



Results from the ALPHA-STAR Trial, a Phase 1b/2 Single and Multiple Dose Study to Assess the Safety, Tolerability, Clinical Activity, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of Navenibart in Participants with Hereditary Angioedema (HAE)

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Speaker Disclosures and Disclaimers



Dr. William R. Lumry

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Navenibart is an investigational therapy and has not yet been approved for any indication

Background

Hereditary angioedema (HAE) is a rare, autosomal dominant disease characterized by unpredictable attacks that impact quality of life.

Navenibart (STAR-0215) is an investigational, long-acting monoclonal antibody inhibitor of plasma kallikrein.

The purpose of this analysis is to describe the safety, clinical activity, pharmacokinetics, and pharmacodynamics evaluated in the open-label Phase 1b/2 ALPHA-STAR trial (NCT05695248) in the target enrollment population (n=16) of adult participants with HAE-C1INH, thereby supporting the doses and dosing regimen selected for the ongoing Phase 3 ALPHA-ORBIT trial (NCT06842823).

Patients with HAE-C1INH Continue to Face Breakthrough Attacks and High Treatment Burden

- HAE-C1INH is a rare, autosomal dominant disease characterized by unpredictable attacks that impact quality of life^{1,2}
- Approved long-term prophylaxis (LTP) therapies have substantially reduced the rate of angioedema attacks in the past 5 years
 - Current therapies can be burdensome³⁻⁶
 - Some patients on LTP therapies continue to experience a high frequency of attacks⁷

Current long-term prophylaxis therapies

| Therapy | Administration frequency | Mean attack reduction |
|----------------------------|--------------------------|-----------------------|
| IV C1INH ^{3,4} | 3-4 days | 52% |
| SC C1INH ^{5,6} | 3-4 days | 84% |
| Lanadelumab ⁸ | 2-4 weeks | 73% to 87% |
| Berotralstat ⁹ | Daily | 30% to 44% |
| Garadacimab ¹⁰ | 4 weeks | 87% to 89% |
| Donidalorsen ¹¹ | 4-8 weeks | 55% to 81% |

Navenibart is an investigational, long-acting monoclonal antibody inhibitor of plasma kallikrein with an extended half-life that is being studied in Phase 3 trials for prevention of HAE attacks and that can potentially be administered 2 or 4 times annually.

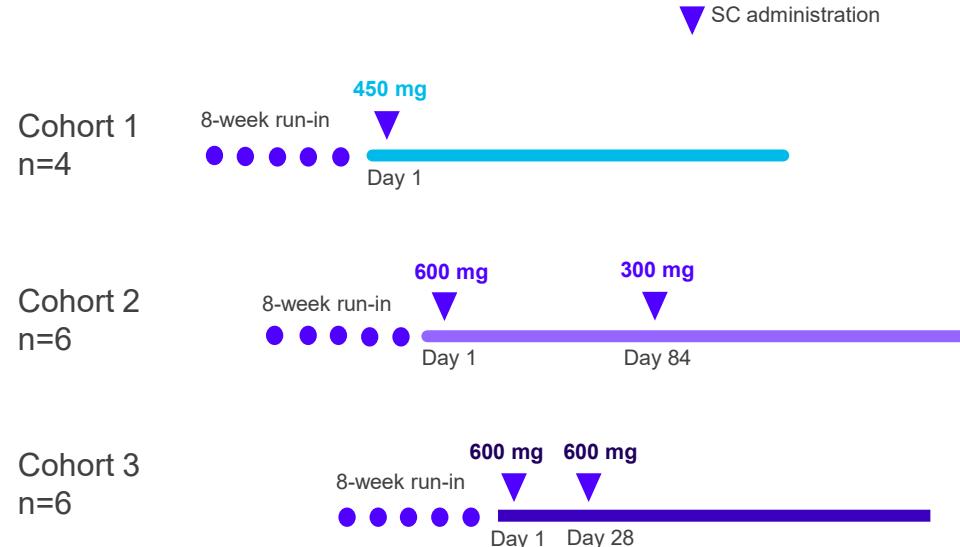
C1INH, C1 esterase inhibitor; HAE-C1INH, hereditary angioedema; IV, intravenous; LTP, long-term prophylaxis; SC, subcutaneous.

1. Zuraw et al. *N Engl J Med.* 2008;359:1027-1036. 2. Guan et al. *Orphanet J Rare Dis.* 2024;19:256. 3. Cinryze. Prescribing information. Takeda Pharmaceuticals; 2023. 4. BioSpace. Press release. March 18, 2008. <https://www.biospace.com/lev-pharmaceuticals-inc-presents-results-of-phase-iii-study-supporting-safety-and-efficacy-of-cinryze-tm-c1-inhibitor-as-prophylactic-therapy-for>. Accessed May 5, 2025. 5. Haegarda. Prescribing information. CSL Behring; 2022. 6. Longhurst et al. *N Engl J Med.* 2017;376:1131-1140. 7. Banerji et al. *Ann Allergy Asthma Immunol.* 2020;124:600-607.

Confidential

ALPHA-STAR Clinical Trial Design

In this dose-ranging, proof of concept **Phase 1b/2 trial** (NCT05695248), in the target enrollment population (n=16) of adult participants with HAE-C1INH were assigned to one of three subcutaneous havenibart dosing cohorts



Participants are observed for 6 months after the last administered dose.

Endpoints Focused on the Safety, Clinical Activity, Pharmacokinetics, and Pharmacodynamics of Navenibart



- Primary endpoint: incidence of TEAEs
 - Safety monitoring included vital signs, electrocardiograms, physical examinations, and clinical laboratory testing
- Secondary endpoints include clinical efficacy, pharmacokinetics, pharmacodynamics, and immunogenicity
- Pharmacokinetics were evaluated through validated immunoassay measurements of navenibart concentrations
- Pharmacodynamic assessments measured plasma kallikrein activity by changes in cHMWK measured via western blot



Adult HAE Participant Demographics Were Similar

| | Navenibart 450 mg (N = 4) | Navenibart 600/300 mg (N = 6) | Navenibart 600/600 mg (N = 6) | Navenibart Total (N = 16) |
|--|---------------------------------|-------------------------------------|-------------------------------------|---------------------------------|
| Age (Years), Mean (SD) | 51 (21) | 39 (15) | 49 (24) | 46 (20) |
| Sex, n (%) | | | | |
| Female | 3 (75) | 4 (67) | 2 (33) | 9 (56) |
| Race, n (%) | | | | |
| White | 4 (100) | 5 (83) | 5 (83) | 14 (88) |
| Black or African-American | - | 2 (33) | 1 (17) | 3 (19) |
| Multiracial | - | 2 (33) | - | 2 (13) |
| American Indian or Alaska-native | - | 1 (17) | - | 1 (6) |
| HAE-C1INH type, n (%) | | | | |
| Type 1 | 4 (100) | 5 (83) | 5 (83) | 14 (88) |
| Type 2 | - | 1 (17) | 1 (17) | 2 (13) |
| Age at the onset of first HAE symptoms (Years), Mean (SD) | 11 (11) | 14 (8) | 12 (6) | 13 (8) |
| Baseline (run-in) monthly attack rate, Mean (SD) | 2.7 (1.3) | 2.3 (1.5) | 1.8 (0.6) | 2.2 (1.2) |

Race categories are not mutually exclusive in the Phase 1b/2 trial.

BMI, body mass index; HAE-C1INH, hereditary angioedema; SD, standard deviation.

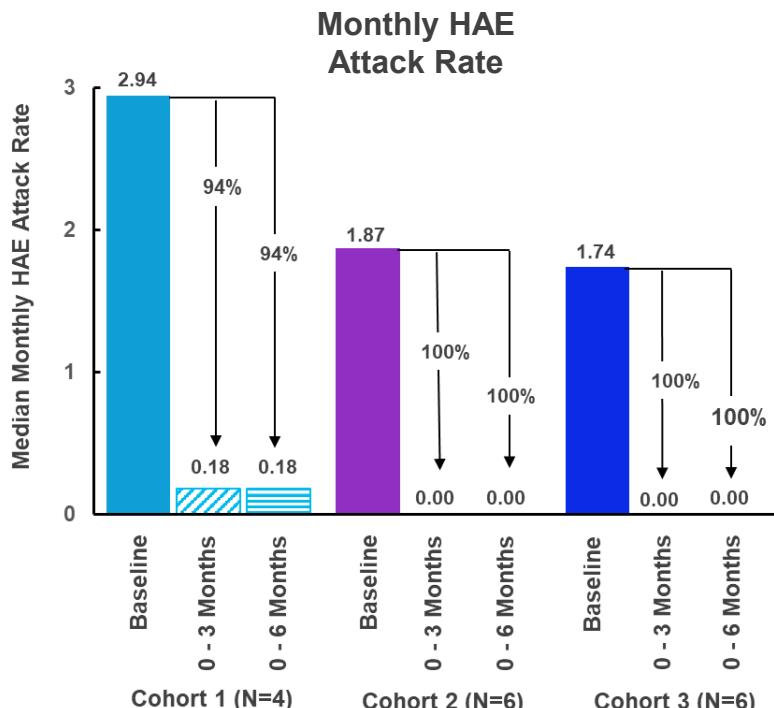
Data on file, Astria Therapeutics, Inc. Data cut-off on September 18, 2024

Navenibart Was Well Tolerated, With a Favorable Safety Profile

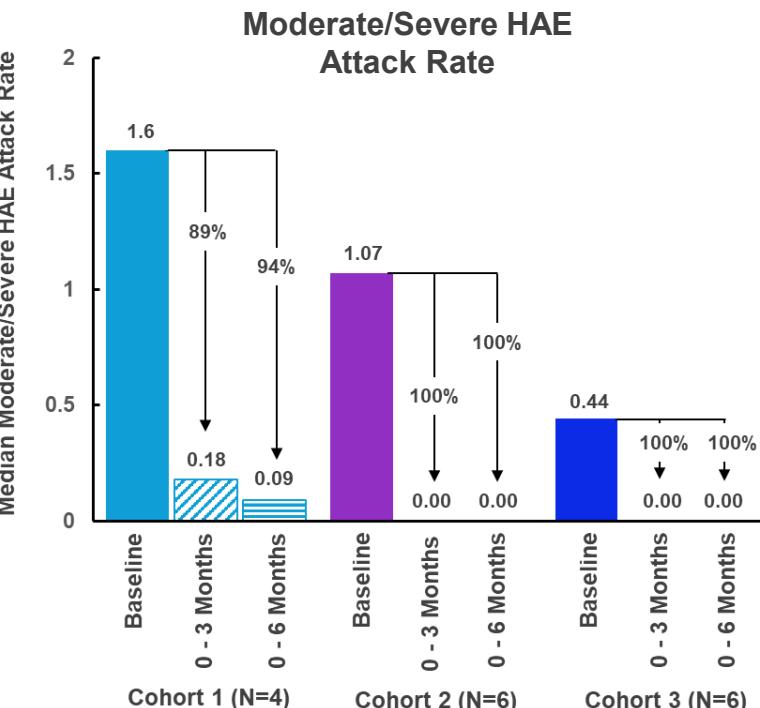
| | Navenibart 450 mg (N = 4) | Navenibart 600/300 mg (N = 6) | Navenibart 600/600 mg (N = 6) | Navenibart Total (N = 16) |
|---|---------------------------------|-------------------------------------|-------------------------------------|---------------------------------|
| At least 1 TEAE, n (%) | 4 (100) | 5 (83) | 6 (100) | 15 (94) |
| TEAEs occurring in ≥2 participants | | | | |
| Nasopharyngitis | 1 (25) | 1 (17) | 2 (33) | 4 (25) |
| Sinusitis | - | 1 (17) | 1 (17) | 2 (13) |
| Headache | 2 (50) | - | - | 2 (13) |
| Participants with ≥1 navenibart-related TEAE, n (%) | - | - | 2 (33) | 3 (19) |
| Injection site erythema | - | - | 1 (17) | 1 (6) |
| Injection site pruritic | - | - | 1 (17) | 1 (6) |
| Injection site rash | - | - | 1 (17) | 1 (6) |
| Dizziness | - | 1 (17) | - | 1 (6) |
| Serious TEAE, n (%) | - | - | - | - |
| TEAE leading to trial discontinuation, n (%) | - | - | - | - |
| TEAE leading to death, n (%) | - | - | - | - |

Navenibart Reduced Monthly HAE Attack Rates

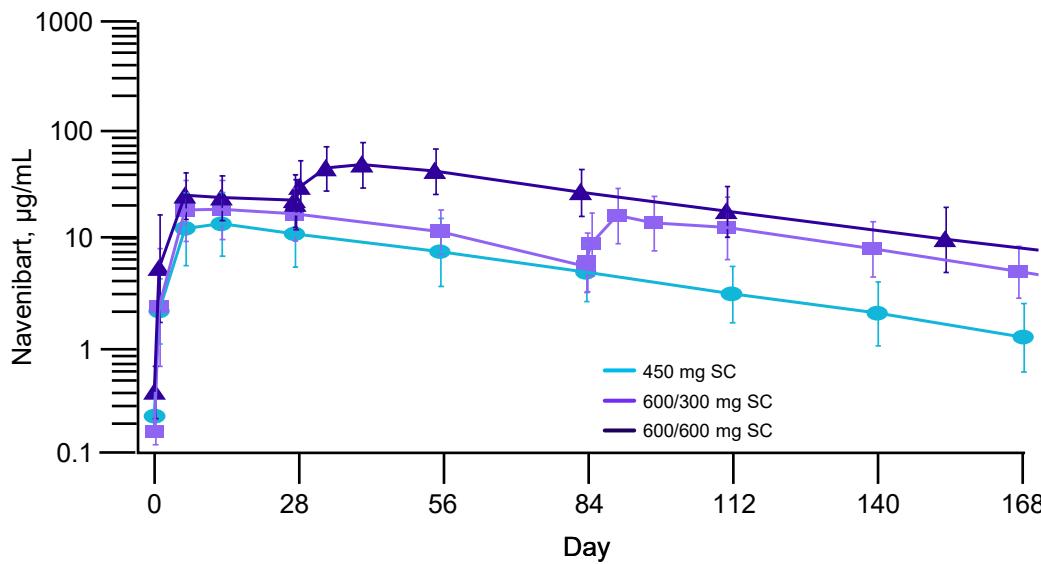
A



B

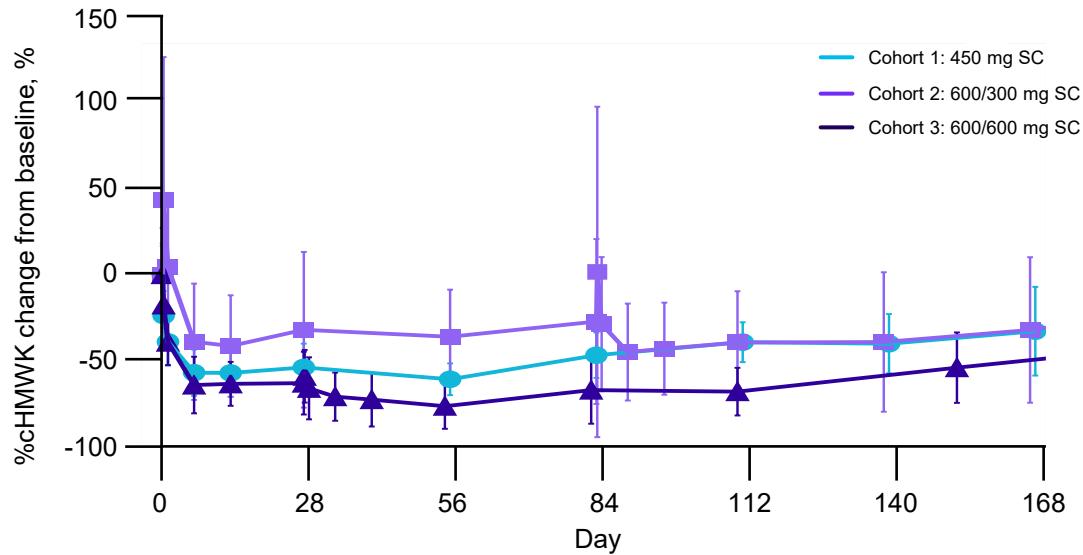


Rapid Increase and Sustained Concentrations Throughout the 6-month follow up



Treatment-emergent anti-drug antibodies were detected in 5/16 participants with no apparent impact on PK/PD.

Navenibart Induced Rapid and Sustained Inhibition of Plasma Kallikrein Activity



cHMWK, cleaved high-molecular-weight kininogen; FXIIa, factor XIIa; HAE-C1INH, hereditary angioedema; SC, subcutaneous.
Data on file, Astria Therapeutics, Inc. Data cut-off on September 18, 2024

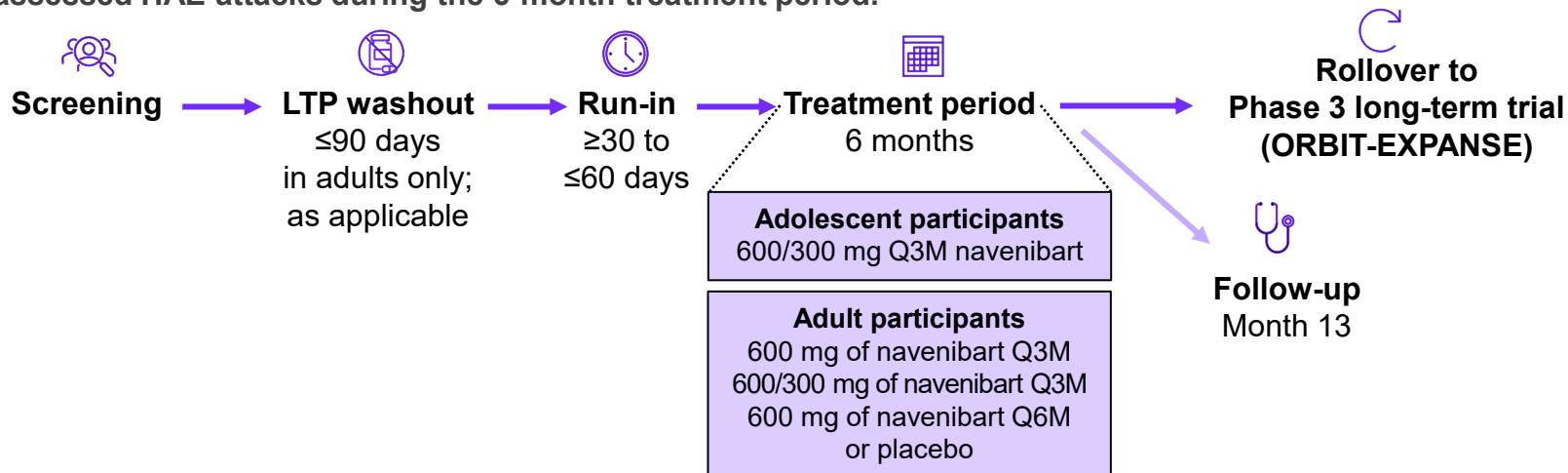
Navenibart Demonstrated Sustained Reductions in HAE Attack Rates with a Favorable Safety and Immunogenicity Profile

- Navenibart demonstrated a favorable safety profile, with no dose-related TEAEs.
- Navenibart showed a 94-100% reduction in median monthly attack rate compared to run-in baseline.
- Navenibart rapidly and durably reduced plasma kallikrein activity after single and multiple doses.

Navenibart has the potential to become an effective and safe preventative treatment for HAE, with administration every 3 or 6 months, and is supportive of the ongoing phase 3 global pivotal trial, ALPHA-ORBIT (NCT06842823).

A Phase 3 Trial (ALPHA-ORBIT) Assessing the Efficacy and Safety of Navenibart Is Ongoing

- The global, randomized, double-blind, placebo-controlled trial (NCT06842823) is evaluating the efficacy and safety of navenibart compared with placebo in preventing HAE attacks in adult participants with HAE-C1INH.
- Adolescent participants with HAE-C1INH will also be enrolled and treated with open-label navenibart.
- The primary endpoint for adult and adolescent participants is the number of time-normalized, investigator-assessed HAE attacks during the 6-month treatment period.





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- Study design, data analysis, and abstract preparation were a collaborative effort of the full author team, which, in addition to today's speaker, includes **Raffi Tachdjian,¹ Michele Gunsior,² Ganesh Mugundu,² Theodora Cohen,² and Christopher Morabito.²**

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