Design of ALPHA-STAR, a Phase 1b/2 proof-of-concept trial of STAR-0215 as a long-acting preventative therapy in patients with hereditary angioedema (HAE) Types I or II

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Disclosures

- **Marcus Maurer (Presenting Author) is or recently was a speaker and/or advisor for and/or has received research funding from Allakos, Allvotech, Amgen, Aquestive, Aralez, AstraZeneca, Astria, Bayer, BioCryst, Celldex, Celltrion, CSL Behring, Evommune, GSK, Ipsen, Kalvista, Leo Pharma, Lilly, Menarini, Mitsubishi Tanabe Pharma, Moxie, Noucor, Novartis, Orion Biotechnology, Pharvaris, Resonance Medicine, Sanofi/Regeneron, Septerna, Takeda, Teva, Third HarmonicBio, Trial Form Support International AB, ValenzaBio, Yuhan Corporation, Zurabio**

- **Christopher Morabito, Chris Stevens, Marianne Magill, Kristine Bernard, Jou-Ku Chung, and Michele Gunsior are or have been full-time employees of or part-time consultants to Astria Therapeutics**

- **Claire VanEenwyk is a full-time employee of Parexel International**

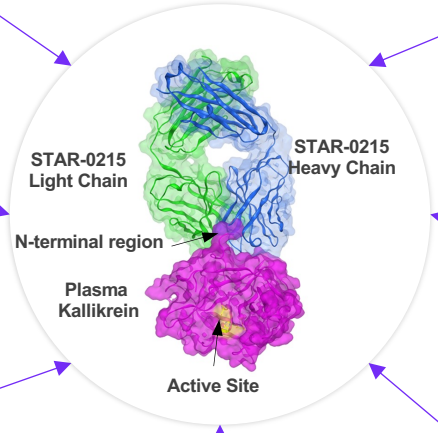
STAR-0215
Anti-Plasma Kallikrein mAb Engineered for Long Half-Life

STAR-0215 Product Characteristics

Humanized IgG1 kappa light chain mAb

Potent allosteric inhibition of plasma kallikrein activity

Novel CDRs



High selectivity for plasma kallikrein

Fc engineered with YTE modifications for half-life extension

Formulated to reduce pain

High concentration formulation supports SC dosing

mAb = monoclonal antibody; IgG1 = immunoglobulin G subclass 1; SC = subcutaneous; CDR = Complementarity-determining regions; YTE = triple mutation (M252Y/S254T/T256E)

STAR-0215: Clinical Development

In development as a long-acting preventative treatment for HAE-C1INH (Types 1 or 2), administered every 3 or 6 months

Phase 1a Healthy Subject SAD
Ongoing

Initial results presented at AAAAI 2023; 6-month data for cohort 4 and 5 and final results from cohorts 1-3 expected Q4 2023

- Healthy volunteer single ascending dose trial
  - Randomized, placebo-controlled trial (3:1 randomization per cohort)
  - 5 single-dose cohorts, with 224 days of safety follow-up planned for each
- Initial results are available through day 84 (3 months) on next slides
  - Cohorts 1 (100 mg SC), 2 (300 mg SC) and 3 (600 mg SC)
- Ongoing cohorts
  - Cohorts 4 (1200 mg SC) and 5 (600 mg IV)

Phase 1b/2 Proof-of-Concept - ALPHA-STAR
Ongoing

Initial proof-of-concept results anticipated mid-2024

- Proof-of-concept trial in HAE patients

SC = subcutaneous; IV = intravenous

Phase 1a Initial Results Suggest that STAR-0215 is Well-Tolerated and Has a Favorable Safety Profile

Cohorts 1-3 through Day 84 (3 Months)

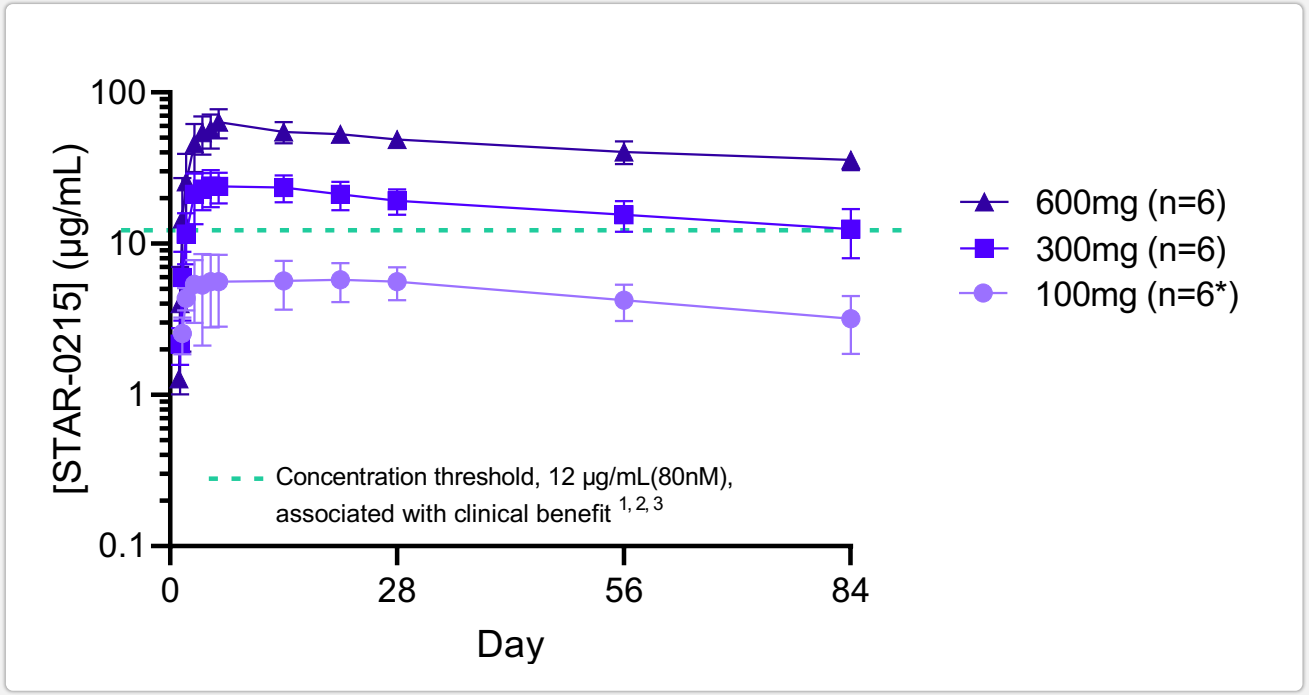
Phase 1a Healthy Volunteer Trial (Cohorts 1-3; n=25 to date):

- Related TEAEs were seen in 8 subjects (STAR-0215 n=7; placebo n=1)
  - 6 subjects (STAR-0215) had ISRs (all mild), most commonly site erythema; no reports of pain
  - 1 subject (STAR-0215, 100 mg) experienced unexpected weight gain
  - 1 subject (placebo) experienced headache
  - All related TEAEs were mild (Grade 1) and resolved.
- No clinically relevant changes in vital signs, ECG parameters, or laboratory values.
- No clinically relevant changes in liver enzymes or coagulation parameters.
- No SAEs and no discontinuations due to TEAEs.

Immunogenicity: No treatment-emergent ADAs were detected

1. TEAE= Treatment-emergent adverse event; ISR = injection site reaction; SAE = serious adverse events: ADA = anti-drug antibody
2. 15 Grade 1 (mild) ISRs occurred in 6 subjects, including erythema (site redness), pruritus, swelling and inflammation.

Initial Phase 1a Healthy Subjects STAR-0215 Pharmacokinetic Results Show Long Half-Life

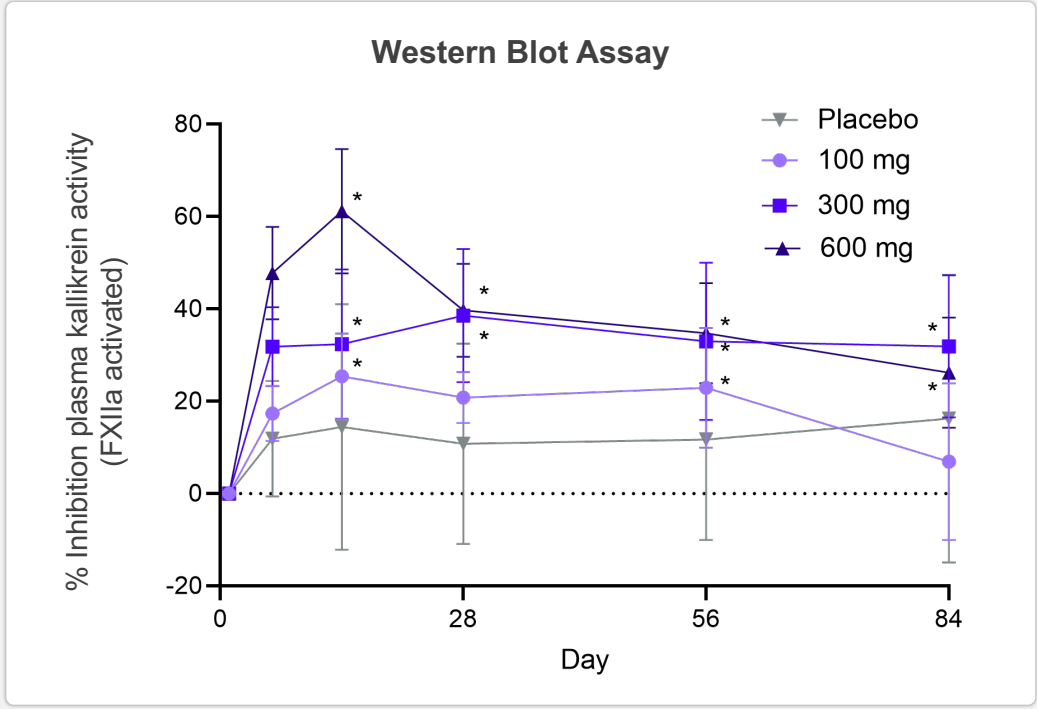


- Results show rapid and sustained achievement of STAR-0215 concentrations consistent with clinical benefit (≥12 µg/ml[1-3]) after single subcutaneous doses
- Concentrations are proportional to dose
- Estimated half-life is up to 117 days, >5 times longer than lanadelumab
- Long elimination phase consistent with YTE-modification

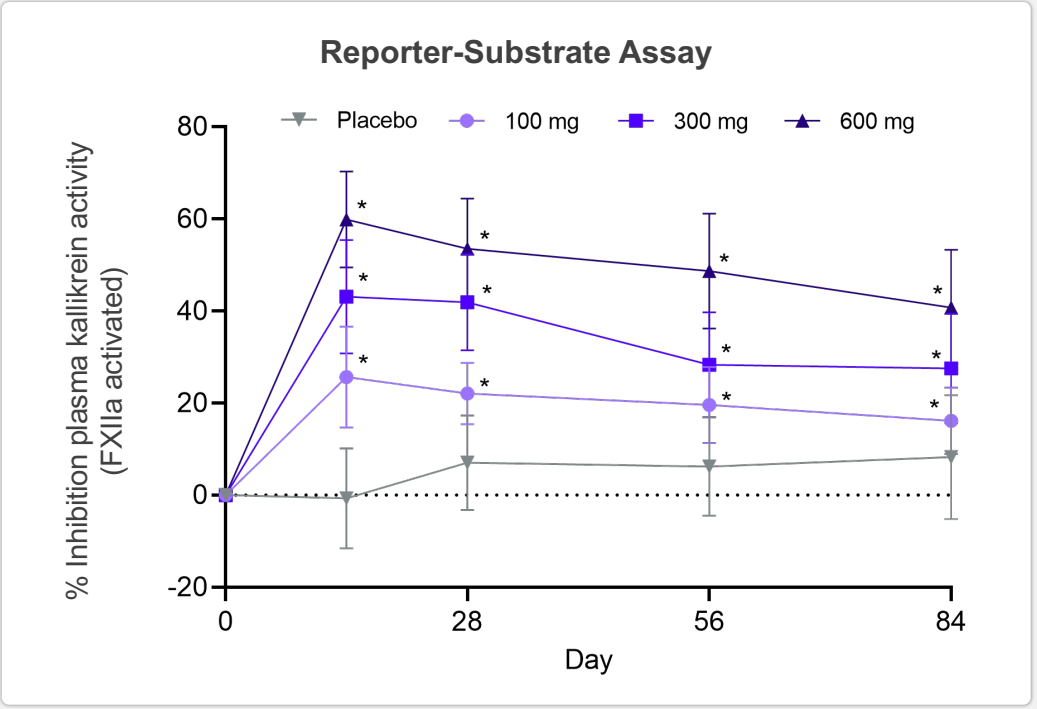
1. Kaufman 1991 June 15. Blood 77(12): 2660-2667
2. Wang et al. Clin Transl Sci. 2020 Nov, 13(6): 1208-1216. doi 10-1111/cts. 12806 Epub 2020 May 26.
3. Ecallantide EMA Assessment Report. 2011 June 23. EMA/CHMP/476618/2011

Mean (SD) concentrations over time. Estimated half-life of up to 117 days is for the 600 mg dose. Data cutoff is Day 84. Results will be finalized after the end of the observation period
*One subject excluded from the analysis due to partial dose administered.
The comparison presented between STAR-0215 and lanadelumab represents a cross-trial comparison and does not involve data from a head-to-head clinical trial

Initial Phase 1a Healthy Subjects Pharmacodynamic Results Show Sustained Inhibition of Plasma Kallikrein



Significant inhibition of plasma kallikrein activity at all post-dose timepoints for 300 mg and 600 mg



Significant inhibition of plasma kallikrein activity at all post-dose timepoints for 100 mg, 300 mg, and 600 mg

Data are Mean ± SD. One subject excluded from the analysis due to partial dose administered.

- * = $p < 0.05$ from pre-dose at indicated doses and timepoints; non-significant (ns) difference at all timepoints for placebo
- Statistical Test: 2-Way ANOVA with Dunnett's test for multiple comparisons

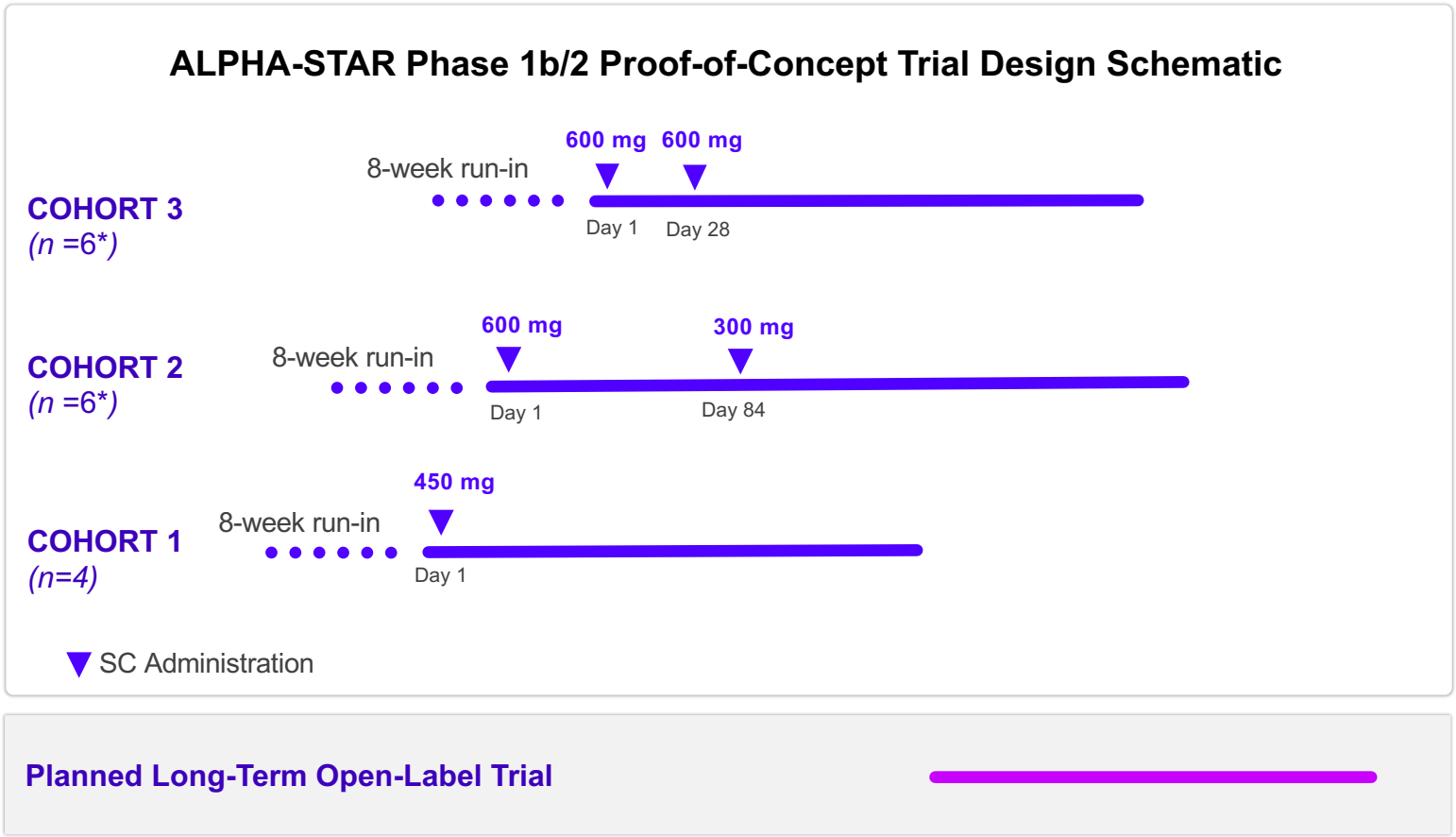
The comparison presented between STAR-0215 and the lanadelumab data on the prior slide represents a cross-trial comparison and does not involve data from a head-to-head clinical trial.

alpha-star

Astria Long-Acting Prophylaxis for Hereditary Angioedema-STAR-0215

Full Title: A Phase 1b/2 Single and Multiple Dose Study to Assess the Safety, Tolerability, Clinical Activity, Pharmacokinetics, Pharmacodynamics, and Immunogenicity of STAR-0215 in Participants with Hereditary Angioedema (The ALPHA-STAR Trial)

ALPHA-STAR Trial Design and Overview



- **Three dose-ranging cohorts to inform pivotal trial design**
- **For each cohort, efficacy will be assessed at 3 months and 6 months after the last STAR-0215 dose administered**
- **Initial proof-of-concept results**
  - Assessing safety and tolerability, PK, PD, attack rate, and QOL in these 3 cohorts
  - Goal: significant reduction in attacks following STAR-0215 treatment

Includes details of the planned amendment
Cohorts planned to be opened sequentially
*Up to 6 additional subjects may be added to Cohorts 2 and/or 3; additional cohorts may be added
For more detailed information, visit www.clinicaltrials.gov, NCT05695248

Population Characteristics

Key Inclusion/Exclusion Criteria

- 18 years old or older
- Documented diagnosis of HAE due to C1-Inhibitor deficiency or dysfunction
- Must have 2 or more HAE attacks in the 8-week run-in period to qualify for STAR-0215 administration

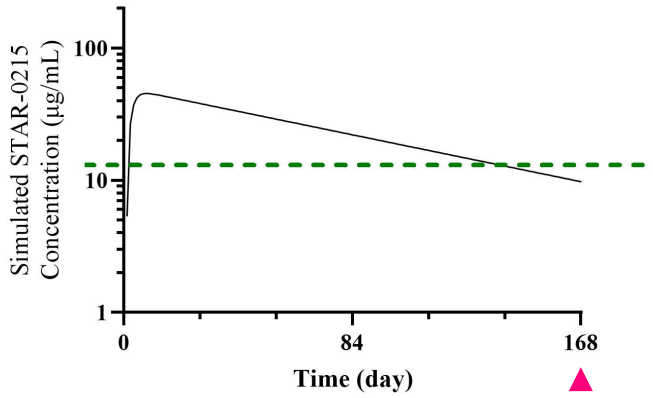
- Any concomitant diagnosis of another form of chronic angioedema, such as acquired C1 inhibitor deficiency, HAE with normal C1-INH (also known as HAE type 3), idiopathic angioedema, or angioedema associated with urticaria.
- Use of therapies prescribed for the prevention of HAE attacks prior to Screening:
  - lanadelumab within 90 days
  - berotralstat within 21 days
  - all other prophylactic therapies, within 7 days
- Any exposure to androgens within 7 days prior to screening.

Dose Selection Rationale

Dose regimens selected based on potential to provide long-term benefit (HAE attack prevention)

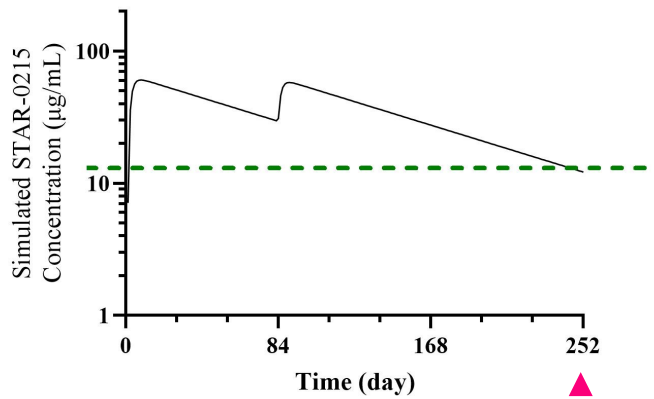
Model and Simulations of ALPHA-STAR Dose Regimens:

Simulation of **Cohort 1** PK Profile
450 mg

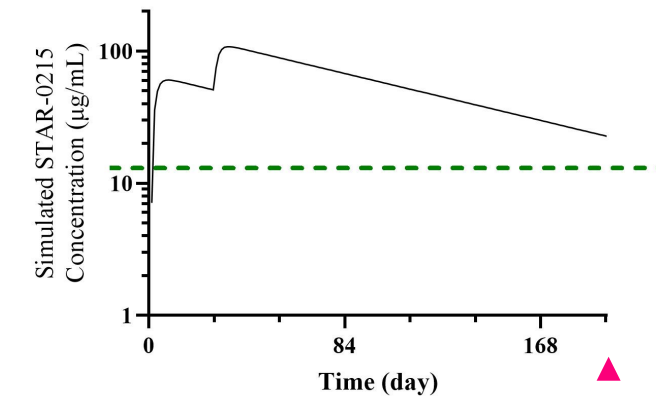


▲ = end of follow-up period

Simulation of **Cohort 2** PK Profile
600 mg / 300 mg at Day 84



Simulation of **Cohort 3** PK Profile
600 mg / 600 mg at Day 28



Targeting STAR-0215 concentrations above 12 µg/mL is expected to confer HAE attack prevention[1-3] (green dashed line)

1. Compartmental PK model built from available Phase 1a healthy subject data.
2. Kaufman 1991 June 15. Blood 77(12): 2660-2667
3. Wang et al. Clin Transl Sci. 2020 Nov, 13(6): 1208-1216. doi 10-1111/cts. 12806 Epub 2020 May 26.
4. Ecallantide EMA Assessment Report. 2011 June 23. EMA/CHMP/476618/2011

Statistical Considerations

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Primary Outcome Measure:

Safety: Number of Participants Experiencing Treatment-Emergent Adverse Events

Secondary Outcome Measures:

Efficacy:

- Change From Baseline in Monthly HAE Attack Rate
- Severity of HAE Attacks Experienced By Participants
- Duration of HAE Attacks
- Number of Participants Experiencing HAE Attacks Requiring On-Demand Therapy
- Time to First HAE Attack After First And Last Dosing

PK and PD:

- Serum Concentration of STAR-0215
- Plasma Levels of Cleaved High-Molecular-Weight Kininogen

Immunogenicity: Number of Participants with Anti-Drug Antibodies to STAR-0215

Open-Label Trial:

Endpoints are objective and change-from-baseline HAE attacks will inform efficacy

HAE attacks are confirmed by investigators

Sample size: Up to 28 participants*

astria THERAPEUTICS

* Planned amendment will increase sample size to maximum 28 participants
For more detailed information, visit www.clinicaltrials.gov, NCT05695248

Partnering with the HAE Community

Pre-Trial

Established relationships with advocacy leaders

- Incorporated feedback into protocol design and available solutions for trial experience
- Engaged global advocacy leaders to advise on trial sites

Engaged patients

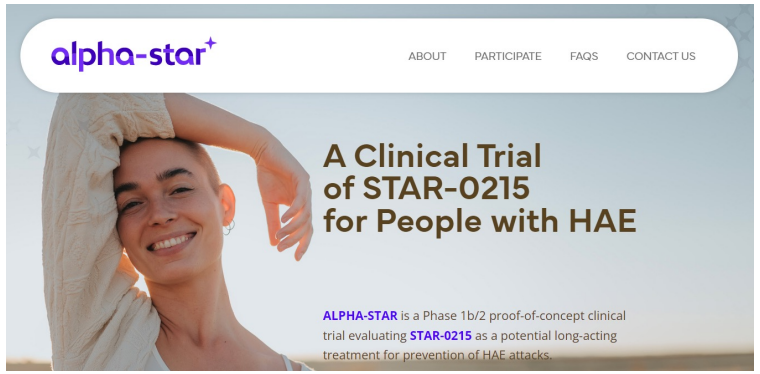
- Conducted patient interviews to understand unmet needs, most meaningful endpoints; input on design
- Review ICFs and recruitment materials to ensure simplicity, clarity

Collaboration with trial sites to mitigate potential patient challenges

During Trial

Advocacy group has mechanisms for trial awareness

- Inclusion in newsletters, “clinical trials” pages on website
- Proactive regional outreach by some groups to patients



Operational Considerations

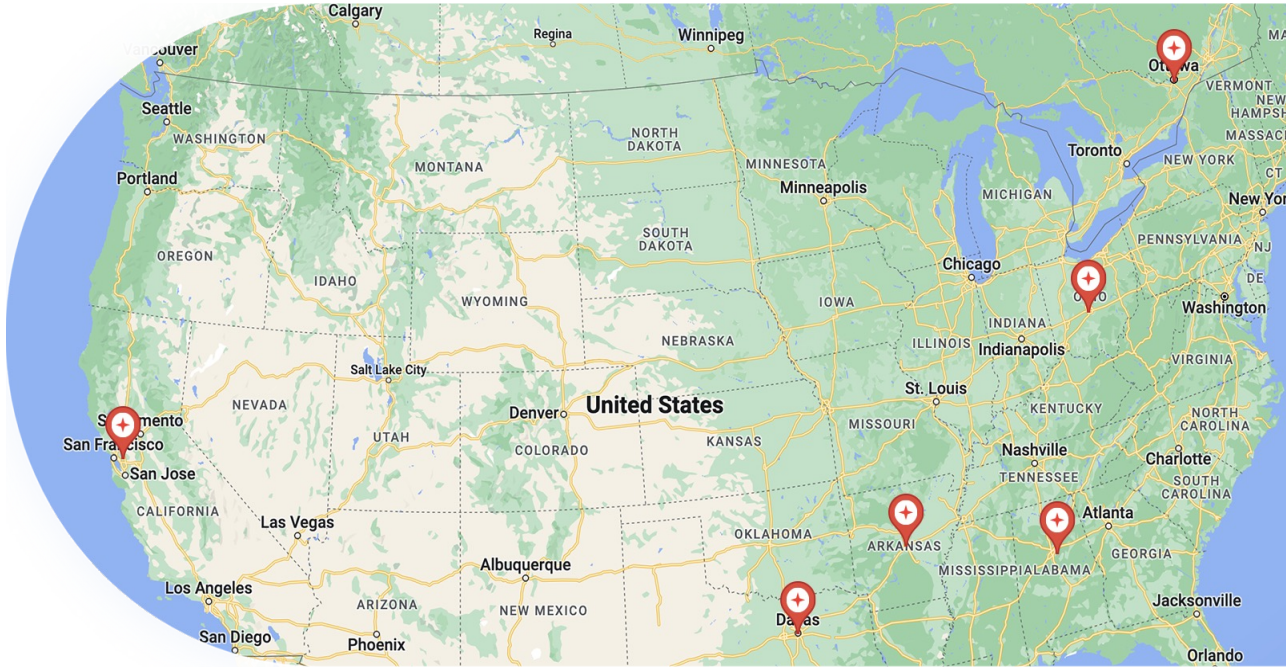
Approximately 25 sites in US, Canada, UK, and EU

- Initiated in US and Canada; UK and EU site initiations are in process

Expect initial proof-of-concept results in mid-2024

- Results will inform plans for the Phase 3 trial, if favorable

Long-Term Open Label trial planned to open in time for the first completers of ALPHA-STAR to opt-in



Initiated ALPHA-STAR Sites (as of 26-April-2023)

See www.astriatx.com/for-patients/alpha-star-trial/ for up-to-date map information.
For more detailed information, visit www.clinicaltrials.gov, NCT05695248

Conclusions

STAR-0215 is a **potential long-term preventative treatment** for HAE-C1INH (Type 1 or 2), administered SC every 3 or 6 months

Phase 1a healthy volunteer results show **potential best-in-class pharmacokinetic profile** and **durable plasma-kallikrein inhibition** for at least 3 months after single doses

ALPHA-STAR is a **proof-of-concept trial** of STAR-0215 in adults living with HAE

- Proof-of-concept will be defined by ability to achieve durable clinical benefits safely when administered every 3 or 6 months
- Trial has initiated and enrollment is on-going
- Initial results are expected in mid-2024

SC = subcutaneous