase 3 for navenibart in patients with HAE.