



# Corporate Presentation

August 2023

# Forward Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements within the meaning of applicable securities laws and regulations including, but not limited to, statements regarding: expectations regarding the potential significance of the results from the Phase 1a STAR-0215 trial and the anticipated nature and timing of receipt of additional data from the trial; expectations regarding the timing and nature of the anticipated initial proof of concept results from the ALPHA-STAR Phase 1b/2 clinical trial; the longer term development plans for STAR-0215, including the plan, pending proof-of-concept results from the ALPHA-STAR trial, to progress directly to a pivotal trial; the timing of, and plans to, initiate a long-term open label trial; the potential attributes and differentiated profile of STAR-0215 as a treatment for HAE, including those suggested by the results from the STAR-0215 Phase 1a trial, market research, mechanistic modeling and patient feedback, and our goals and vision for STAR-0215; the potential commercial opportunity for STAR-0215 in HAE and the likelihood that it can effectively compete in HAE, assuming its approved; the size of the HAE market and the need for effective treatments for HAE; the potential for three and six-month administration and potential for suppression of HAE attacks of STAR-0215; anticipated cash runway; and the goal to meet the unmet needs of patients with rare and niche allergic and immunological diseases. The use of words such as, but not limited to, “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “goals,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would,” or “vision,” and similar words expressions are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on the Company’s current beliefs, expectations and assumptions regarding the future of its business, future plans and strategies, future financial performance, results of pre-clinical and clinical results of the Company’s product candidates and other future conditions. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including risks and uncertainties: changes in applicable laws or regulations; the possibility that we may be adversely affected by other economic, business, and/or competitive factors, including the COVID-19 pandemic; risks inherent in pharmaceutical research and development, such as: adverse results in our drug discovery, preclinical and clinical development activities, the risk that the results of pre-clinical studies may not be replicated in clinical studies, that the preliminary results from the Phase 1a trial may not be indicative of the final results, that the results of early stage clinical studies, such as the preliminary results from the Phase 1a trial, may not be replicated in later stage clinical studies, including the ALPHA-STAR trial, the risk that we may not be able to enroll sufficient patients in our clinical trials on a timely basis, and the risk that any of our clinical trials may not commence, continue or be completed on time, or at all; decisions made by, and feedback received from, the U.S. Food and Drug Administration and other regulatory authorities on our regulatory and clinical trial submissions and other feedback from potential clinical trial sites, including investigational review boards at such sites, and other review bodies with respect to STAR-0215 and any other future development candidates; our ability to manufacture sufficient quantities of drug substance and drug product for STAR-0215 and any other future product candidates on a cost-effective and timely basis, and to develop dosages and formulation for STAR-0215 and any other future product candidates that are patient-friendly and competitive; our ability to develop biomarker and other assays, along with the testing protocols therefore; our ability to obtain, maintain and enforce intellectual property rights for STAR-0215 and any other future product candidates; our potential dependence on collaboration partners; competition with respect to STAR-0215 or any of our other future product candidates; the risk that survey results and market research may not be accurate predictors of the commercial landscape for HAE, the ability of STAR-0215 to compete in HAE and the anticipated position and attributes of STAR-0215 in HAE based on clinical data to date, its pre-clinical profile, pharmacokinetic modeling, market research and other data; our ability to manage our cash usage and the possibility of unexpected cash expenditures; our ability to obtain necessary financing to conduct our planned activities and to manage unplanned cash requirements; the risks and uncertainties related to our ability to recognize the benefits of any additional acquisitions, licenses or similar transactions; and general economic and market conditions; as well as the risks and uncertainties discussed in the “Risk Factors” section of our Annual Report on Form 10-K for the period ended December 31, 2022 and in other filings that we may make with the Securities and Exchange Commission (“SEC”). New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. The Company may not actually achieve the forecasts or expectations disclosed in our forward-looking statements, and investors and potential investors should not place undue reliance on the Company’s forward-looking statements. Neither the Company, nor its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company’s views as of any date subsequent to the date hereof.

# Investment Highlights



Astria (Nasdaq: ATXS) is developing differentiated therapeutics for patients with rare and niche allergic and immunological diseases



Our lead program, **STAR-0215**, is a monoclonal antibody inhibitor of plasma kallikrein for the preventative treatment of Hereditary Angioedema (HAE)

- STAR-0215 has shown early proof of concept for its target profile: long-acting preventative therapy, best-in-class PK profile, and dosing once every 3 or 6 months
- HAE market is large and growing, expected to reach \$4.2B by 2028<sup>1,2</sup>



Phase 1b/2 ALPHA-STAR trial in HAE patients is underway and is enrolling and administering STAR-0215 to patients. Initial proof-of-concept results expected in mid-2024



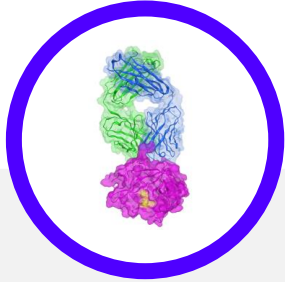
Pursuing opportunities to expand our pipeline in allergic and immunological diseases



Cash, cash equivalents and short-term investments of \$203M<sup>3</sup>  
Expected cash runway through H1 2025 based on current operating plan

# Our Vision for STAR-0215

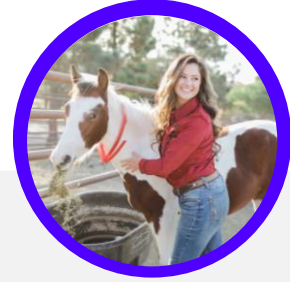
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**First-choice  
preventative  
treatment for HAE**



**Q3 or Q6 month  
administration**







**Normalize the lives  
of people with HAE**

*Allow patients to focus their time and energy on what matters most to them*

# STAR-0215 Development Strategy




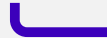

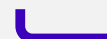
1

## Transform treatment paradigm with Q3 month dosing

-  Evaluated safety, PK, and PD in healthy subjects
-  Confirmed strong demand with patients and physicians
-  Evaluate safety and efficacy in patients  
 *In progress, initial results expected mid-2024*

2

## Explore Q6 month dosing interval

-  Evaluate safety, PK, and PD in healthy subjects  
 *In progress, initial results expected Q4 2023*
-  Understand patient and physician interest  
 *In progress in 2023*
-  Evaluate safety and efficacy in patients  
 *In progress, initial results expected mid-2024*

# Hereditary Angioedema (HAE): A Rare, Disfiguring, and Potentially Life-Threatening Disease

Rare genetic disorder characterized by severe, unpredictable, sometimes **life-threatening** swelling<sup>1</sup>

Affects **<8,000 in the U.S. and <15,000 in Europe**,<sup>2, 3, 4</sup> average age of onset is 11 years old<sup>5</sup>

Standard of care has evolved to both **on-demand** and **preventative treatments** with room for improvement



1. Zuraw BL. N Engl J Med. 2008;359:1027-36.
2. Busse, P.J. et al. N Engl J Med. 2021; 132-150.
3. Lumry, W.R. Front Med. 2018; 5, 22.
4. Aygören-Pürsün, E. et.al. Orphanet J Rare Dis. 2018; 13:73.

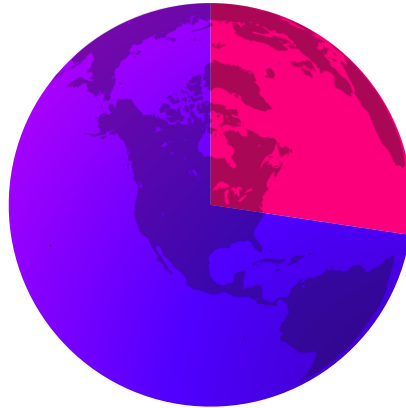
5. Bork K, et al. Am J Med. 2006;119:267-274.
6. Images obtained by haeimages.com

# Global HAE Treatment Market is Substantial and Growing

The HAE market is expected to grow substantially by 2028,<sup>1,2</sup> driven by:

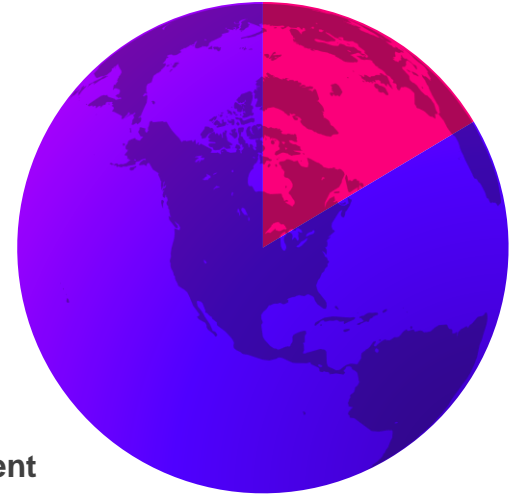
- Patients being diagnosed earlier<sup>3</sup>
- More patients taking preventative treatments<sup>4</sup>
- Geographic expansion for currently available therapies<sup>5</sup>

2022 HAE Market<sup>1</sup>



**\$2.6B**

2028 Estimated HAE Market<sup>1,2</sup>







**\$4.2B**

HAE Treatment



- Preventative
- On-Demand

# Approved and Late-Stage Preventative HAE Treatments

## Approved Therapies

Product	Mechanism of Action	Administration	Mean Attack Reduction*	% of Attack- Free Patients
<b>CINRYZE</b>	Plasma derived C1-INH	2x/week 	52%	18% (12 weeks) <sup>1</sup>
<b>HAEGARDA</b>	Plasma derived C1-INH	2x/week 	88%	40% (16 weeks) <sup>2</sup>
<b>TAKHZYRO</b> ( <i>lanadelumab</i> )	Plasma kallikrein inhibitor	1-2x/month 	73-87%	31-44% (26 weeks) <sup>3</sup>
<b>ORLADEYO</b> ( <i>berotralstat</i> )	Plasma kallikrein inhibitor	1x/day 	30-44%	2-8% (24 weeks) <sup>4</sup>

## Late-Stage Development Programs

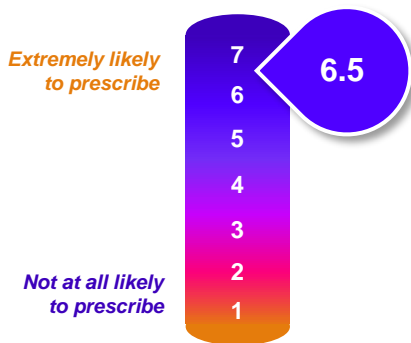
Program	Mechanism of Action	Administration	Mean Attack Reduction*	% of Attack- Free Patients
<b>garadacimab</b>	Factor XIIIa inhibitor	1x/month 	87%	62% (26 weeks) <sup>5</sup>
<b>donidalorsen</b>	Prekallikrein inhibitor	1x/1-2 months 	TBD	TBD <sup>6</sup>

There remains a need for an effective, infrequent treatment that can help normalize the lives of people with HAE

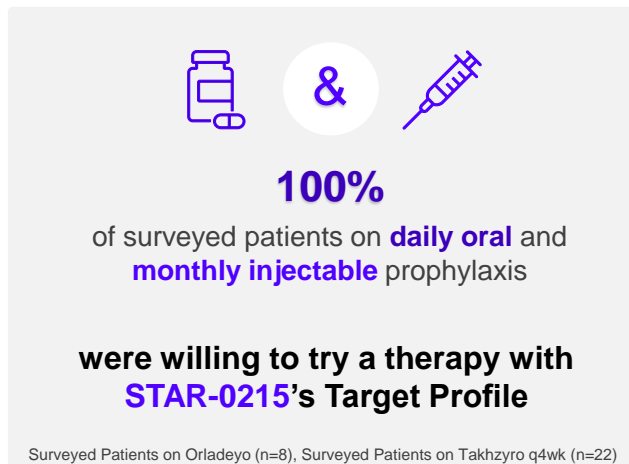
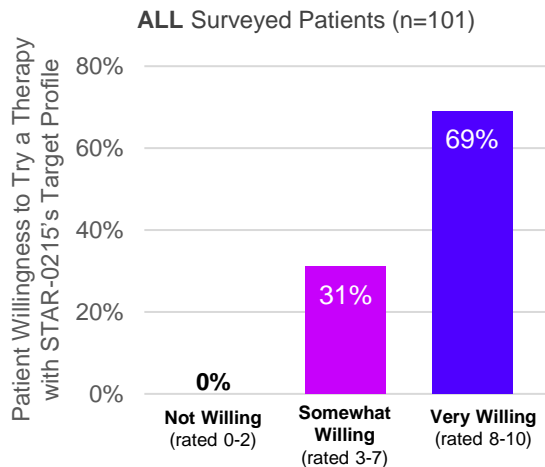


# STAR-0215's Target Efficacy and Dosing is Compelling to Surveyed HAE Treatment Providers and Patients

Surveyed Prescribers Were Highly Motivated to Prescribe a Product with STAR-0215's Q3 Month Target Profile<sup>1</sup>



All Surveyed Patients Were Willing to Try an Effective Q3 Month Product<sup>2</sup>

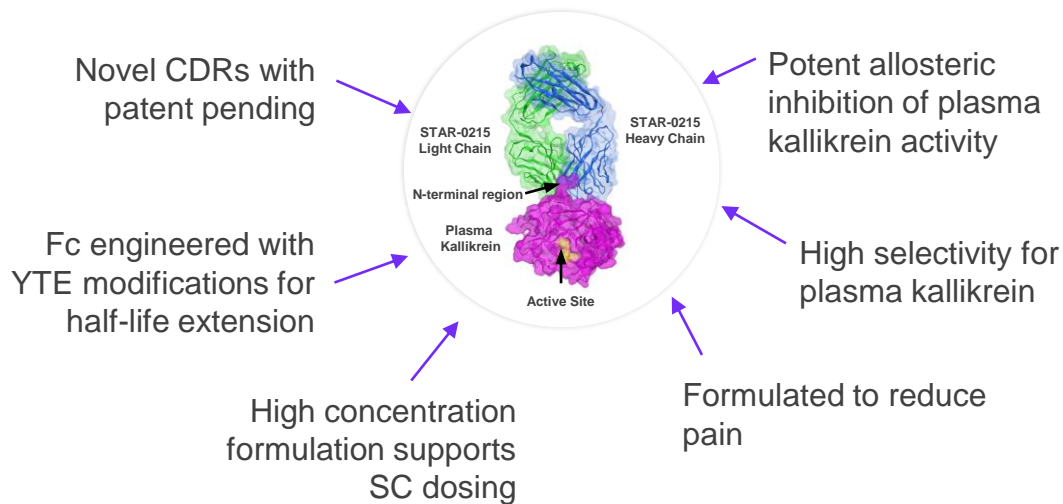


Results suggest that STAR-0215 would gain strong patient share in a future HAE market

# STAR-0215

## Potential for Best-in-Class in HAE

### Preclinical Profile of STAR-0215



#### Encouraging initial clinical results

Demonstrated best-in-class PK profile with long plasma half-life and sustained inhibition of plasma kallikrein

#### Differentiated profile

Potential benefits include long duration without breakthrough attacks and infrequent SC dosing- once every 3 or 6 months

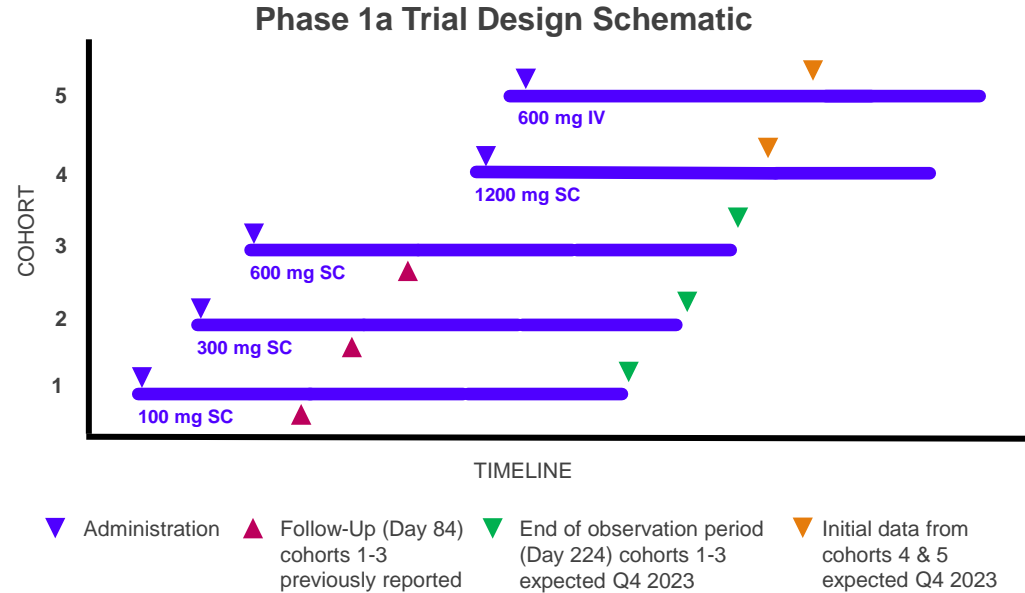
#### Trusted modality

Monoclonal antibody inhibitors of plasma kallikrein are clinically and commercially validated in HAE<sup>2,3</sup>

*Astria wholly owns an international patent application directed to STAR-0215. If nationalized in the U.S. and granted, the patent would expire in 2042, excluding any potential patent term extension<sup>1</sup>*

# STAR-0215 Phase 1a Trial

- Randomized, double-blind, placebo-controlled in healthy adult subjects
  - 5 single ascending doses (6:2 randomization)
  - Endpoints: Safety, tolerability, PK, PD, ADA
- Data in Q4 2023 expected to enable updates to PK and QSP models, anticipated to support 3 and 6-month administration strategies



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

## Cohorts 1-3 through 3-Month Timepoint

### **STAR-0215<sup>1</sup>:**

- 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 redness; no reports of pain
- All related TEAEs were mild (Grade 1) and resolved. No Grade 2, 3, or 4 TEAEs. There were no SAEs and no discontinuations due to TEAEs.

**Immunogenicity:** No treatment-emergent ADAs were detected

### **Lanadelumab<sup>2</sup>:**

The most common adverse reactions associated with lanadelumab are:

- Injection site reactions, most commonly pain (52%)
- Upper respiratory tract infection (29%)
- Headache (21%)

TEAE= Treatment-emergent adverse event; ISR = injection site reaction; SAE = serious adverse events; ADA = anti-drug antibody

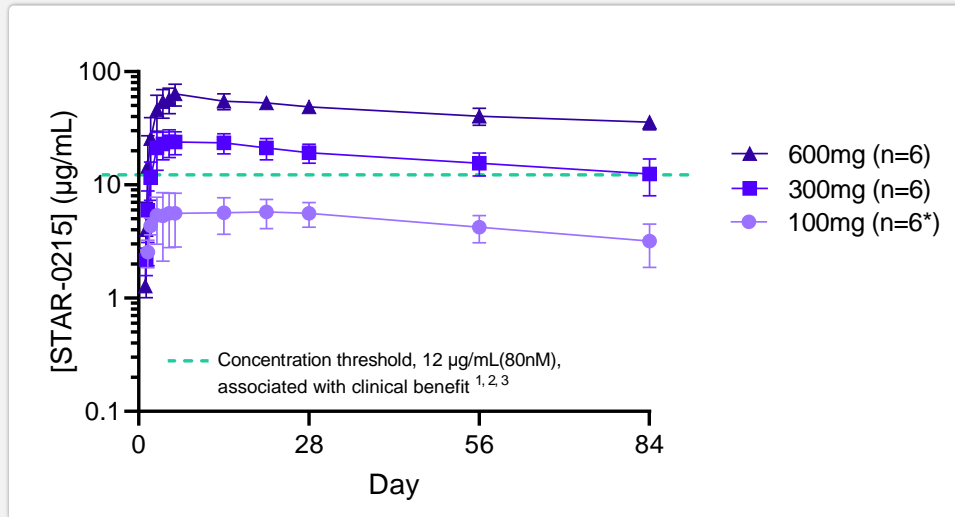
1. Other related TEAEs were headache (1 subject receiving placebo) and unexplained weight gain (1 subject receiving STAR-0215), both in Cohort 1 (100 mg). 15 Grade 1 (mild) ISRs occurred in 6 subjects, including erythema (site redness), pruritus, swelling and inflammation.

There were no clinically relevant changes in vital signs, ECG parameters, or laboratory values. No clinically relevant changes in liver enzymes or coagulation parameters. No deaths, or adverse events leading to study discontinuation.

2. TAKHZYRO US Prescribing Information, Feb 2023.

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. Data cutoff is Day 84.

# Initial Results Show **STAR-0215** Has a Potential Best-In-Class PK Profile



- Results show rapid and sustained achievement of STAR-0215 concentrations consistent with clinical benefit ( $\geq 12 \mu\text{g/ml}^{1-3}$ ) 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.

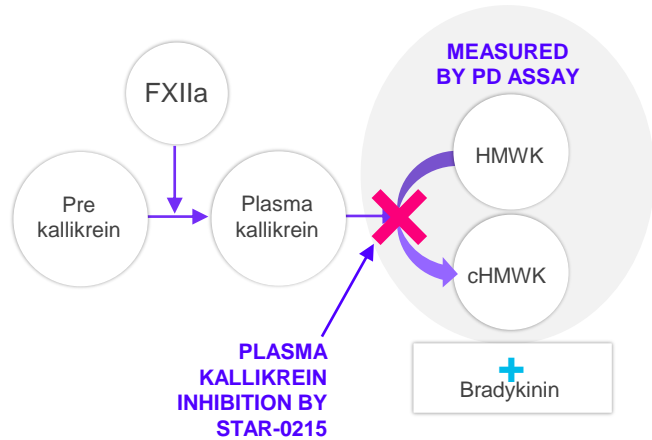
3. Ecallantide EMA Assessment Report. 2011 June 23. EMA/CHMP/476618/2011

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

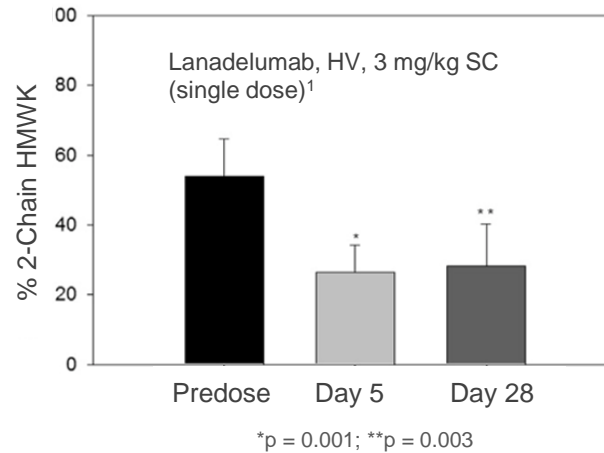
\*One subject excluded from the analysis due to partial dose administered.

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

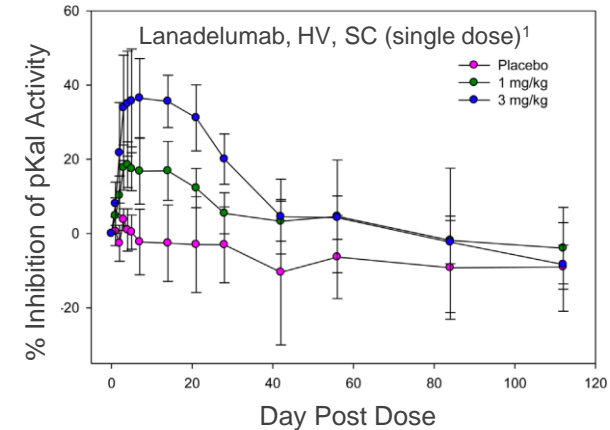
# Assessing Plasma Kallikrein Target Engagement



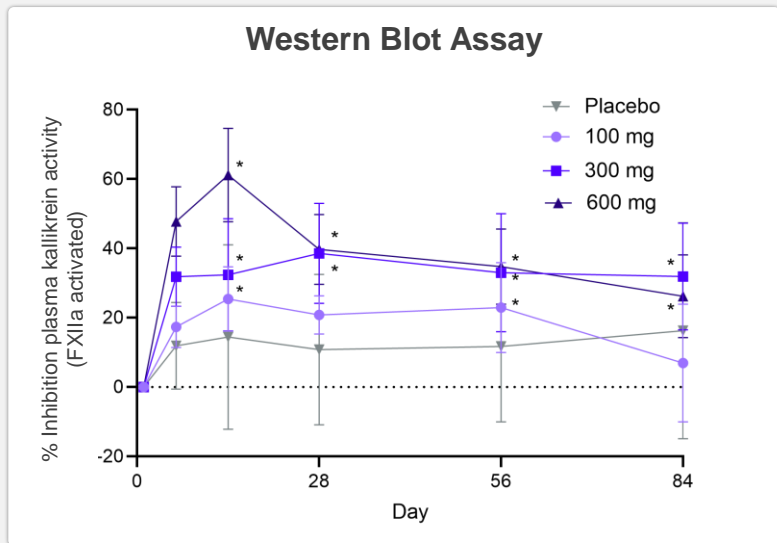
## Western Blot Assay Cleavage of HMWK



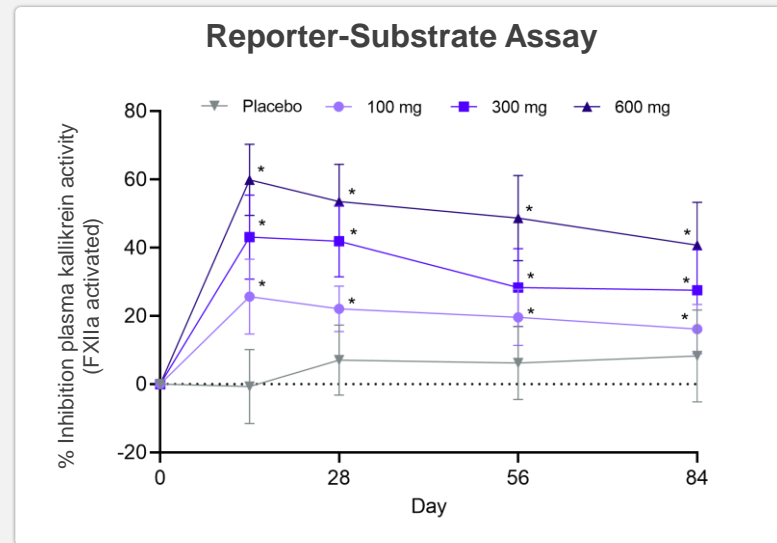
## Reporter-Substrate Assay Cleavage of Peptide Substrate



# Initial Results Show **STAR-0215** Achieves Sustained Inhibition of Plasma Kallikrein



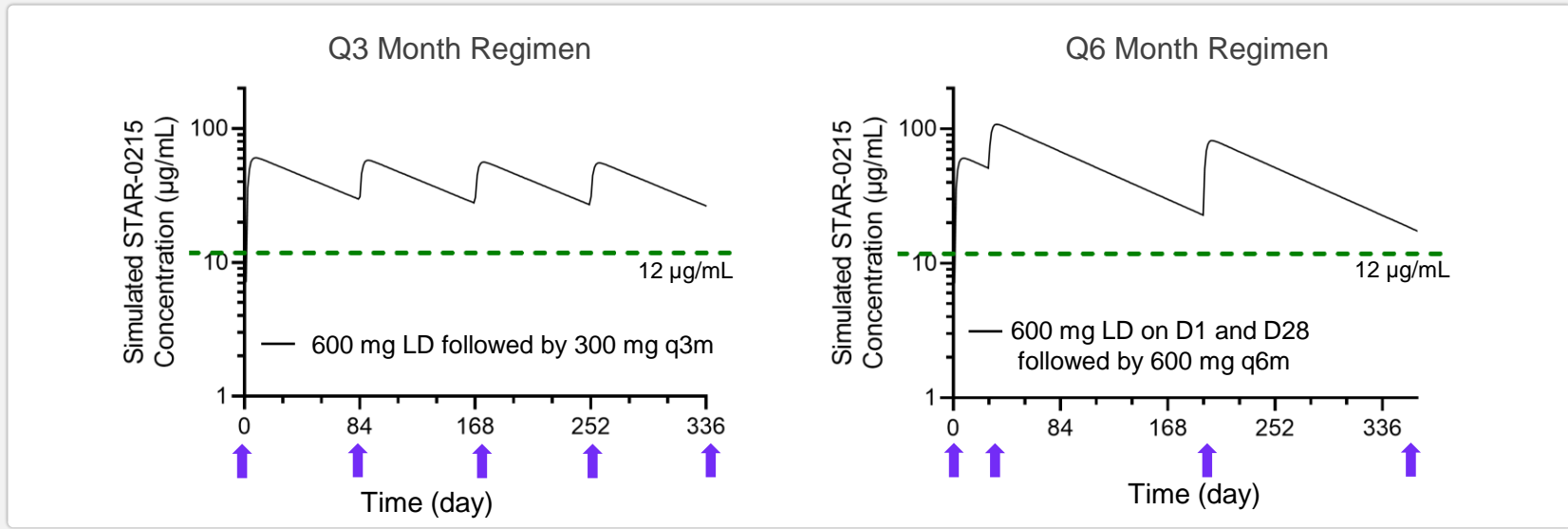
Significant inhibition of plasma kallikrein activity at all post-dose timepoints for 300 mg and 600 mg



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

# STAR-0215 Could Sustain Exposure Above Target Threshold with Both Q3 and Q6 Month Regimens

## Human Pharmacometric Model



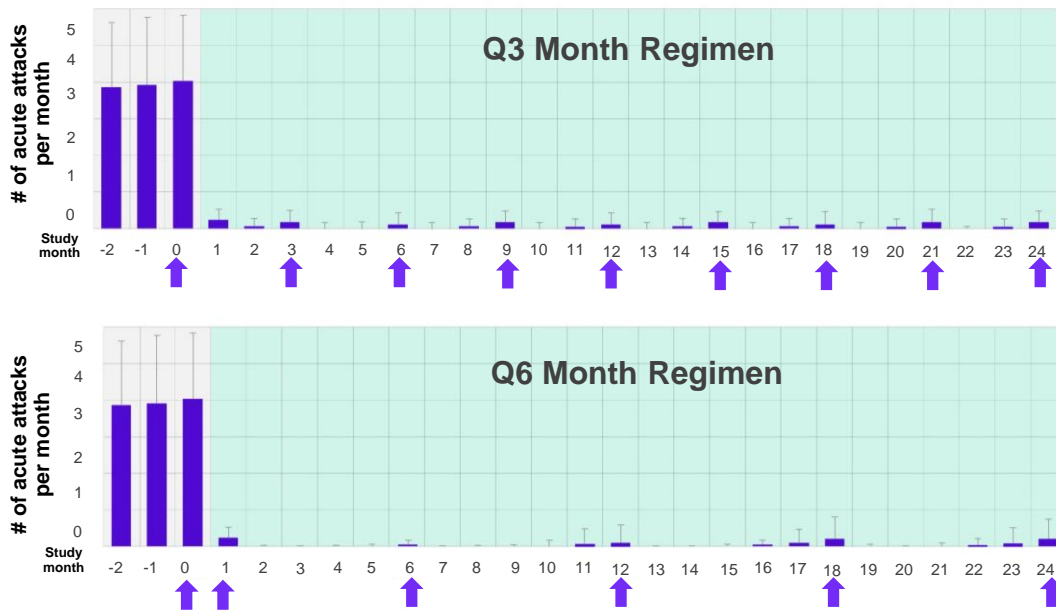
$C_{min}$  steady state concentrations remain above target threshold (12 µg/mL) associated with clinical benefit<sup>1,2,3</sup>



1. Kaufman 1991 June 15, Blood 77(12):2660-2667  
2. Wang et al. Clin Transl Sci. 2020 Nov, 13(6):1208-1216  
3. Ecallantide EMA Assessment Report 2011 June 23. EMA/CHMP/476618/2011  
 $C_{min}$ =minimum / trough concentration  
Pharmacometric model is based on initial human pharmacokinetic data from the Phase 1a trial in healthy adult subjects.  
These data were presented at the 13<sup>th</sup> C1-Inhibitor Deficiency and Angioedema Workshop, May 4-7, 2023, Budapest Hungary.



# Validated QSP Model Predicts **STAR-0215** May Produce Robust and Long-Lasting HAE Attack Suppression



- Model estimated a  $\geq 90\%$  reduction in monthly HAE attack rate for both Q3 and Q6 month dose regimens
- Model estimated between 75% - 86% of treated HAE patients would be attack-free during the first 6 months of treatment

A population simulation using virtual patients ( $n=500$  per cohort). The quantitative systems pharmacology (QSP) model was configured to represent the simplified biological process of the contact system, the production of bradykinin and the cleaved HMWK, and to determine the likelihood of a HAE attack.

The QSP model was established based on published reaction parameters for the plasma kallikrein-kininogen pathway.<sup>1, 2, 3</sup>

1. Narayanan, R. et al. 2019, Allergy, Asthma & Clinical Immunology. 15 (Suppl 4):P17.

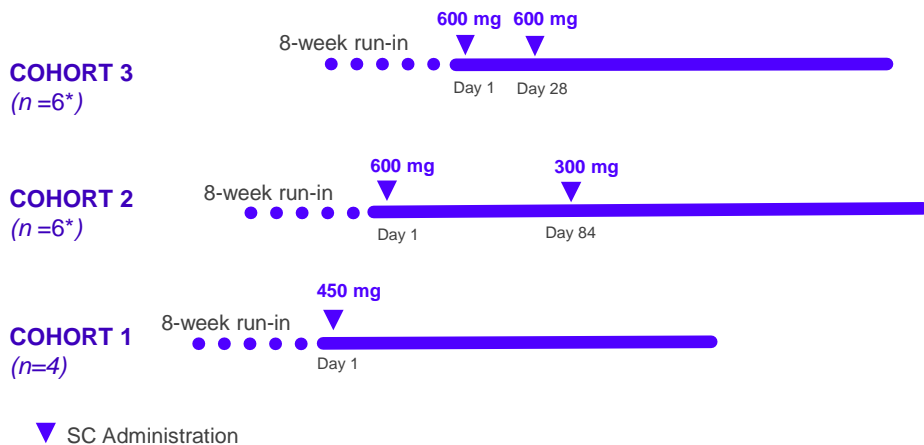
2. López-Lera, A. et al. 2019, Allergy, Asthma & Clinical Immunology. 15 (Suppl 4):P18.

3. Narayanan, R. et al. 2020, The Journal of Allergy and Clinical Immunology. 145, 2 (Suppl) AB105.

Chung, J. et al. Mechanistic Modeling and Simulations Predict Long-Term HAE Attack Prevention with STAR-0215. Poster P-05 presented at the 13<sup>th</sup> C1-Inhibitor Deficiency and Angioedema Workshop.

# ALPHA-STAR Trial Currently Enrolling and Dosing HAE Patients

## ALPHA-STAR Phase 1b/2 Proof-of-Concept Trial Design Schematic



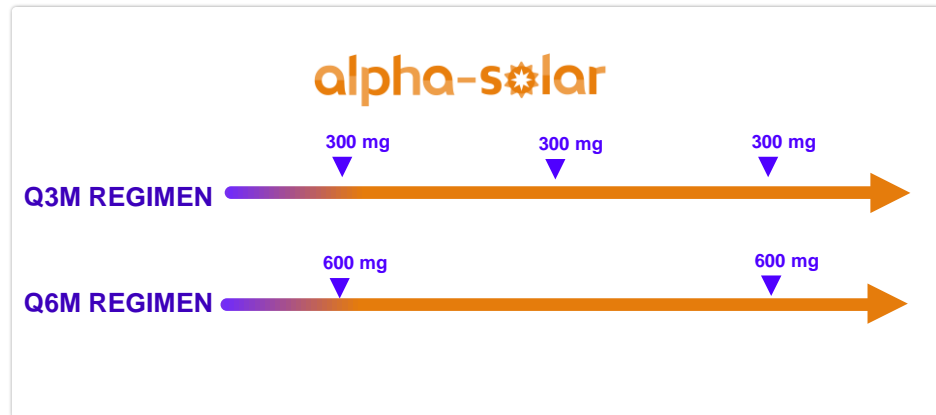
## ALPHA-SOLAR Long-Term Open-Label Trial

- Three dose-ranging cohorts planned 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 expected in mid-2024
  - Results expected from all 3 cohorts
  - Assessing safety and tolerability, PK, PD, attack rate, and QOL in these 3 cohorts
  - Goal: significant reduction in attacks following STAR-0215 treatment

# ALPHA-SOLAR Long-Term Open-Label Trial

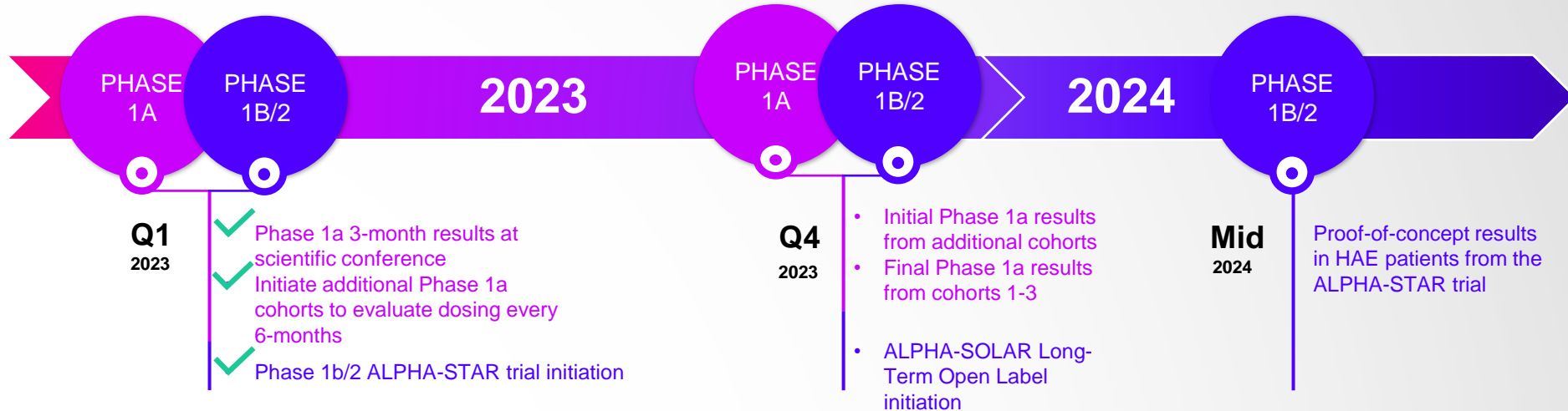
Expected to Initiate Q4 2023

- Expected to be open to participants from ALPHA-STAR
- Trial designed to assess long-term safety, tolerability and clinical activity of STAR-0215
  - Build dataset to support potential regulatory approvals
- **Primary Endpoint:**
  - Safety and tolerability
- **Secondary Endpoints:**
  - Efficacy including attack rate, attack-free participants, PK, and PD



# Astria (Nasdaq ATXS) Well-Positioned for the Future

## Completed and Expected Upcoming Milestones



- Cash, cash equivalents and short-term investments of \$203M<sup>1</sup>
- Expected cash runway through H1 2025 based on current operating plan
- Common shares outstanding on an as-converted basis<sup>1</sup>: 33.2M
  - 28.0M common shares outstanding and 5.2M series X preferred



**astria**  
THERAPEUTICS