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 burdensome[3-6]
  - Some patients on LTP therapies continue to experience a high frequency of attacks[7]

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%

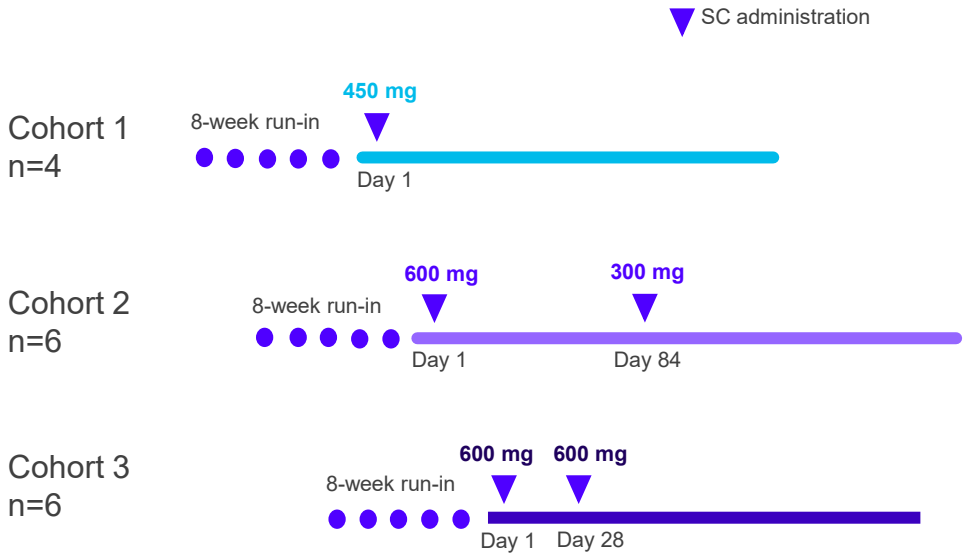
Navenibart is an investigational, long-acting monoclonal antibody inhibitor of plasma kallikrein with an extended half-life that is being studied in Phase 3 trials for prevention of HAE attacks and that can potentially be administered 2 or 4 times annually.

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. **8.** Takhzyro. Prescribing information. Takeda Pharmaceuticals; 2023. **9.** Orladeyo. Prescribing information. BioCryst Pharmaceuticals; 2023.**10.** Andembry™ (garadacimab-gxii) Prescribing Information. CSL Behring LLC; 2025. **11.** Dawnzera™ (donidalorsen) Prescribing Information. Ionis Pharmaceuticals, Inc.; 2025.

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 navenibart dosing cohorts



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

HAE-C1INH, hereditary angioedema with C1INH deficiency; IV, intravenous; SC, subcutaneous.
Data on file, Astria Therapeutics, Inc.Data cut-off on September 18, 2024

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**

cHMWK, cleaved high-molecular-weight kininogen; TEAE, treatment-emergent adverse event.

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 Black or African-American Multiracial American Indian or Alaska-native	4 (100) - - -	5 (83) 2 (33) 2 (33) 1 (17)	5 (83) 1 (17) - -	14 (88) 3 (19) 2 (13) 1 (6)
HAE-C1INH type, n (%) Type 1 Type 2	4 (100) -	5 (83) 1 (17)	5 (83) 1 (17)	14 (88) 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 (%)	-	-	-	-

aPTT, activated partial thromboplastin time; ECG, electrocardiogram; TEAE, treatment-emergent adverse event.
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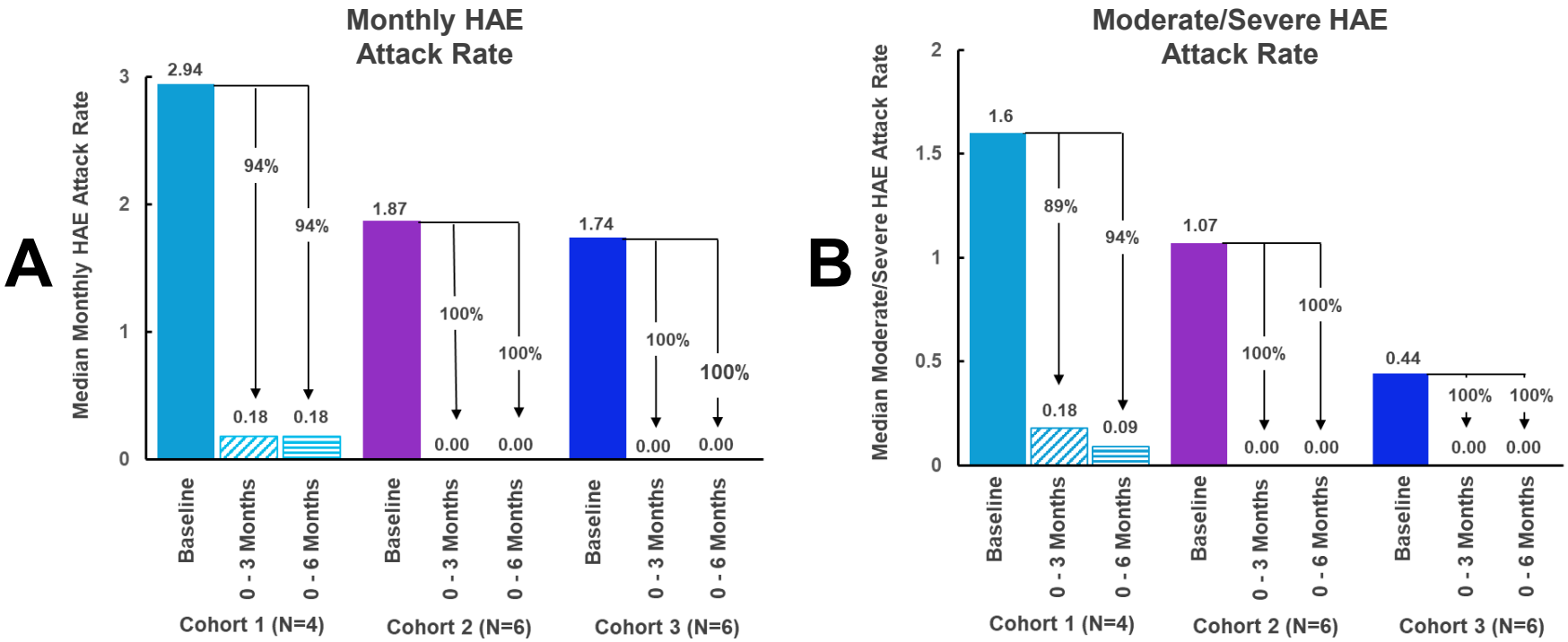
Navenibart Reduced Monthly HAE Attack Rates



cHMWK, cleaved high-molecular-weight kininogen; FXIIa, factor XIIa; HAE-C1INH, hereditary angioedema; SC, subcutaneous.
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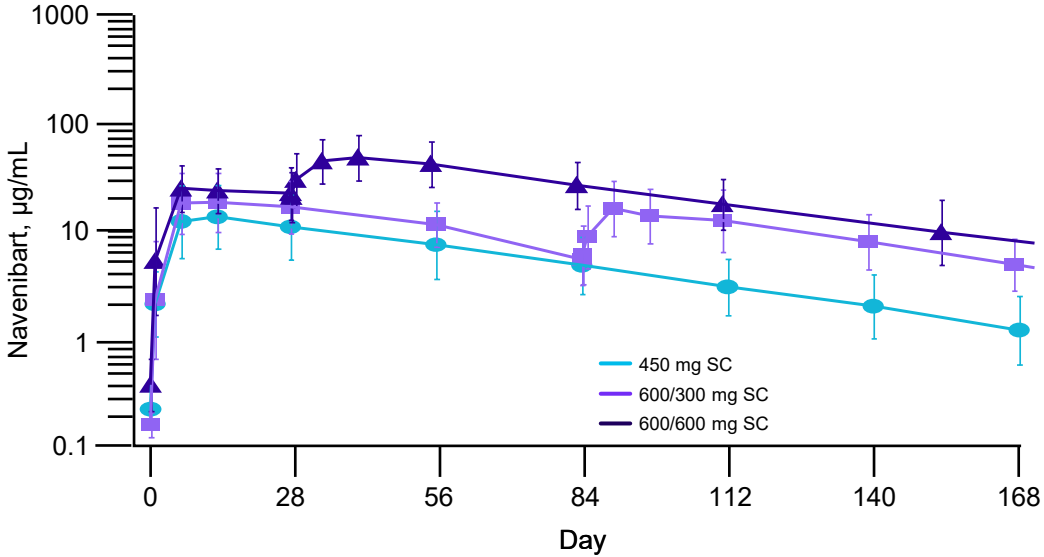
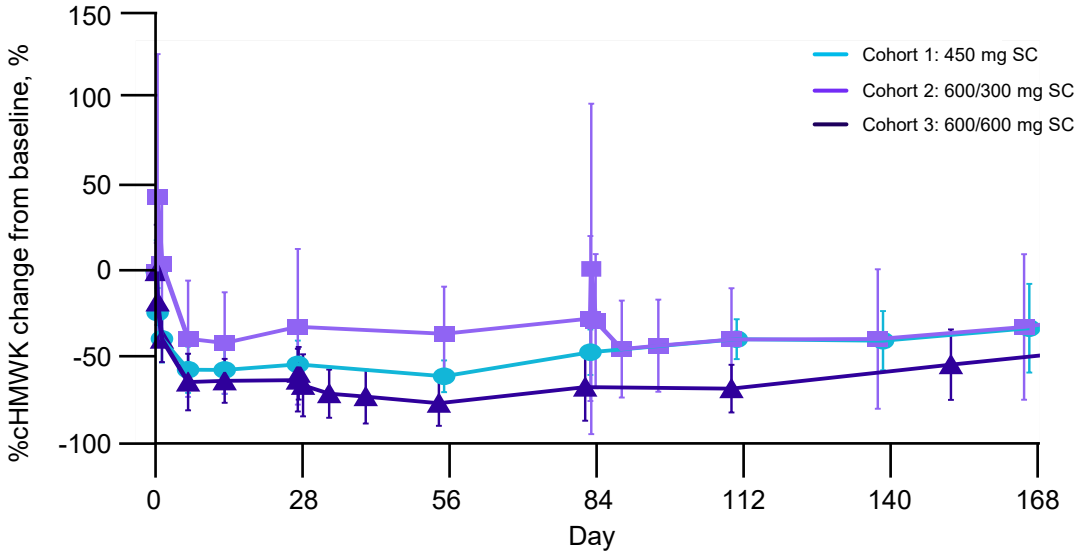
Rapid Increase and Sustained Concentrations Throughout the 6-month follow up



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

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

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

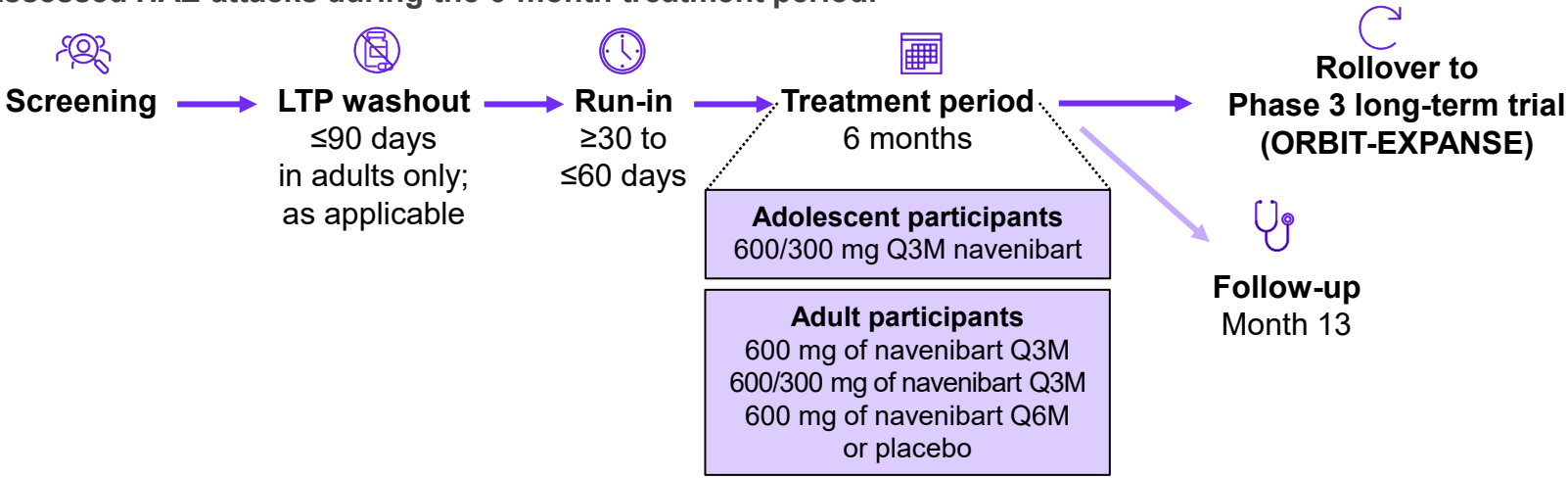
- Navenibart demonstrated a favorable safety profile, with no dose-related TEAEs.
- Navenibart showed a 94-100% reduction in median monthly attack rate compared to run-in baseline.
- Navenibart rapidly and durably reduced plasma kallikrein activity after single and multiple doses.

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).

HAE-C1INH, hereditary angioedema; Q3M, every 3 months; Q6M, every 6 months; SC, subcutaneous; TEAE, treatment-emergent adverse event.

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.



HAE-C1INH, hereditary angioedema; LTP, long-term prophylaxis; Q3M, every 3 months; Q6M, every 6 months; TEAE, treatment-emergent adverse event.

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