# Astria R&D Day: Update on STAR-0215 and Its Clinical Development for the Prevention of HAE Attacks

**September 30, 2022**

# Forward Looking Statements

This presentation and various remarks we make during this presentation contain forward-looking statements of Astria Therapeutics, Inc. (“Astria,” the “Company,” “we”, “our” or “us”) within the meaning of applicable securities laws and regulations, including statements with respect to: the Company's projected cash runway; expectations regarding the nature, timing and potential significance of the preliminary results from the Phase 1a STAR-0215 trial; the planned timing of initiation of a Phase 1b/2 clinical trial of STAR-0215; the potential Phase 3 development plans for STAR-0215; the potential attributes and differentiated profile of STAR-0215 as a treatment for HAE, including its potential half-life and those suggested by preclinical and pharmacokinetic modeling data; the potential commercial opportunity for STAR-0215 in HAE, including its potential to be a best-in-class and most patient friendly treatment option for HAE; the need for effective treatments for HAE; the planned biomarker assay for STAR-0215; the size and anticipated growth of the HAE market; the expected patent protection of patents directed at STAR-0215; and the Company’s goal to meet the unmet needs of patients with rare and niche allergic and immunological diseases, and expand its pipeline. We use words such as "aims," “anticipate,” “believe,” “estimate,” “expect,” "goals," “hope,” “intend,” “may,” "opportunity," “plan,” “predict,” “project,” “target,” “potential,” “would,” "vision," “can,” “could,” “should,” “continue,” and other words and terms of similar meaning to help identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including risks and uncertainties related to: 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 and that the results of early stage clinical studies may not be replicated in later stage clinical studies, 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. FDA (“FDA”) and other regulatory authorities on our regulatory and clinical trial submissions and other feedback from investigational review boards at clinical trial 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; 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 and the anticipated position and attributes of STAR-0215 in HAE based on its pre-clinical profile, pharmacokinetic modeling 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, 2021, subsequent Quarterly Reports on Form 10-Q, and in other filings that we may make with the Securities and Exchange Commission. These forward-looking statements should not be relied upon as representing our view as of any date subsequent to the date of this presentation, and we expressly disclaim any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

This presentation contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

# Welcome and Introduction to Astria

Our mission is to bring life-changing therapies to patients and families.

We are driven to change the way that people live with HAE by allowing them to focus their time and energy on what matters most to them.

# STAR-0215 Has the Opportunity to Change the Way That People Live With HAE

## PROFILE

**STAR-0215**
is a monoclonal antibody inhibitor of plasma kallikrein designed to provide long-acting, effective attack prevention for HAE with dosing once every three months or longer

## YEAR END RESULTS

**Preliminary clinical results expected to inform the profile of STAR-0215 to prevent HAE attacks**

- Expected results in healthy subjects include safety and tolerability, PK, and PD results

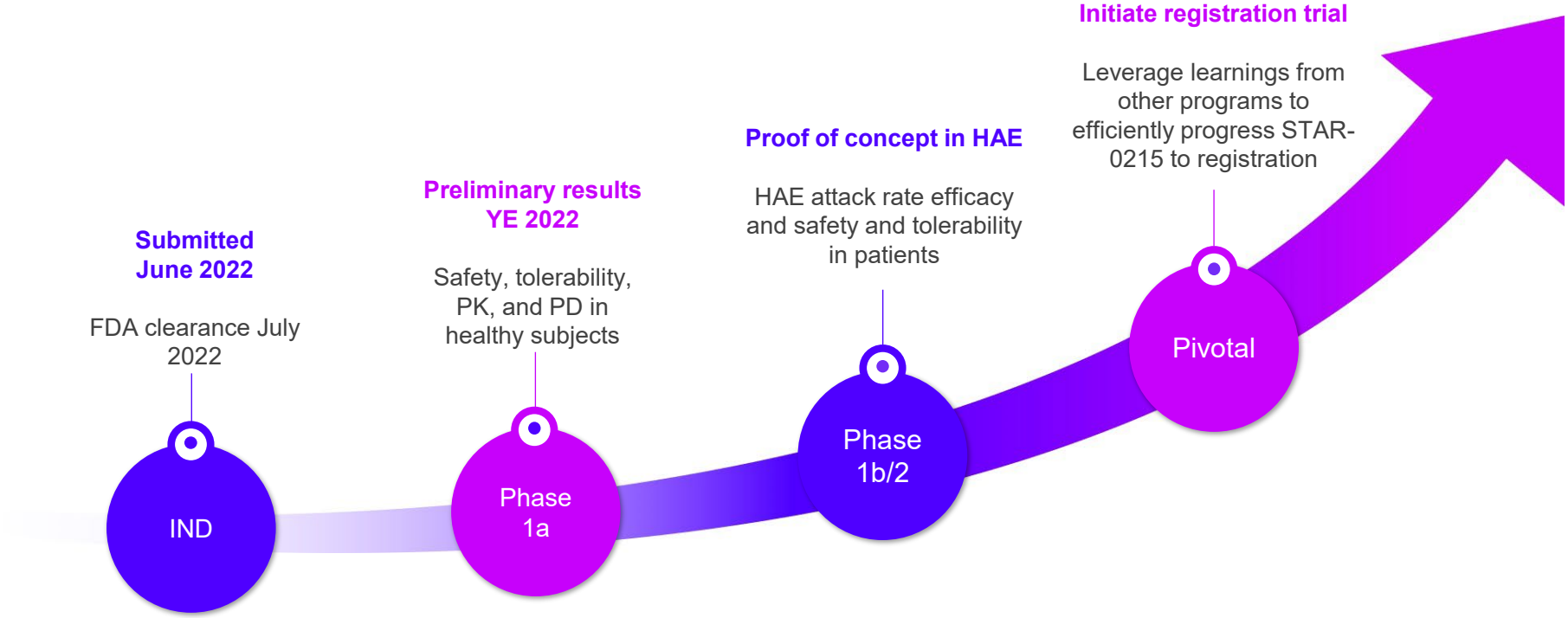
## COMMERCIAL OPPORTUNITY

**STAR-0215 has the potential to significantly reduce treatment burden for patients**

- The HAE global treatment market is substantial and growing, estimated to be $4.5B in 2027
- Patients and physicians are highly interested in STAR-0215's target efficacy and dosing frequency

# Aiming to Progress STAR-0215 Quickly to Patients

## Completed and Expected Upcoming Milestones



# Agenda

## Sessions

**Introduction and Astria Overview**

Jill C. Milne, Ph.D., *Co-Founder and CEO*

**Living With HAE**

US Hereditary Angioedema Association and HAE International

**Hereditary Angioedema (HAE):** ***Current Treatment & Opportunity to Improve Patient Experience***

Dr. Marc Riedl M.D., UC San Diego Professor of Medicine | Clinical Director of US HAEA Angioedema Center UCSD

**HAE Market Insights**

Andrew Komjathy, MBA, *Chief Commercial Officer*

**Characteristics of STAR-0215 and Preclinical Data**

Andy Nichols, Ph.D., *Chief Scientific Officer*

**Clinical Development Plans and Expected Year-End Results for STAR-0215**

Chris Morabito, M.D., *Chief Medical Officer*

**Q&A**

All

**Concluding Remarks**


Living With HAE
HAEA
US HEREDITARY ANGIOEDEMA ASSOCIATION
HAEi
HAE International

# Hereditary Angioedema (HAE):
## Current Treatment & Opportunity to Improve Patient Experience

**Dr. Marc Riedl, M.D.**
UCSD

# Hereditary Angioedema

Marc Riedl MD MS
Professor of Medicine
Clinical Director – US HAEA Angioedema Center at UCSD
Division of Rheumatology, Allergy & Immunology
University of California, San Diego

# Disclosures

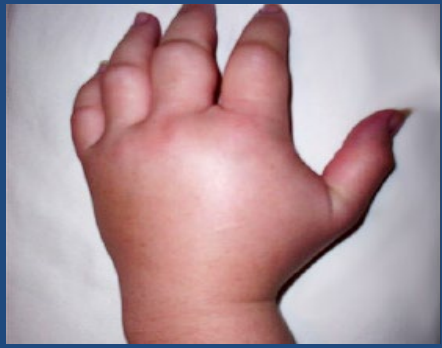
- Research support:  Biocryst, Biomarin, CSL Behring, Ionis, Kalvista, Pharvaris, Takeda
- Consulting:  Astria, Biocryst, Biomarin, CSL Behring, Cycle Pharma, Grifols, Ipsen, Kalvista, Ono Pharma, Pfizer, Pharming, Pharvaris, RegenexBio, Sanofi-Regeneron, Spark, Takeda
- Speaker Presentations: Biocryst, CSL Behring, Grifols, Pharming, Takeda

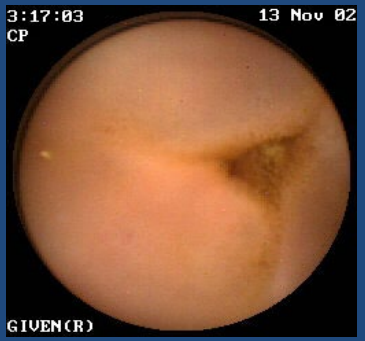
# Objectives

- Review clinical presentation and impact of hereditary angioedema (HAE)
- Discuss current guideline-based treatment of HAE
- Summarize unmet needs and opportunities to improve HAE management

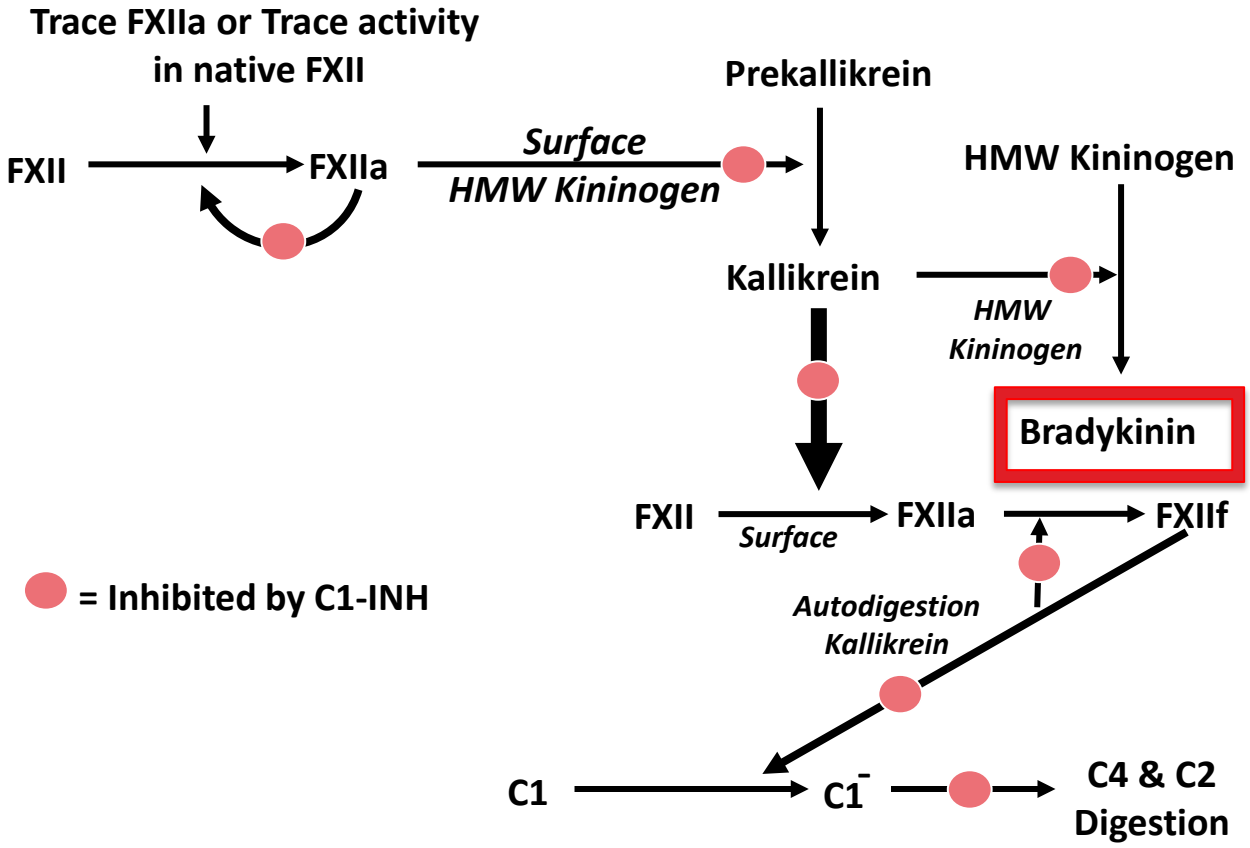
# Clinical Features of Hereditary Angioedema

- Angioedema **without** urticaria
- Angioedema often quite severe
  - Face, oropharynx, extremities, GI system, genitourinary tract
- Attacks prolonged
  - Increasing intensity over 24 hours, resolve in 2-4 days
  - Unresponsive to therapy with antihistamines, corticosteroids, or epinephrine
- Attacks occur unpredictably and are of varying frequency
- Frequently worsened by estrogen-containing oral contraceptives, hormone replacement therapy
- Often precipitated by trauma or stress
- Frequently (+) family history – AUTOSOMAL DOMINANT disorder






# Hereditary Angioedema Pathophysiology



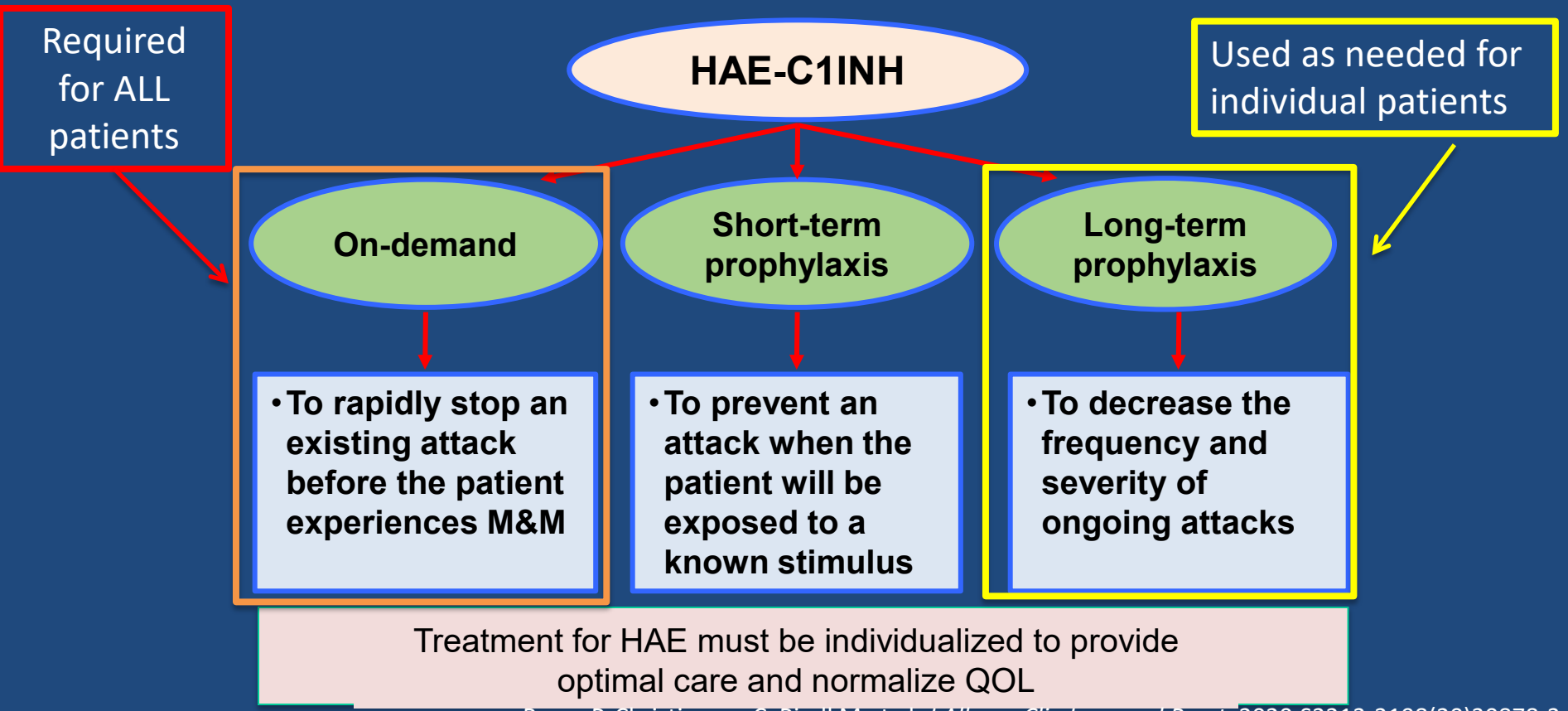
# Categories of HAE

| | Type 1 | Type 2 | HAE-Normal C1INH |
|---|---|---|---|
| Percent of all HAE | ~85% | ~15% | Rare |
| C4 Level | Low | Low | Normal |
| C1-INH antigenic level | Low | Normal | Normal |
| C1-INH antigenic function | Low | Low | Normal |

Maurer M, et al. Allergy. 2018 Aug;73(8):1575-1596.

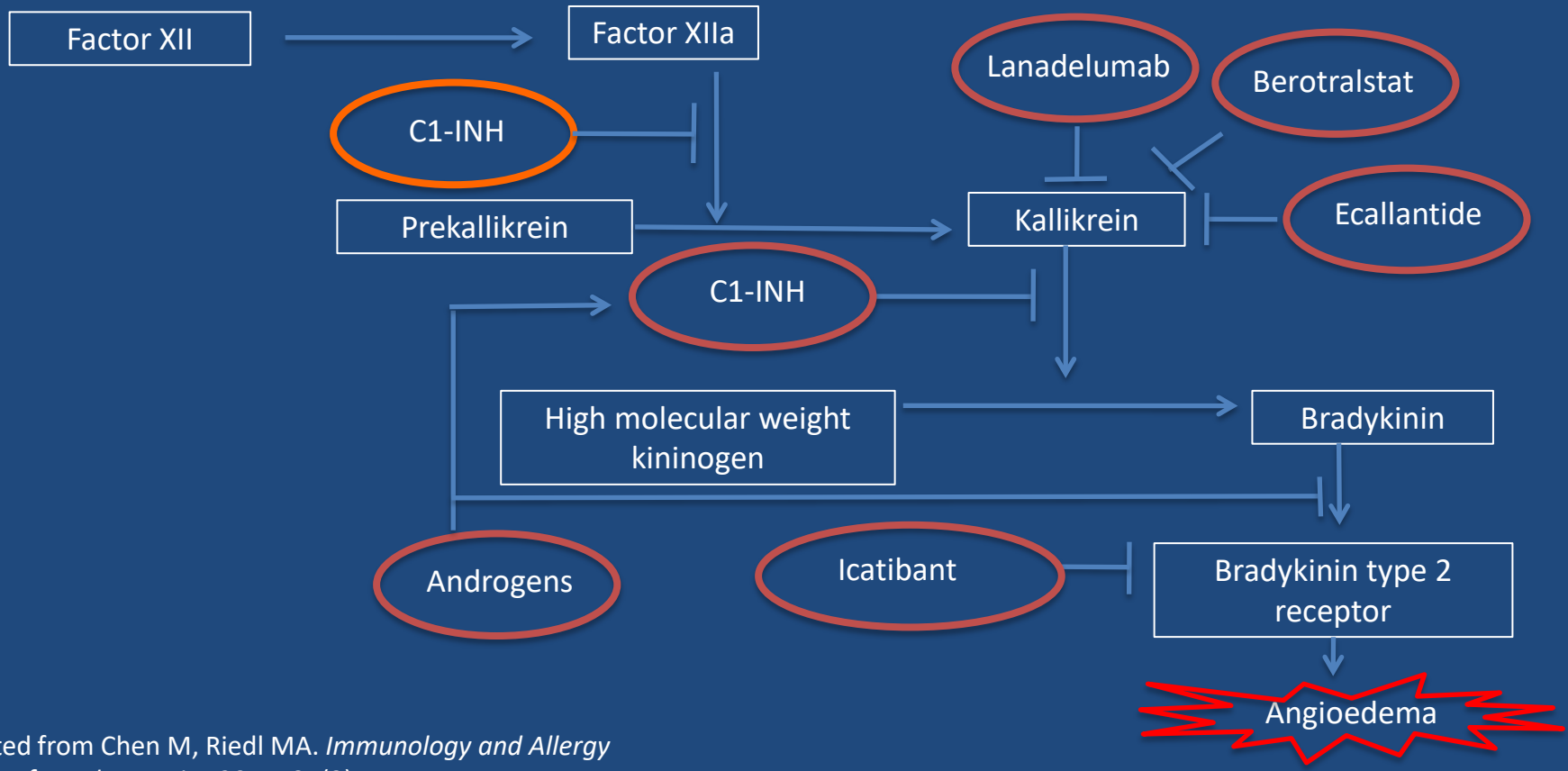
# Evidence-Based HAE Management

# HAE Management: Three Treatment Strategies




Busse P, Christiansen C, Riedl M et al. *J Allergy Clin Immunol Pract.* 2020:S2213-2198(20)30878-3.

# Current HAE Therapies




Adapted from Chen M, Riedl MA. *Immunology and Allergy Clinics of North America* 2017; 37(3).

# HAE Acute Therapies

| Drug | Potential Safety Concerns | Disadvantages | Advantages | Status |
|---|---|---|---|---|
| **Plasma-derived C1-INH** | • Infectious risk<br>• Potential infusion reactions | • Needs IV access<br>• Dependent on plasma supply | • Extensive clinical experience<br>• Relatively long half-life | • **Berinert®:** Approved in USA and many countries worldwide for HAE acute treatment[1]<br>• **Cinryze®:** Approved in USA for HAE long-term prophylactic therapy; in Europe for acute and prophylactic treatment[2,3] |
| **Recombinant C1-INH** | • Potential hypersensitivity | • Needs IV access | • No human virus risk<br>• Scalable supply | • **Ruconest®:** Approved in Europe and USA for HAE acute treatment |
| **Ecallantide** | • Allergic reactions<br>• Antibody formation | • Requires administration by a healthcare provider | • No infectious risk<br>• Subcutaneous administration | • **Kalbitor®:** Approved in the USA for acute HAE therapy[5]; currently not approved in Europe |
| **Icatibant** | • Local injection reactions | | • No infectious risk<br>• Stable at room temperature<br>• Subcutaneous administration | • **Firazyr®:** Approved in USA and numerous other countries for acute HAE therapy[6] |

1. Berinert SPC; 2. CINRYZE USPI; 3. CINRYZE SPC; 4. Ruconest SPC; 5. Kalbitor SPC; 6. Firazyr SPC.

# Acute Treatment Recommendations

- All HAE attacks are considered for on-demand treatment and any attack affecting or potentially affecting the upper airway is treated
- HAE attacks are treated as early as possible
- HAE attacks are treated with either C1-INH, ecallantide, or icatibant
- All patients have sufficient medication for on-demand treatment of two attacks and carry on-demand medication at all times
- All patients who are provided with on-demand treatment licensed for self-administration should be taught to self-administer

Maurer M, et al. Allergy. 2021

# HAE Prophylactic Therapies

| Drug | Mechanism | Patient Age | Potential Safety Concerns | Disadvantages | Advantages |
|---|---|---|---|---|---|
| **Plasma-derived nanofiltered C1 INH (intravenous)[1]** | Inactivation & consumption of C1 inhibitor | 6 years and older | • Infectious risk<br>• Infusion reactions<br>• Thrombosis | • Needs IV access<br>• Dependent on plasma supply | • Extensive clinical experience<br>• Long half-life |
| **Plasma-derived nanofiltered C1INH (subcutaneous)[2]** | Inactivation & consumption of C1-INH | 6 years and older | • Infectious risk<br>• Infusion reactions<br>• Thrombosis | • Needs IV access<br>• Dependent on plasma supply | • Improved steady-state C1INH levels<br>• No IV access required |
| **Lanadelumab[3]** | Monoclonal antibody; binds plasma kallikrein & inhibits its proteolytic activity | 12 years and older | • Unknown safety in pregnancy<br>• Anti-drug antibodies/ hypersensitivity | • Injection site reactions | • No human virus risk<br>• Subcutaneous administration<br>• Less frequent dosing |
| **Berotralstat[4]** | Plasma kallikrein inhibitor | 12 years and older | Abdominal pain, vomiting, diarrhea | | • Oral administration |
| **Danazol[5]** | Unknown | All ages | • Hepatic toxicity, elevated LDL, weight gain, hypertension<br>• Virilization, amenorrhea<br>• Psychological effects | • Contraindicated in pregnancy, lactation, children, cancer | • Oral administration |
| **Tranexamic acid[6]** | Inhibits activation of plasminogen and activity of plasmin | All ages | • Thrombosis, myalgias, abdominal pain, diarrhea | • Inferior efficacy compared to other agents<br>• Off-label for HAE | • Oral administration |

[1]Cinryze. Prescribing information.Shire; 2018. [2] HAEGARDA. Prescribing information. CSL Behring; 2020. [3]Takhzyro. Prescribing information. Dyax Corp; 2018. [4] Zuraw B, et al. *J Allergy Clin Immunol.* 2020:S0091-6749(20)31484-6. [5]Danazol. Prescribing information. Sanofi-aventis; 2011. [6]Tranexamic acid. Prescribing information. Exela Pharma Sciences, LLC; 2019.

# Prophylactic Treatment Recommendations

- Patients are evaluated for long-term prophylaxis at every visit. Disease burden and patient preference should be taken into consideration
- Use of C1-Inhibitor, lanadelumab, or berotralstat for first line long term prophylaxis
- Suggest to use androgens as second-line long-term prophylaxis
- Suggest adaptation of long-term prophylaxis in terms of dosage and/or treatment interval as needed to minimize burden of disease

Maurer M, et al. Allergy. 2021

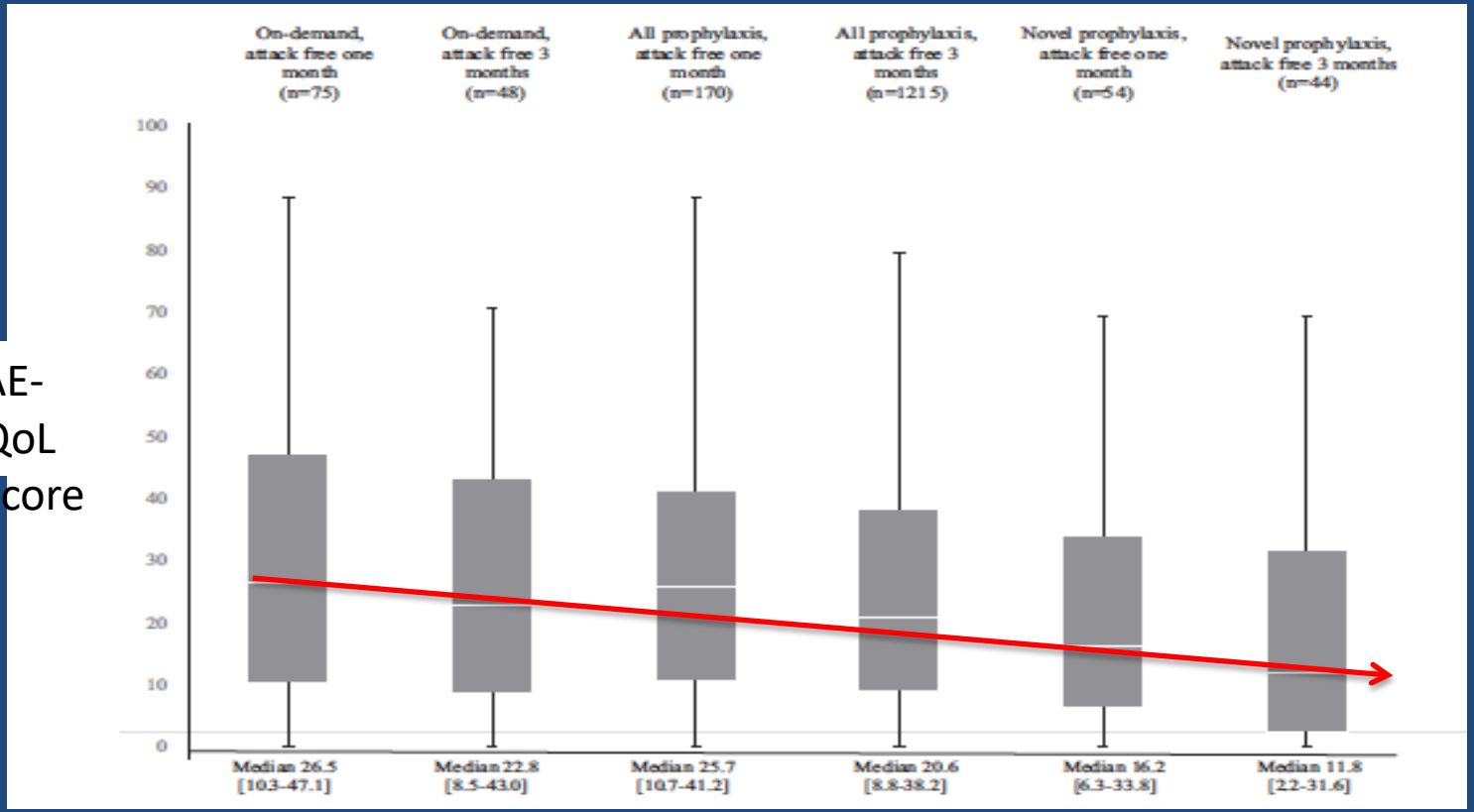
# Real World Data on HAE Treatment Strategies and Quality of Life

| Questionnaire and treatment modality | *n* | % | Mean ± SD | Median [IQR] | Significance *p* value |
|---|---|---|---|---|---|
| AECT | 37 | 100 | 10.2±4.8 | 12.0 [5.5–15.0] | |
| On-demand only | 20 | 54.1 | 7.6±4.6 | 7.0 [4.0–12.0] | **<0.001** |
| Prophylaxis | 17 | 45.9 | 13.2±2.8 | 13 [12.0–15.0] | |
| AE-QoL | 37 | 100 | 31.5±14.3 | 30.6 [21.2–41.2] | |
| On-demand only | 20 | 54.1 | 36.7±14.9 | 34.7 [27.4–50.0] | **<0.001** |
| Prophylaxis | 17 | 45.9 | 24.0±9.6 | 23.5 [18.8–31.5] | |
| GAD-7 | 36 | 97.3 | 6.0±5.2 | 4.0 [2.25–9.0] | |
| On-demand only | 20 | 55.6 | 8.2±5.9 | 8.5 [3.0–12.25] | **0.011** |
| Prophylaxis | 16 | 44.4 | 3.3±2.5 | 4.0 [0.25–4.75] | |
| HADS | 37 | 100 | 10.6±7.6 | 8.0 [5.0–16.0] | |
| On-demand only | 20 | 54.1 | 13.5±7.6 | 14.0 [5.75–17.75] | **0.012** |
| Prophylaxis | 17 | 45.9 | 7.2±6.4 | 5.0 [2.0–10.5] | |
| HADS-A | 37 | 100 | 6.5±4.5 | 7.0 [3.0–10.0] | |
| On-demand only | 20 | 54.1 | 8.1±4.5 | 8.5 [4.0–10.75] | **0.021** |
| Prophylaxis | 17 | 45.9 | 4.7±3.9 | 4.0 [2.0–7.0] | |
| HADS-D | 37 | 100 | 4.1±3.7 | 3.0 [1.0–6.5] | |
| On-demand only | 20 | 54.1 | 5.4±3.8 | 5.0 [3.0–7.0] | **0.008** |
| Prophylaxis | 17 | 45.9 | 2.5±3.1 | 1.0 [0.0–4.0] | |

Scores of questionnaires used (AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; GAD-7, Generalized Anxiety Disorder-7; HADS, Hospital Anxiety and Depression Scale (A, Anxiety; D, Depression); SD, standard deviation; IQR, interquartile range).

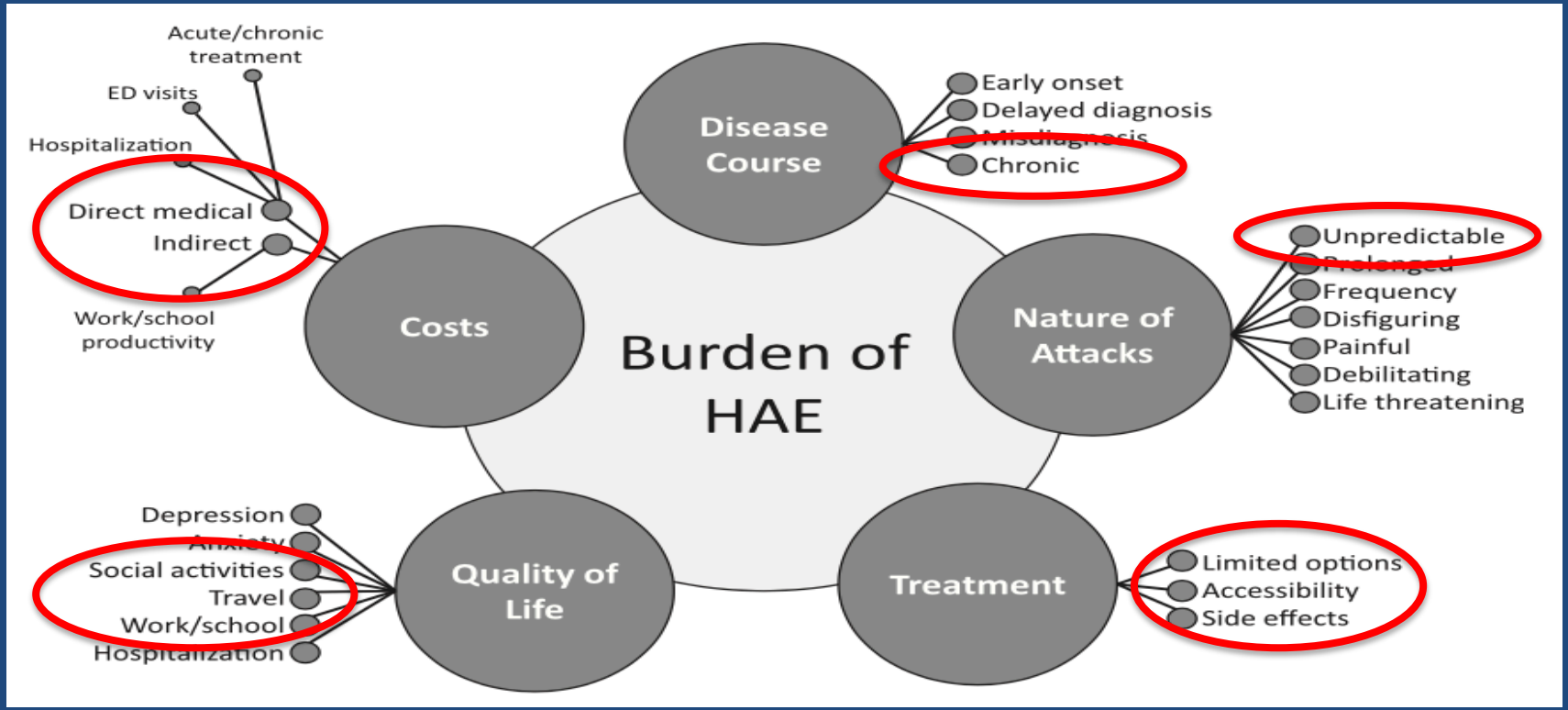
Zarnowski J,et al. Int Arch Allergy Immunol. April 2021

# Real World Data on Modern HAE Treatments and QoL




Castaldo AJ, et al. Allergy Asthma Proc 42:108– 117, 2021;

# HAE Burden of Disease




Banerji A. Ann Allergy Asthma Immunol. 2013

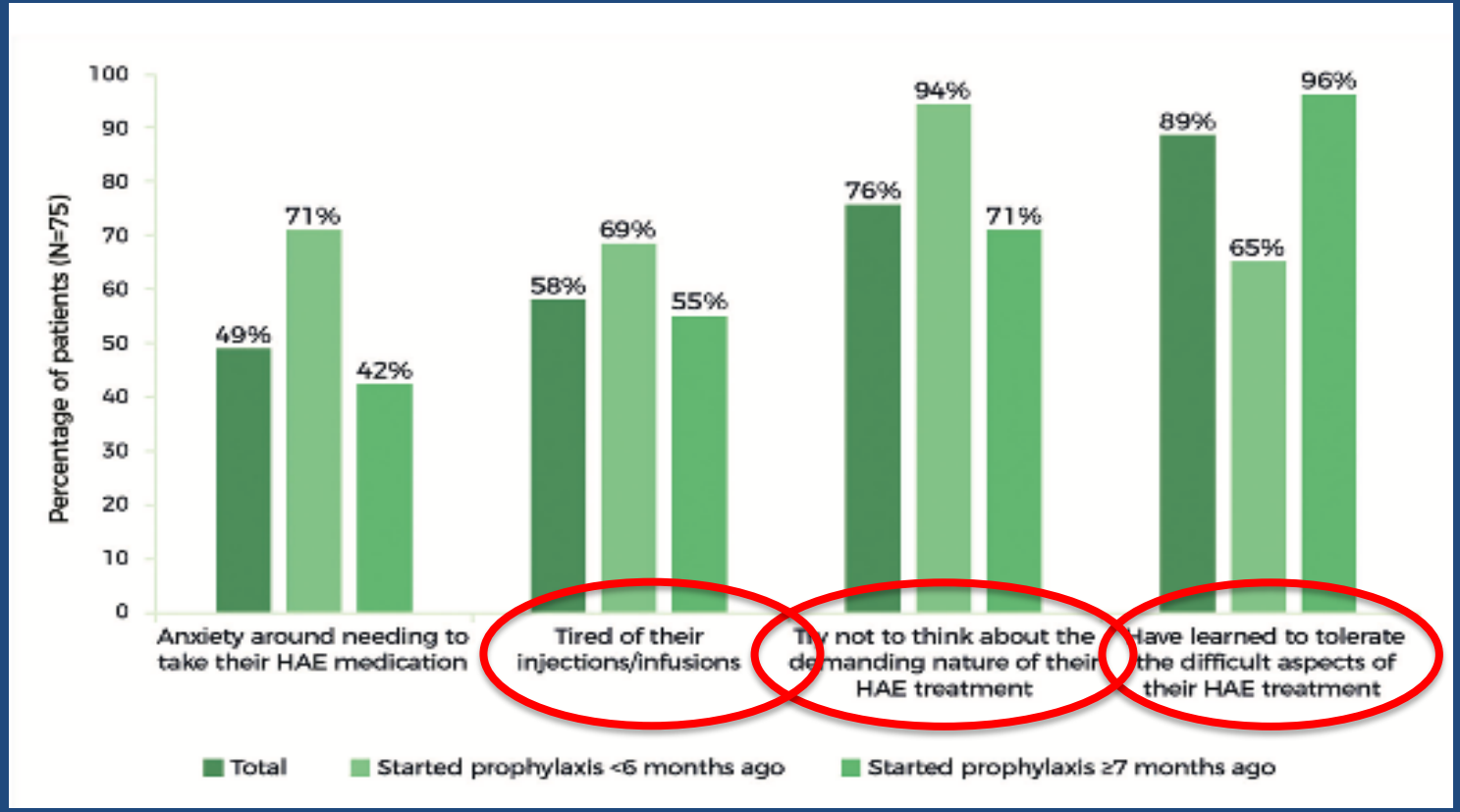
# Consensus on Treatment Goals in Hereditary Angioedema: A Global Delphi Initiative

- Panel of 23 international HAE experts – Consensus agreement of >75%

- One of the ultimate goals of HAE treatment should be to normalize the patient's life (100%)
- One of the ultimate goals of HAE treatment should be to achieve total control of the disease (95%)
- Patients with HAE should provide input on how they or their treating physician should assess whether HAE is well controlled or their life is normalized (100%)
- Patients with HAE will benefit from the development of novel tools that help them to assess whether their HAE is well controlled or whether their life is normalized (89%)
- Physicians who treat HAE patients will benefit from the development of novel tools that help them to assess whether a patient's HAE is well controlled or whether the life of a patient with HAE is normalized (89%)

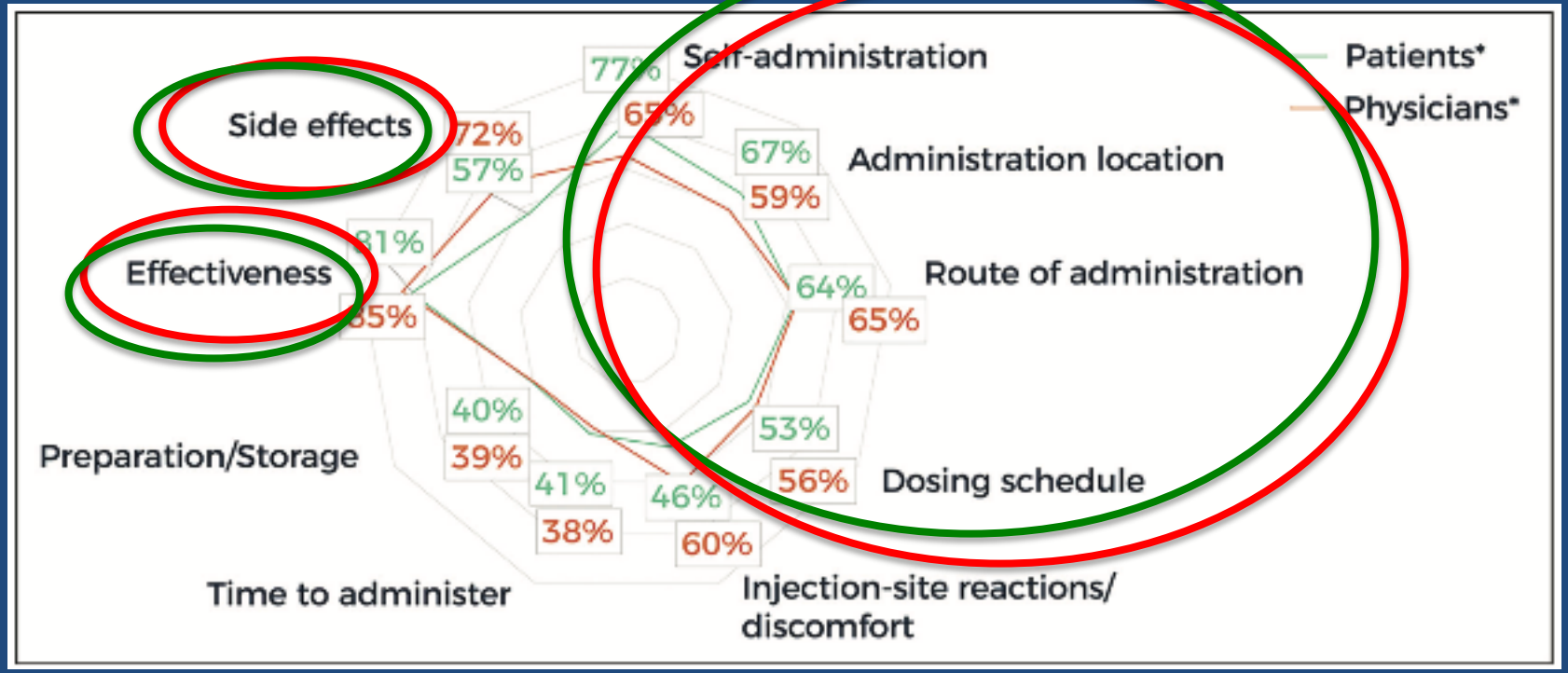
Maurer M, et al. JACI. May 2021

# Patient Concerns Related to HAE Treatment




Radojicic C, et al. Allergy Asthma Proc. 2021

# Patients and Physicians: Important Factors in Selecting HAE Prophylactic Therapy




Riedl MA, et al. Allergy Asthma Proc. 2021

# Individualization of HAE Therapy

- PATIENT FACTORS
  - Frequency of attacks
  - Rapidity of attack progression
  - Laryngeal attacks
  - Access to medical care
  - History of frequent hospitalization
  - Treatment complications
  - Quality of life

- MEDICATION FACTORS
  - Efficacy
  - Safety
  - Cost
  - Dosing Schedule
  - Route of administration
  - Patient preference/tolerability

# Themes in the HAE Treatment Pipeline

- Subcutaneous medications with less frequent dosing (prophylactic)
- Targeted oral medications (acute and prophylactic)
- Gene therapy (prophylactic)

# Re-thinking The HAE Discussion

- “How are you?”
- “Tell me about your HAE symptoms, ED visits, hospitalizations…”

- “Is your treatment plan working well for you… specifically: Do you feel in control of HAE?”
- “Do you have any specific concerns about the HAE medications?”
- “What are you NOT doing (or not doing well) in your life because of HAE that you would like to be doing?”
  - Work
  - School
  - Relationships
  - Travel
  - Exercise
  - Hobbies
  - Family planning
  - Effects of anxiety or depression


THANK YOU

# HAE Market Insights

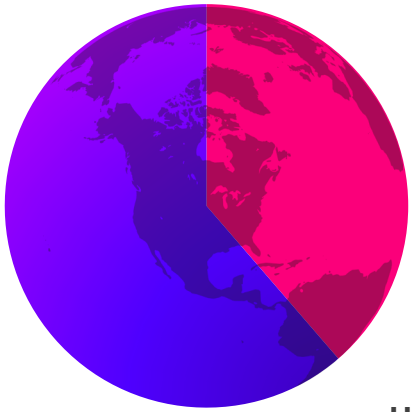
**Andrew Komjathy**
Chief Commercial Officer

# Global HAE Treatment Market is Substantial and Growing

**The HAE market is expected to double by 2027[1,2], driven by:**

- Patients being diagnosed earlier[3]
- More patients taking preventative treatments[4]
- Geographic expansion for currently available therapies[5]

**2021 HAE Market[1]**

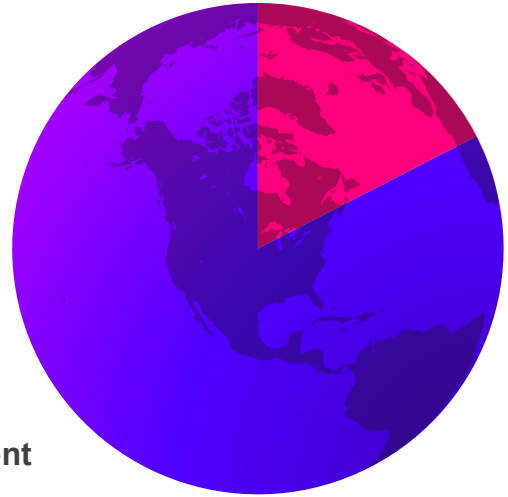


**$2.3B**

**HAE Treatment**

- Preventative
- On-Demand

**2027 Estimate HAE Market[1,2]**



**$4.5B**

1. Company-reported sales (Takeda, CSL Behring, Pharming, BioCryst)
2. Analyst consensus forecasts compiled by Clarivate's Cortellis, Astria company research and analysis.
3. Zanichelli A. Clin Transl Allergy. 2018: doi: 10.1186/s13601-018-0229-4
4. Astria company research and analysis
5. Company-reported expectations (Takeda, CSL Behring, BioCryst)

# Opportunities Exist to Improve the Patient Experience in HAE

## Selected Analog Markets May Teach Us About the Impact of Reduced Treatment Burden

### *Published Literature*

**HAE Patients**

Patient-reported burden of hereditary angioedema: findings from a patient survey in the United States

Aleena Banerji, MD [*]; Kimberly H. Davis, MS, RPh [†]; T. Michelle Brown, PhD [†]; Kelly Hollis, MBA [†]; Shannon M. Hunter, MS [†]; Janet Long, MSLIS [†]; Gagan Jain, PhD [§]; Giovanna Devercelli, PhD [§]

Ann Allergy Asthma Immunol 124 (2020) 600–607

**HAE Treaters**

Current medical management of hereditary angioedema
Follow-up survey of US physicians

Marc A. Riedl, MD [*]; Aleena Banerji, MD [†]; Richard Gower, MD [‡]

Ann Allergy Asthma Immunol 126 (2021) 264–272

### *HAE Market Research*

**HAE Patients**

**HAE Treaters**

### *Selected Analog Markets*

**Hemophilia**

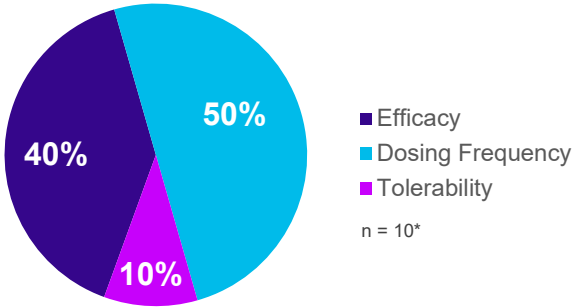
**Psoriasis Treatment**

**Multiple Sclerosis**
(Relapse Remitting)

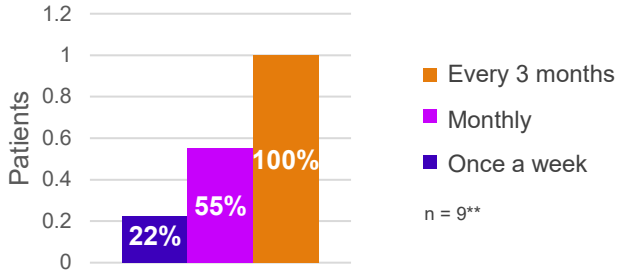
# Efficacy and Dosing Improvements Would Compel Patients to Switch to a New Therapy

## Based on Market Research With HAE Patients

### Top Improvement That Would Compel a Therapy Switch




### Minimal Dosing Frequency That Would Compel a Therapy Switch




*"I'd choose 'efficacy,' but I don't know how much more effective it could get --Takhzyro is… 80-90% effective. But if something is equally effective, and it's easier to integrate into my life, that would make me change."*

*— HAE Patient 9*

1. * Two of the ten patients were unable to choose between efficacy and dosing; their answers were counted in both categories
2. ** One of the ten patients was unable to specify an answer.
3. Source: Company qualitative market research with 10 U.S. HAE patients. Patient Interview data presented at the 2021 NORD Virtual Summit

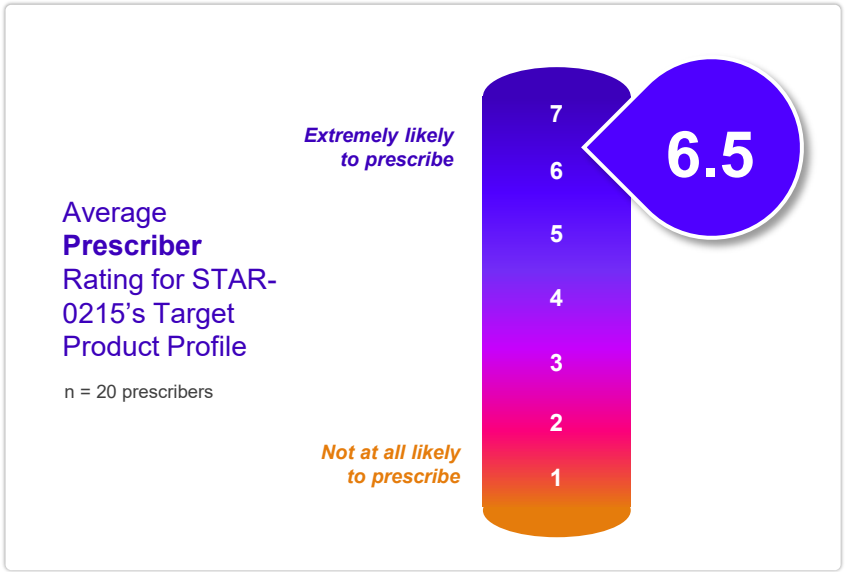
# Health Care Providers Viewed STAR-0215 Target Profile as the Potential Next Generation of HAE Treatment

## Blinded Qualitative Market Research

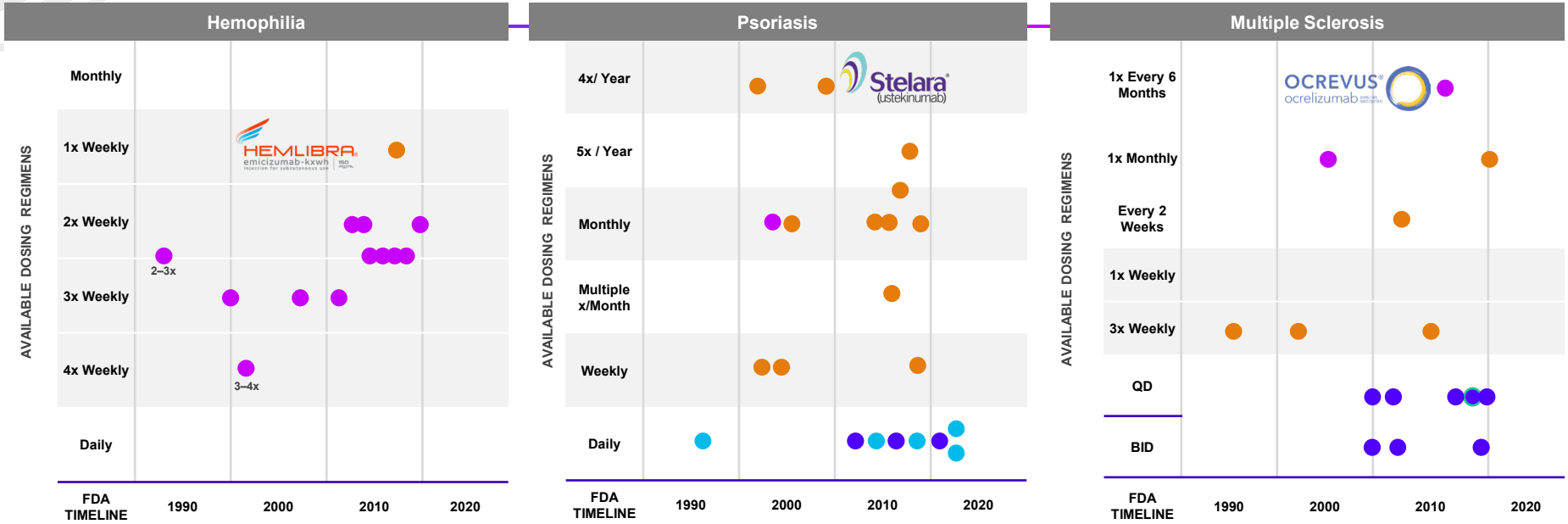
### Blinded Product Profile

- A monoclonal antibody inhibitor of plasma kallikrein that helps prevent HAE attacks by suppressing the pathway that generates bradykinin and causes excessive swelling
- Efficacy on par with current subcutaneous therapies
- Dosing once every 3 months or longer

> *"[if this were available], this would be my first choice. I've looked through all the products [in development], this is the first one which is really exciting. This is a generation leap; anybody who is on medication now either daily, every three days, or every two or four weeks, why wouldn't they want to do this?"*
>
> *— HAE Prescriber 16*



# Therapies Providing Less Frequent Dosing Regimens in Selected Analog Markets Have Established Market Success




Sources: Company Websites, FDA CenterWatch Approved Drugs Listings: https://www.centerwatch.com/directories/1067-fda-approved-drugs, DataBridge Market Research Migraine Market Syndicated Report 2022, Global Market Insights Hemophilia Market Syndicated Report, February 2022, Fortune Business Insights Psoriasis Market Syndicated Report March 2022, Fortune Business Insights Multiple Sclerosis Market Syndicated Report May 2022, Coherent Market Insights HAE Syndicated Report, August 2022.

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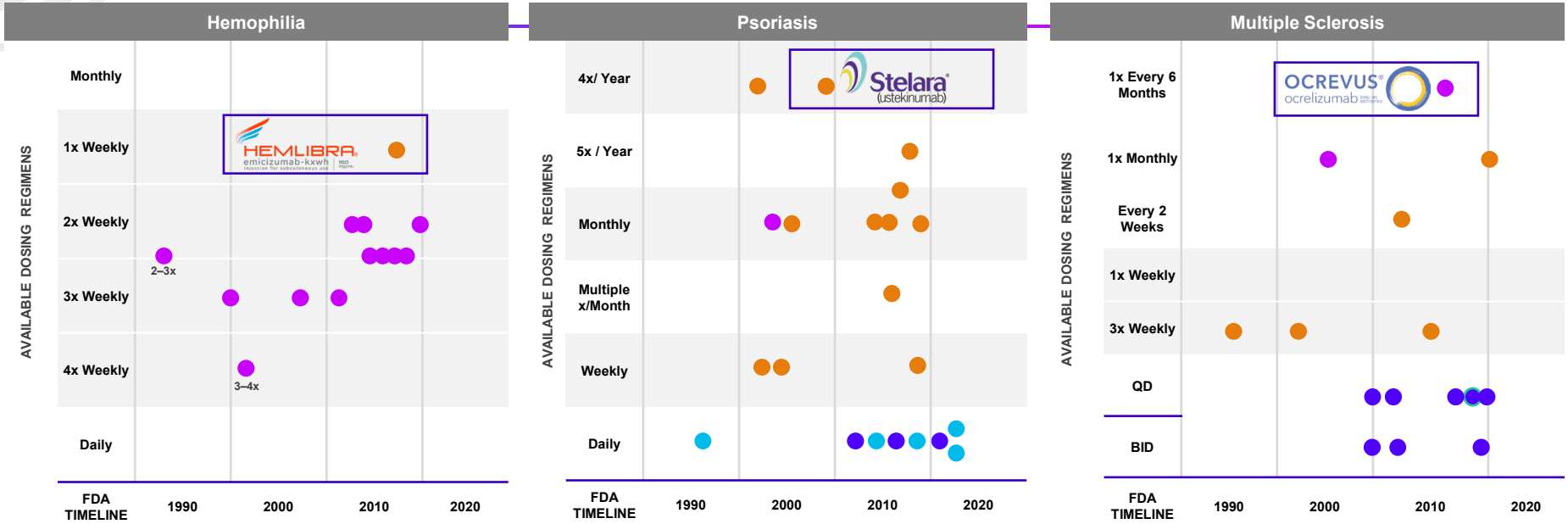


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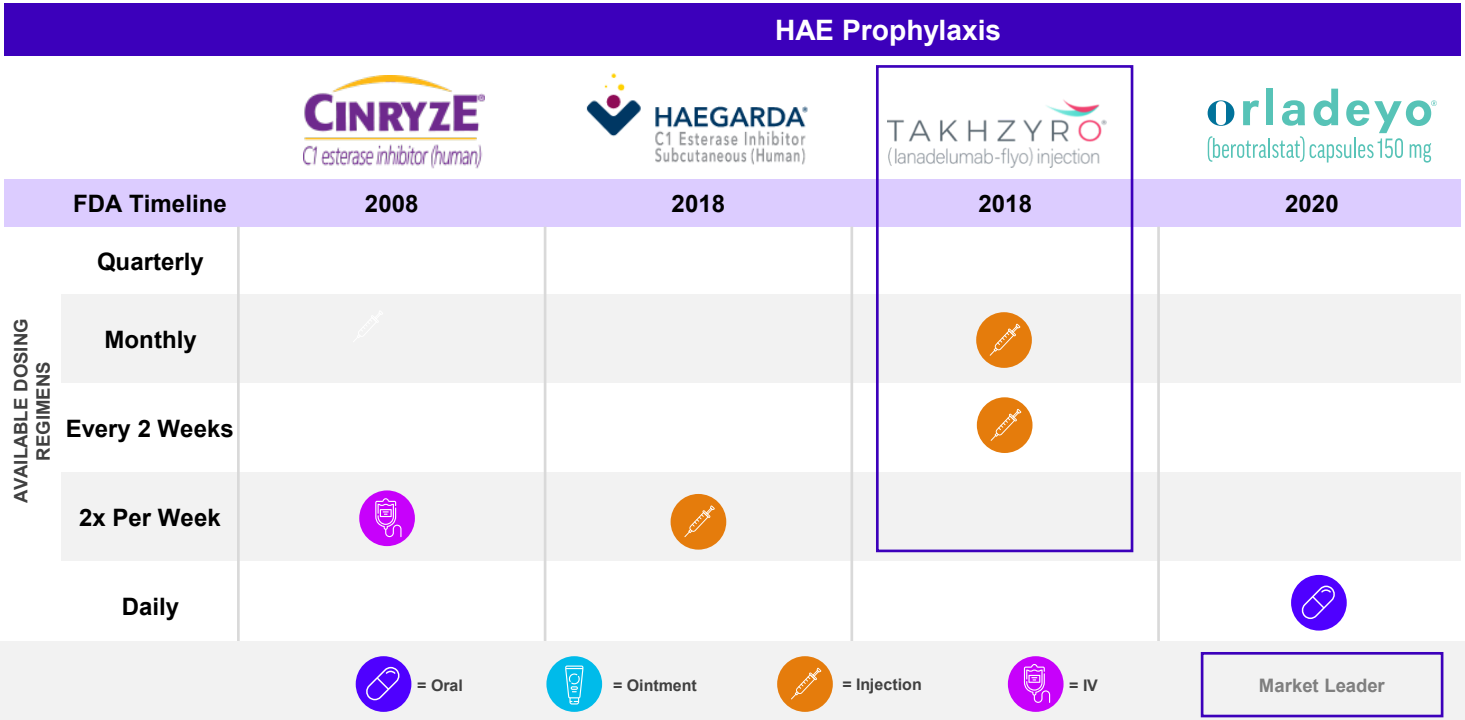
# STAR-0215 Has the Potential to Offer Patients Longer-Acting and Less Frequently Dosed Prophylaxis

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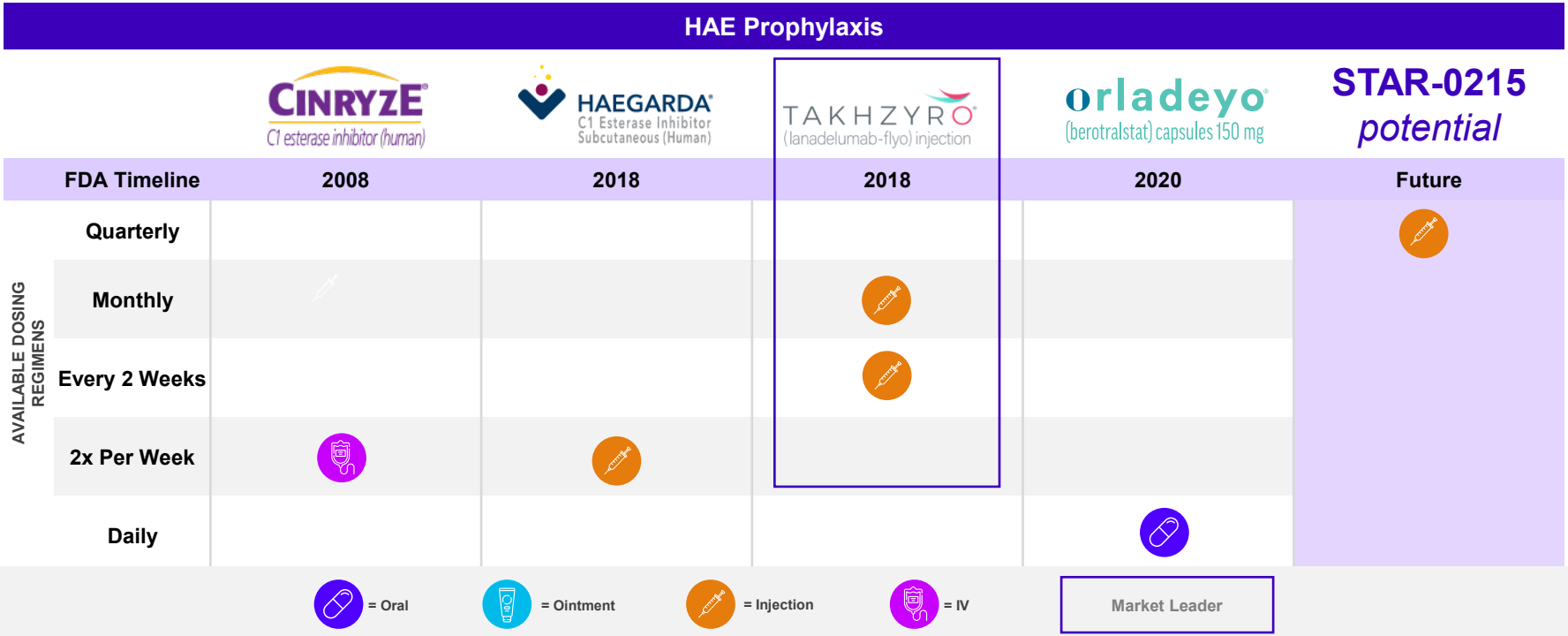


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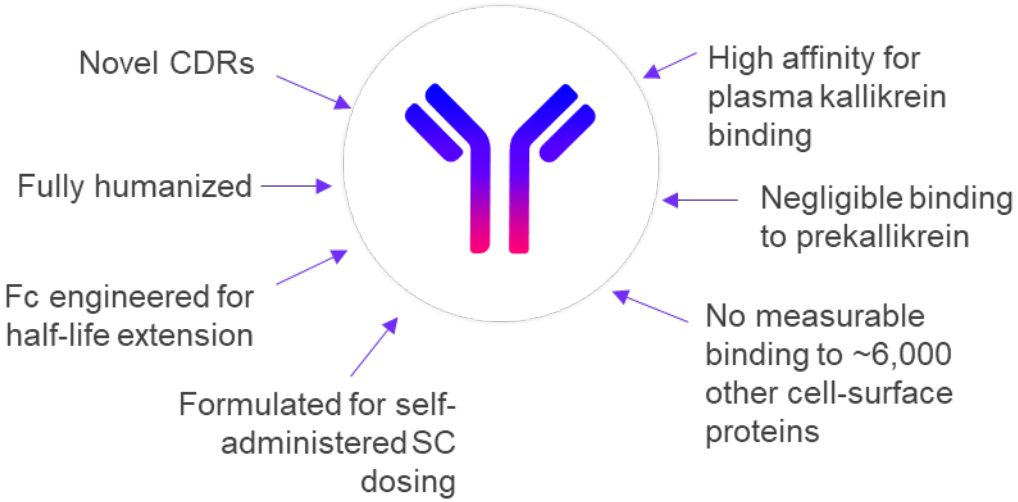
# Characteristics of STAR-0215 and Preclinical Data

**Andy Nichols, Ph.D.**
Chief Scientific Officer

# STAR-0215: Designed to Provide a Potential Solution to the Normalization of Life With HAE

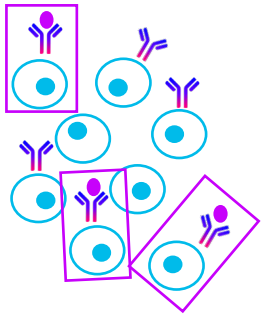
## Preclinical Profile of STAR-0215

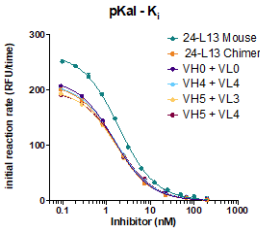


# Discovery of STAR-0215, a Monoclonal Antibody Targeting Plasma Kallikrein

pKal -/-

Immunized with human plasma kallikrein






20 hits selected from hybridomas for binding to plasma kallikrein and 1 selective inhibitor identified

STAR-0213

Sequence humanized and optimized

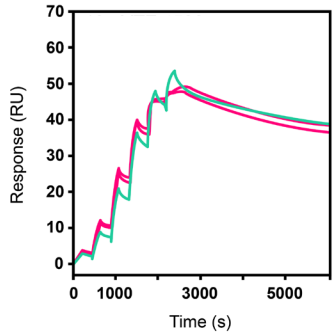

STAR-0215

Half-life extended

# STAR-0215 is a Potent Inhibitor of Plasma Kallikrein

## Nanomolar Binding Affinity

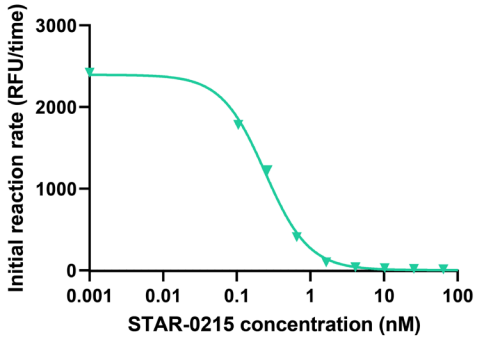
Surface Plasmon Resonance




$K_D$ (pH 7.4) = 1.1 nM

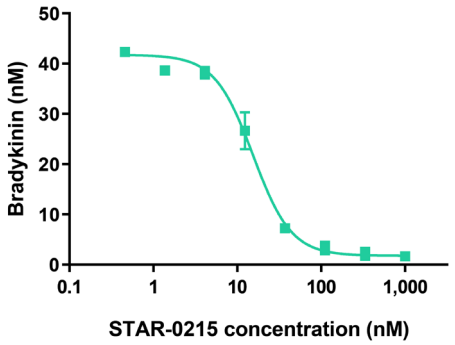
## Potent Functional Inhibition

Artificial Substrate (PFR-AMC)
Fluorescent Reporter Assay



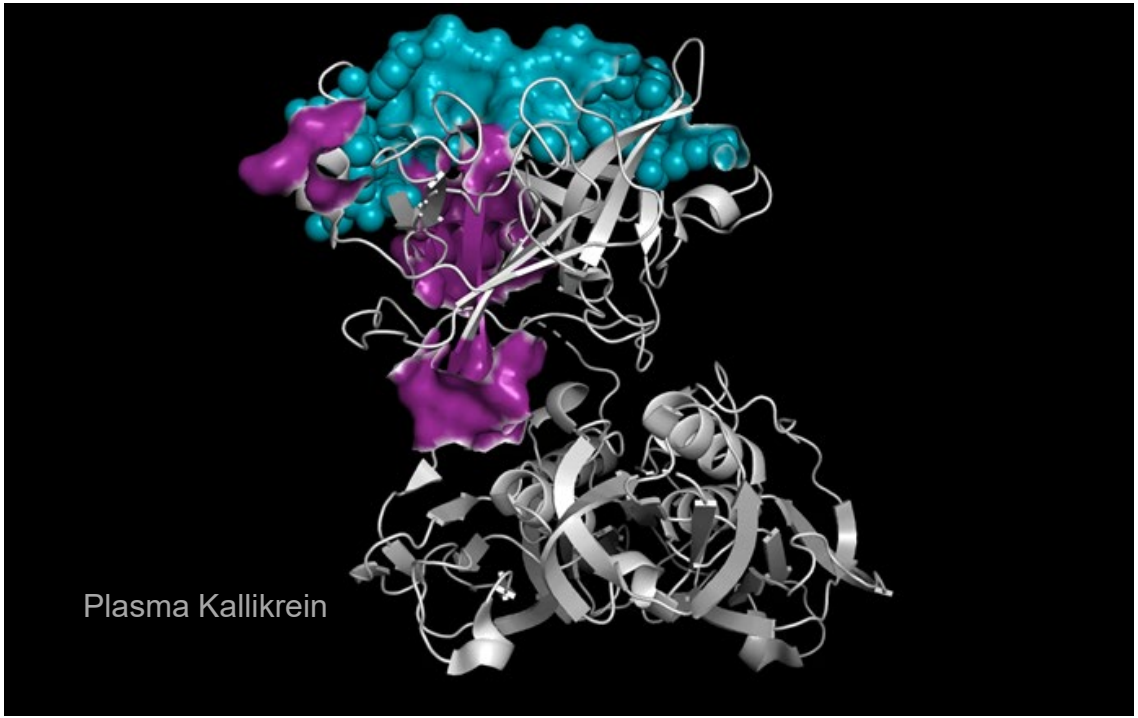

$IC_{50}$ = 0.3 nM

Natural Substrate (HMWK)
Bradykinin Release Assay




$IC_{50}$ = 15 nM

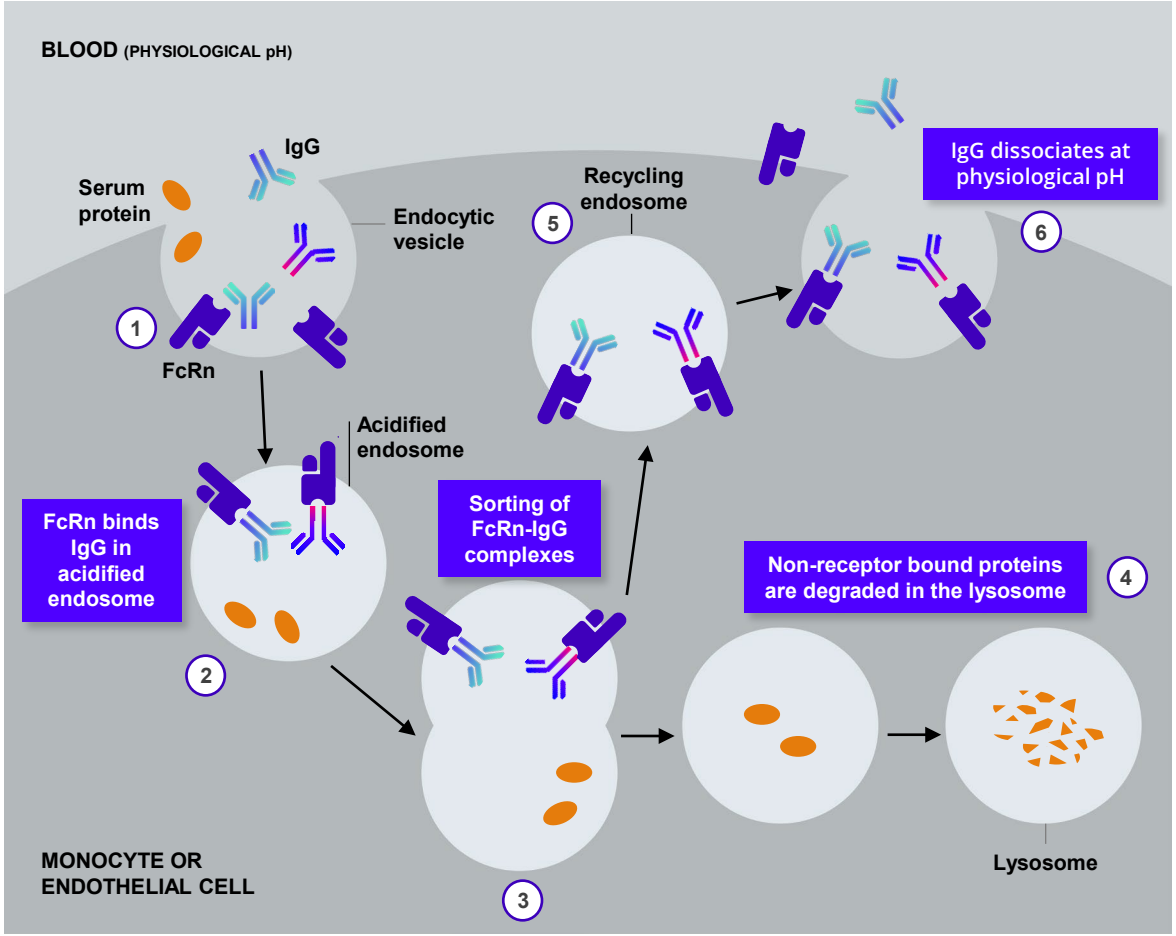
# STAR-0215 Binds to a Novel Region of Plasma Kallikrein




STAR-0215 interaction surface

Lanadelumab interaction surface

# STAR-0215
# Leverages the Mechanism of pH-Dependent FcRn Recycling to Extend Circulating Half-Life




Modified from: https://www.news-medical.net/whitepaper/20211110/FcRn-and-its-role-as-a-therapeutic-target.aspx

# YTE Fc Modifications Have Led to Substantial Half-Lives of Monoclonal Antibodies in Humans

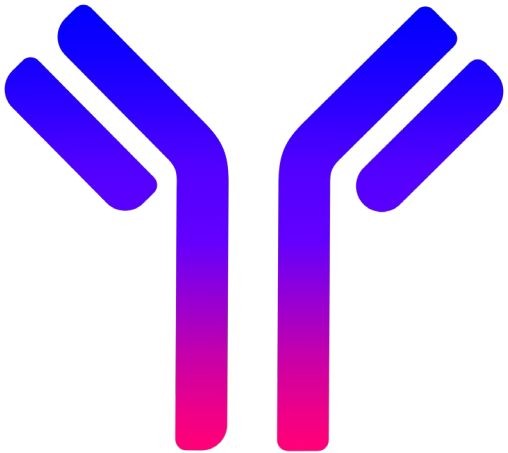
- Introduction of YTE into the anti-RSV mAb, motavizumab, prolonged half-life ~3.5-fold in both NHP and humans
- The approved YTE antibodies have half-lives of 83-88 days in humans
- Across a range of YTE Fc modified mAbs against non-cellular targets that are not subject to target mediated drug disposition (TMDD), the half-life is ~80-90 days in humans
- For targets affected by TMDD (e.g. KIT) the half-life is extended by YTE Fc modification is 2-4-fold but is shorter than 80 days (30 – 40 days)

| | Antibody | Target | NHP $T_{1/2}$ (Days) | Human $T_{1/2}$ (Days) |
|---|---|---|---|---|
| | Motavizumab | RSV | 6 | 24 |
| | Motavizumab-YTE | RSV | 21 | **82** |
| Approved | Tixagevimab-YTE / Cilgavimab-YTE (Evusheld) | SARS-CoV-2 | ~19<br>~19 | **88**<br>**83** |


1. Dall'Acqua et al. J Biol Chem.2006 Aug 18;281(33):23514-24. doi: 10.1074/jbc.M604292200. Epub 2006 Jun 21.
2. Robbie et al. J Biol Chem. 2006 Aug 18;281(33):23514-24. doi: 10.1074/jbc.M604292200. Epub 2006 Jun 21.
3. Loo et al. Sci Transl Med. 2022 Mar 9;14(635):eabl8124. doi: 10.1126/scitranslmed.abl8124. Epub 2022 Mar 9.
4. Evusheld EUA Review: https://www.fda.gov/media/155107/download

# STAR-0215 Incorporates YTE Fc Modifications to Extend Half-Life

STAR-0213



## hFcRn Binding at pH 6.0[1]

| | $k_a$ (1/Ms) | $k_d$ (1/s) | $K_D$ (M) |
|---|---|---|---|
| **STAR-0213** | $2.70 \times 10^{5}$ | $2.29 \times 10^{-1}$ | $8.48 \times 10^{-7}$ |
| **STAR-0215** | $1.84 \times 10^{5}$ | $2.77 \times 10^{-2}$ | $1.50 \times 10^{-7}$ |

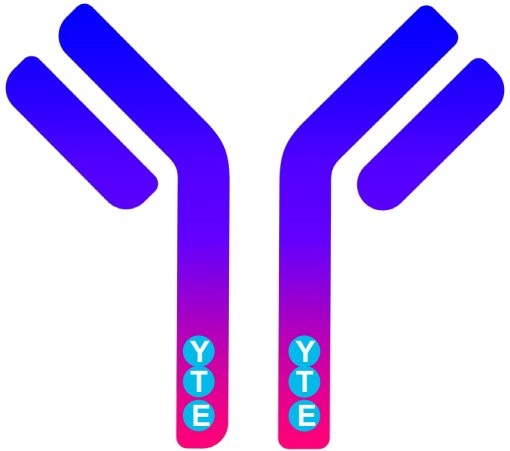
STAR-0215 has increased pH-dependent hFcRn binding due to a reduced off rate compared to parent mAb, STAR-0213

## PK Parameters in Cynomolgus Monkeys[2]

| | Vss (mL/kg) | Cl (mL/day/kg) | $T_{1/2}$ (days) |
|---|---|---|---|
| **STAR-0213** | 72 | 4.85 | 10.9 |
| **STAR-0215** | 67 | 1.44 | 33.6 |

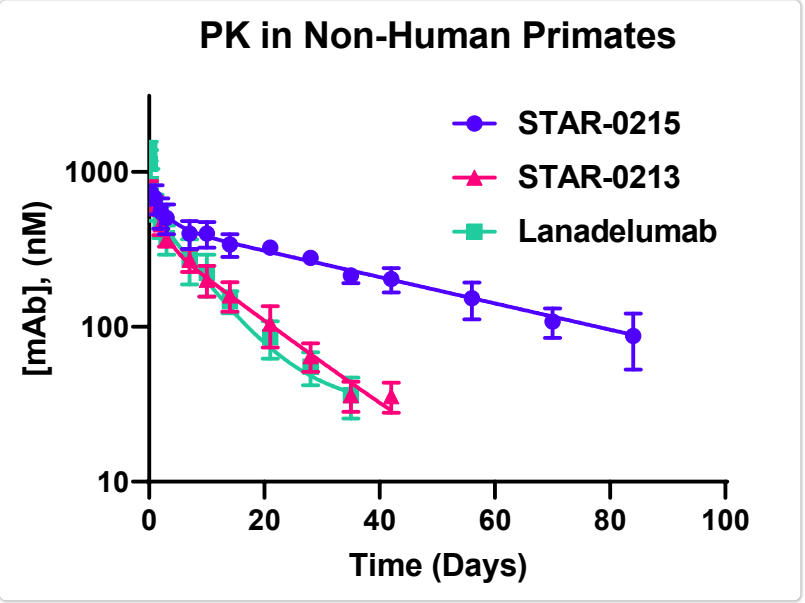
Increased pH-dependent FcRn binding translates into slower clearance and extended half-life in cynomolgus monkeys

STAR-0215



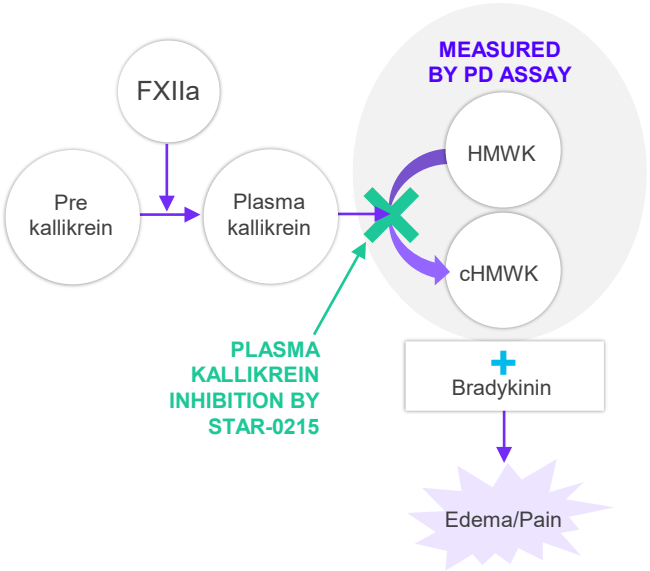

1. No binding at pH 7.4
2. Dose of 5 mg/kg IV

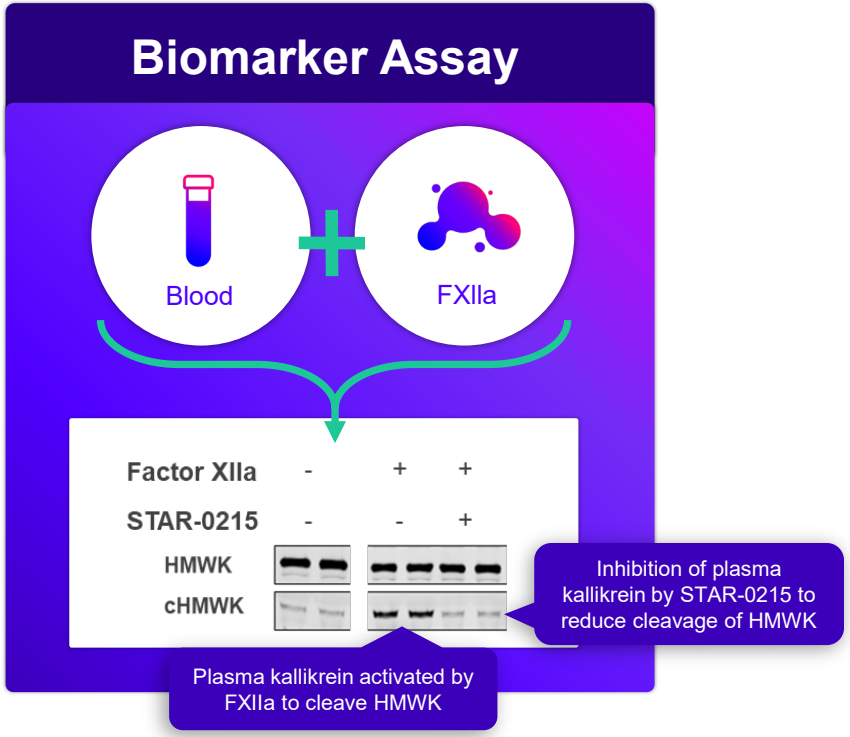
# STAR-0215 Has Shown Substantially Prolonged Plasma Half-Life Compared to Lanadelumab in Non-Human Primates




| Mean non-human primate half-life in days (SD) | Lanadelumab | STAR-0213 | STAR-0215 |
|---|---|---|---|
| | 10.5 (1.6) | 10.9 (0.4) | 33.6 (8.3) |

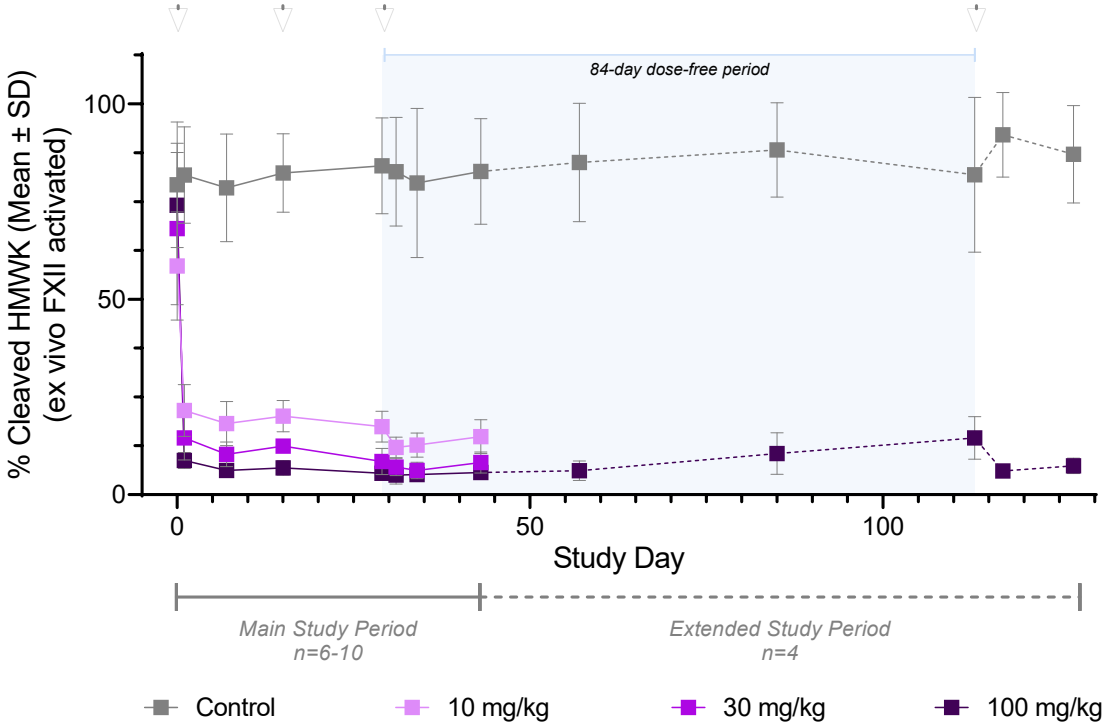
# Biomarker Assay to Assess Plasma Kallikrein Activity Following STAR-0215 Dosing



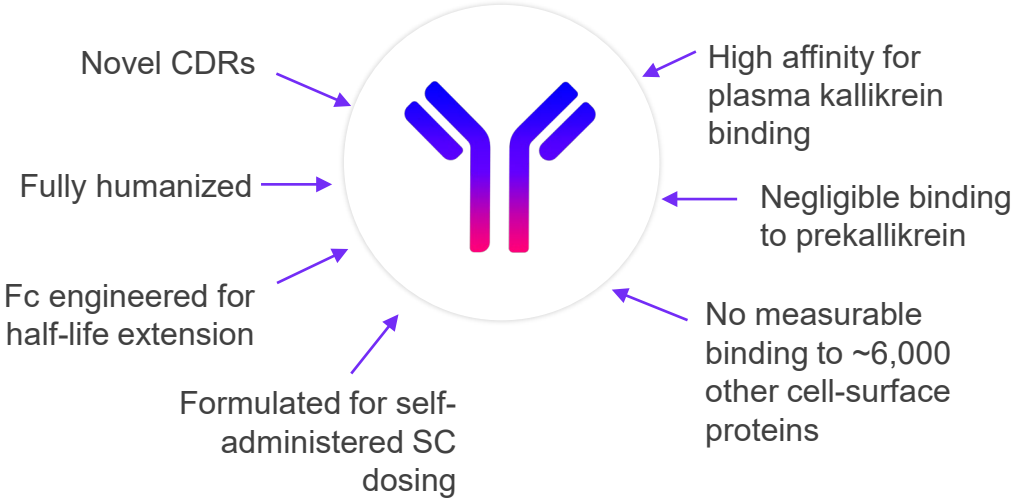

HMWK = high molecular weight kininogen
cHMWK = cleaved high molecular weight kininogen
FXII = Factor XII
FXIIa = activated Factor XII

# STAR-0215 Produces Rapid and Sustained Inhibition of FXIIa-Activated HMWK Cleavage in Cynomolgus Monkeys



# STAR-0215
# Potential for Best-in-Class Profile in HAE

## Preclinical Profile of STAR-0215




**Encouraging preclinical results**
Demonstrated high potency for plasma kallikrein and long plasma half-life

**Differentiated profile**
Potential benefits include long duration without breakthrough attacks and infrequent SC dosing- once every 3 months or longer

**Trusted modality**
To provide patients with improved quality of life

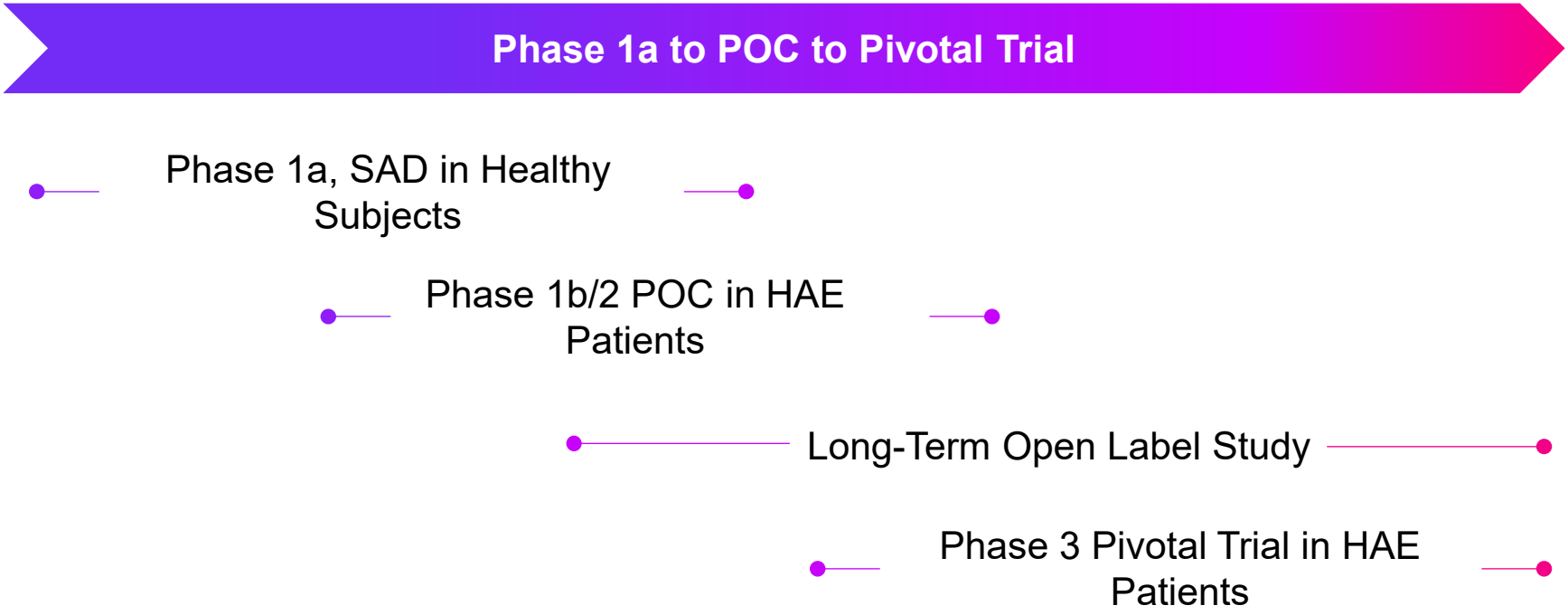
*Astria wholly owns an international patent application directed to STAR-0215. If nationalized in the U.S. and granted, the patent would expire in 2042, excluding any potential patent term extension[1]*

1. If this application is nationalized in PCT member states ex-U.S., the term of any resulting patents would also be to 2042, exclusive of any available term extensions.

# Clinical Development Plans for STAR-0215

**Chris Morabito, M.D.**
Chief Medical Officer

# Overview of the Expected Clinical Development Plan

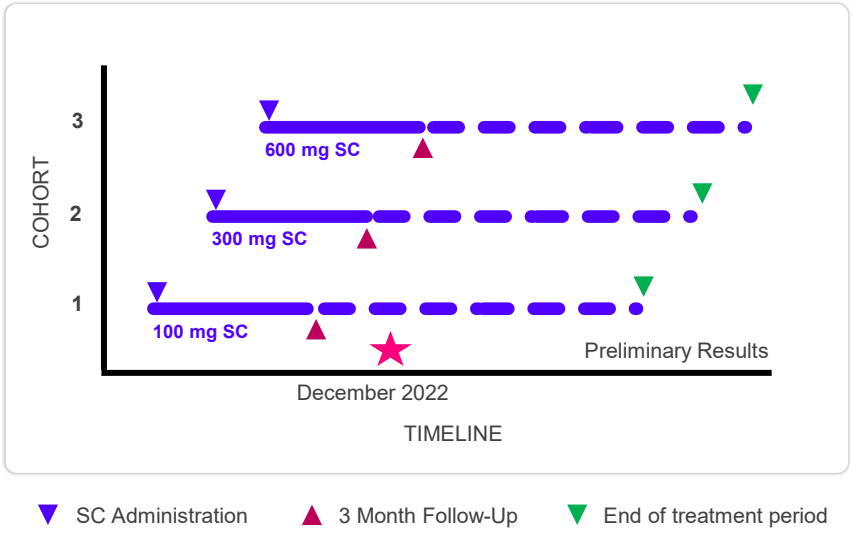



1. Timeline for clinical trials are to be determined. Bars are representative descriptions of trial durations only.

# STAR-0215 Phase 1a: Dosing is Complete

## Phase 1 Healthy Subject Trial Overview

- At least three single ascending dose cohorts
  - 100 mg, 300 mg, and 600 mg
  - Healthy adult subjects
  - Subcutaneous dosing
- Randomized, double-blind, placebo-controlled
  - 6 active to 2 placebo randomization
- Single U.S. center study
- Observation period through multiple half-lives
- 3-month data will inform on the target profile



# STAR-0215 Phase 1a Trial Will Inform on Target Profile

**Preliminary data expected to be available by year-end 2022**

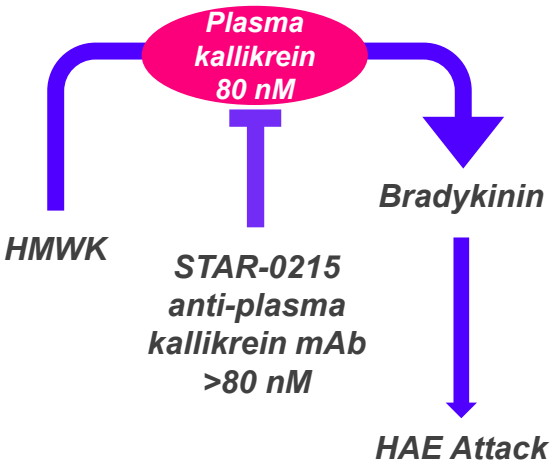
**Phase 1a Endpoints**

- Safety and tolerability
- Pharmacokinetics: blood concentrations over time
- Pharmacodynamics: inhibition of bradykinin production via inhibition of plasma kallikrein

**Target Profile**

- Small volume subcutaneous administration
- Durable activity
- Administered once every 3 months or less frequently
- Safe and well tolerated

# Phase 1a Dose Selection and Interpretation of Results




**Mechanism of HAE Attack:**

- To prevent an HAE attack, anti-plasma kallikrein concentrations need to be greater than plasma kallikrein concentrations
- In HAE: ecallantide effectively reduces acute attacks at 80 nM[1]; $C_{min}$ of lanadelumab > 67 nM is effective at preventing attacks[2]

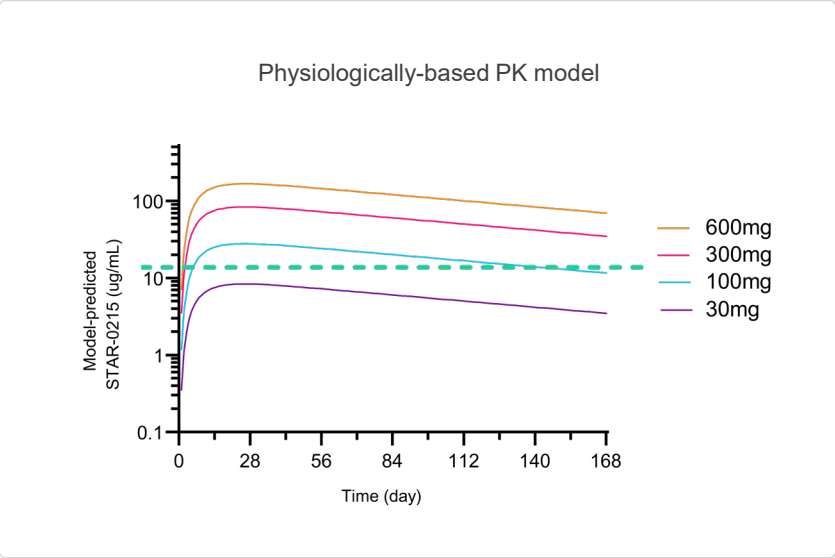
**We hypothesize that the bar for clinical effectiveness of STAR-0215 is $C_{min}$ >80 nM (12 µg/mL) in healthy subjects**

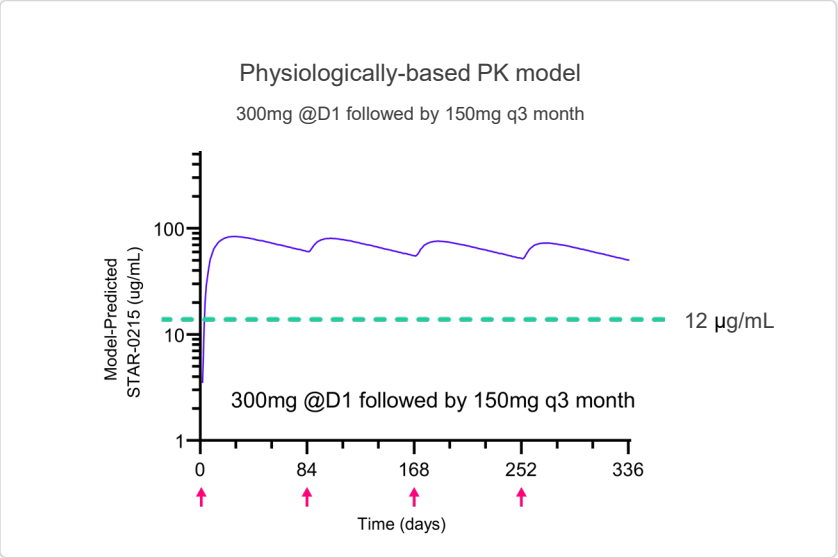
- STAR-0215 may achieve a concentration >12 µg/mL at 3 months in the Phase 1a healthy subject trial
- Multiple doses of STAR-0215 may be required to achieve sufficiently high $C_{min}$ steady-state concentrations

1. Dyax corporate presentation Feb 2014. Ecallantide mean Cmax is 80 nM after 30 mg SC administration.
2. Wang et al. Clin Transl Sci. 2020 Nov;13(6):1208-1216. doi: 10-1111/cts.12806. Epub 2020 May 26.

# Model Simulations Predict That Doses in Phase 1a May Be Clinically Effective

## Physiologically-Based Model and Simulations

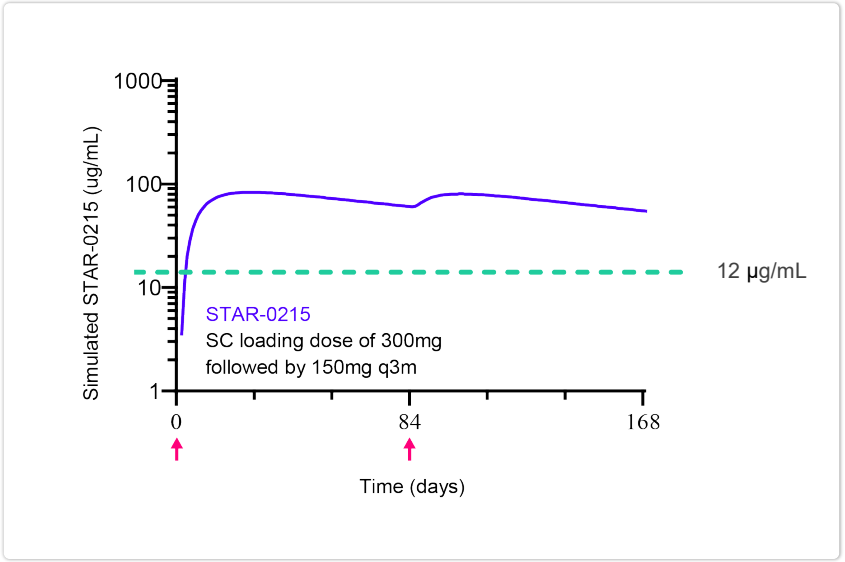


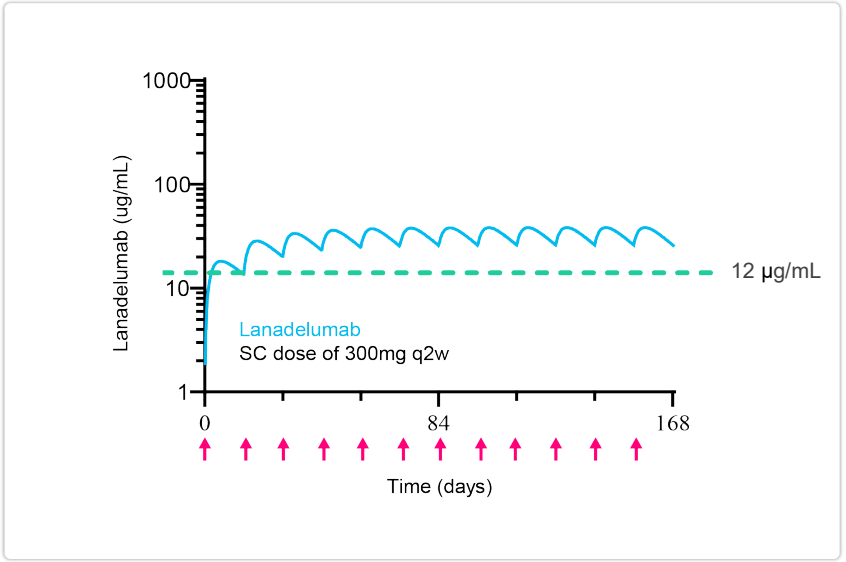




3 months is approximately Day 84
Arrows indicate simulated drug dosing
Green dashed line is 12 µg/mL

# STAR-0215 Loading Dose Followed by Q3 Month Maintenance Dose May Achieve More Rapid and Sustained Effects Compared to Lanadelumab

## Physiologically-Based Model and Simulations




3 months is approximately Day 84
Arrows indicate simulated drug dosing
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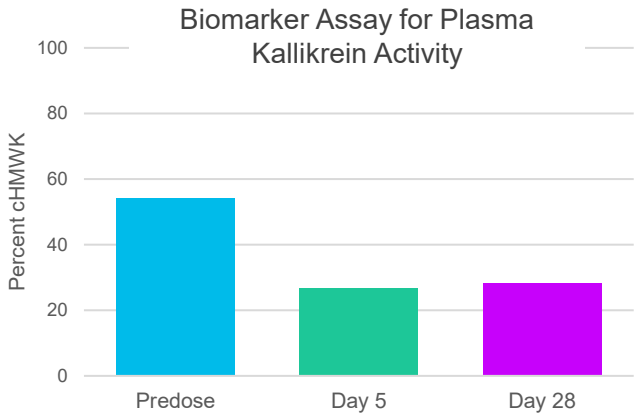
Bista, P et al, EAACI 2022 Poster #100242
Wang et al. Clin Transl Sci 2020 Nov;13(6):1208-1216. doi: 10-1111/cts.12806. Epub 2020 May 26.

# Inhibition of Plasma Kallikrein Reduces cHMWK, Correlating to Clinical Benefit in HAE

## STAR-0215 May Achieve More Sustained Reductions in cHMWK Compared to Lanadelumab

**Healthy Subjects Phase 1a:**
Lanadelumab 3mg/kg (avg. weight 83 kg) (single dose)[1]




**Phase 1a Healthy Subject PD Target:**

STAR-0215 is expected to produce similar changes to cHMWK

1. Chyung et al. Ann Allergy Asthma Immunol. 2014 Oct;113(4):460-6.e2. doi: 10.1016/j.anai.2014.05.028. Epub 2014 Jun 26.

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


Phase 1b/2 Proof of Concept Trial

# Planning for ALPHA-STAR Trial

## Expect to Initiate in Q1 2023, Subject to Favorable Phase 1a Results

### DESIGN

- HAE patients, multiple sites, global
- Phase 1b/2
- Single and multiple dose cohorts
- Small sample size
- Each qualifying participant will receive at least one dose of STAR-0215
- Each participant may roll-into a long-term open label study

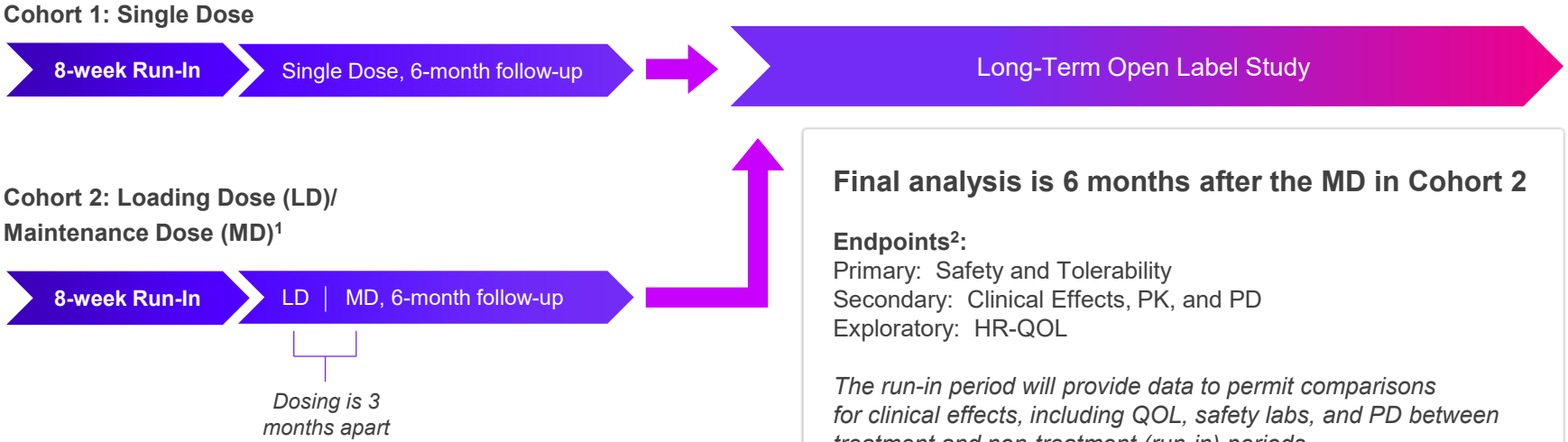
### EXPECTED RESULTS

**Proof of concept**

- Well tolerated, durable activity compatible with robust clinical benefit
- SC administration
- Results inform the dose selection for the pivotal Phase 3 trial

# ALPHA-STAR Expected Trial Design Schematic

## Open-Label Single and Multiple Dose Phase 1b/2 Proof-of-Concept (POC) Clinical Trial in HAE




**Final analysis is 6 months after the MD in Cohort 2**

**Endpoints[2]:**
Primary: Safety and Tolerability
Secondary: Clinical Effects, PK, and PD
Exploratory: HR-QOL

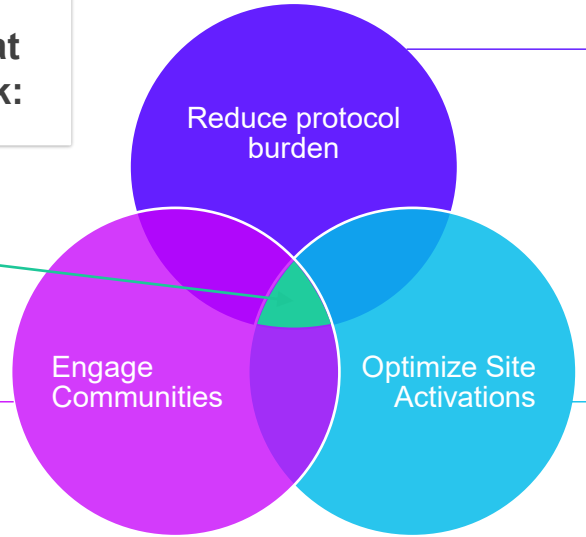
*The run-in period will provide data to permit comparisons for clinical effects, including QOL, safety labs, and PD between treatment and non-treatment (run-in) periods.*

1. Additional cohorts may be added based on emerging data
2. Preliminary and subject to change. The list does not include the full-set of planned endpoints or measurements.

# ALPHA-STAR Optimizing Enrollment

## Success depends on focus on execution

**Proactive steps underway that we expect to mitigate this risk:**




- Access to investigational drug for all qualifying participants
- Minimal in-person assessments

*Enrollment sweet spot*

- Active trial advocacy across patient, partner and caregiver communities

- Smart site selections
- Boosting site activations to facilitate rapid enrollment

# Planned Future Clinical Trials

**Phase 1a to POC to Pivotal Trial**

Phase 1a, SAD in Healthy Subjects

Phase 1b/2 POC in HAE Patients

Long-Term Open Label Study

Phase 3 Pivotal Trial in HAE Patients

1. Timeline for clinical trials are to be determined. Bars are representative descriptions of trial durations only.


Q&A

# Concluding Remarks

**Jill C. Milne, Ph.D.**
Chief Executive Officer


astria
THERAPEUTICS