Rationale and Design of the ALPHA-SOLAR Clinical Trial of STAR-0215 for the Treatment of Hereditary Angioedema (HAE)

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SUMMARY

1 ALPHA-SOLAR LONG-TERM OPEN-LABEL TRIAL EVALUATES THE LONG-TERM SAFETY AND EFFICACY OF STAR-0215

2 INITIAL RESULTS OF THE ALPHA-STAR TRIAL DEMONSTRATED A FAVORABLE SAFETY AND TOLERABILITY PROFILE OF STAR-0215

3 ALPHA-STAR AND ALPHA-SOLAR SUPPORT THE POTENTIAL OF STAR-0215 TO PROVIDE DISEASE CONTROL AND NORMALIZE THE LIVES OF PATIENTS WITH HAE

OBJECTIVES

- The goal of the ALPHA-SOLAR clinical trial is to enable the collection of information about long-term safety and efficacy of STAR-0215 in participants with HAE.

INTRODUCTION

- Hereditary angioedema (HAE), a rare genetic disorder, causes episodic attacks of localized swelling which can be disabling and potentially fatal.
- In patients with HAE due to C1-inhibitor deficiency or dysfunction, normal regulation of plasma kallikrein activity is lacking leading to increases in plasma kallikrein activity and release of bradykinin resulting in angioedema attacks.
- STAR-0215 is an investigational monoclonal antibody inhibitor of plasma kallikrein with long-lasting activity enabled by a YTE-modified Fc domain.
- Results from the single ascending dose Phase 1a trial (NCT05477160) demonstrated that STAR-0215 was well tolerated at all doses administered and achieved clinically relevant kallikrein inhibition after single doses > 100 mg.[1]
- These results support the ongoing Phase 1b/2 ALPHA-STAR trial (NCT05695248); initial results demonstrate a rapid reduction in monthly attack rates (90-96%) after 3 and 6 months of follow up, coupled with a favorable safety profile.
- There were no reports of injection site pain with administration of STAR-0215 in HAE patients in ALPHA-STAR.
- Here, we describe the design of the ongoing Phase 2 extension study (NCT06007677) that is investigating the long-term safety of STAR-0215 in patients with HAE.

METHODS

- ALPHA-SOLAR is an open-label, phase 2 clinical trial (NCT06007677) open to participants in the ongoing Phase 1b/2 ALPHA-STAR trial (adults, HAE type 1 or 2) who meet eligibility requirements. This trial will enroll up to 56 participants globally. Enrolled participants will receive a subcutaneous (SC) loading dose (600 mg) and either 300 mg SC every 3 months (Q3M) or 600 mg SC every 6 months (Q6M) of STAR-0215. ALPHA-SOLAR participants who continue from ALPHA-STAR cohorts 1 and 2 will receive a SC loading dose and Q3M; participants from ALPHA-STAR cohort 3 will receive a SC loading dose and Q6M. The assessments occur every 3 and 6 months. The trial is expected to continue for 5 years (**Figure 1**).

KEY INCLUSION CRITERIA

- Open to participants from (NCT05695248) who have met one of the following conditions:
  - Completed ALPHA-STAR (follow up through 6 months after their last dose);
  - Eligible for ALPHA-STAR and entered the Run-In period but did not qualify for the Treatment Period because they did not meet the criterion for the minimum number of HAE attacks;
  - Eligible for ALPHA-STAR and entered the Run-In period but did not complete it for reasons other than not meeting the criterion for the minimum number of HAE attacks (eligibility requires consultation with the Medical Monitor); or
  - Discontinued ALPHA-STAR (for reasons other than safety) after having completed at least 84 days of trial follow-up since their last dose of STAR-0215 (eligibility requires consultation with the Medical Monitor).

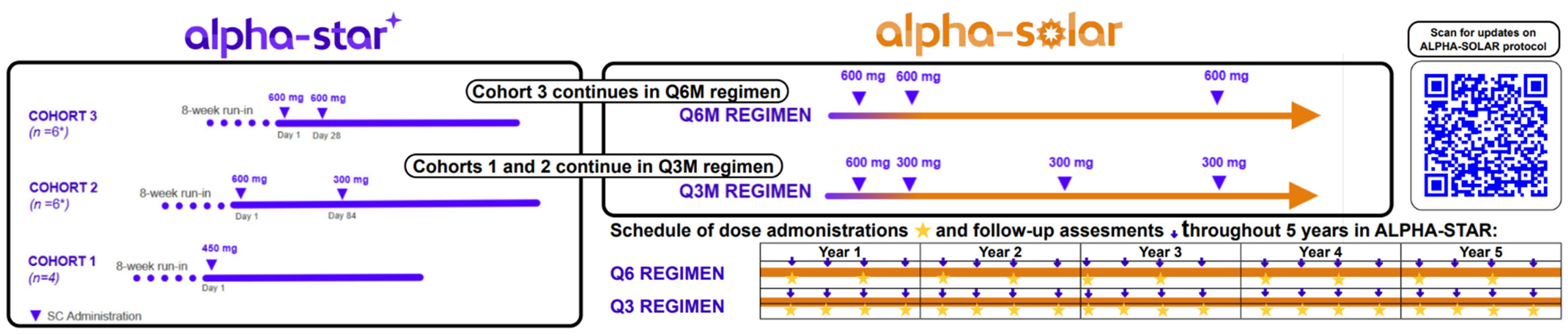
KEY EXCLUSION CRITERIA

- Any concomitant diagnosis of another form of chronic angioedema, such as acquired C1 inhibitor deficiency, HAE with normal C1-esterase inhibitor protein (also known as HAE Type III), idiopathic angioedema, or angioedema associated with urticaria.
- Any exposure to angiotensin-converting enzyme inhibitors or any estrogen-containing medications with systemic absorption (such as hormonal contraceptives or hormone replacement therapy) within 28 days prior to Screening.
- Any exposure to androgens (for example, stanozolol, danazol, oxandrolone, methyltestosterone, testosterone) within 7 days prior to Screening.
- 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, discuss with the Medical Monitor.
- Note: Other inclusion and exclusion criteria may apply.

ALPHA-SOLAR ENDPOINTS

- Primary endpoint
  - To assess long-term safety and tolerability of STAR-0215 in participants with Type 1 or Type 2 HAE
- Secondary endpoints:
  - To assess the long-term clinical efficacy of STAR-0215 in participants with Type 1 or Type 2 HAE
  - Pharmacokinetics
  - Pharmacodynamics
  - Immunogenicity

Figure 1. ALPHA-STAR and ALPHA-SOLAR clinical trial design



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CONCLUSIONS

- **The goal of the ALPHA-SOLAR long-term open-label trial is to evaluate the long-term safety and efficacy of STAR-0215 as a potential long-acting preventative therapy for HAE. Initial results from the ongoing ALPHA-STAR trial demonstrate a favorable safety and tolerability profile, clinically relevant prevention of HAE attacks, and potential for Q3M and Q6M administration. These results support the potential of STAR-0215 to provide disease control and normalize the lives of HAE patients, which is the overarching goal of HAE management. The ALPHA-SOLAR clinical trial will provide additional data of STAR-0215 in patients with HAE.**

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REFERENCES: 1. Lumry, W. et al. *Journal of Allergy and Clinical Immunology,* 2024;153(2).

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