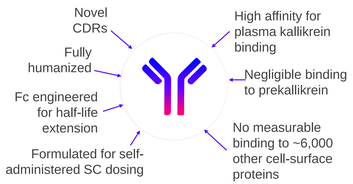
# STAR-0215, a Long-Acting Monoclonal Antibody Plasma Kallikrein Inhibitor in Development for Treatment of HAE, Demonstrates Sustained Functional Inhibition in Subcutaneously Dosed Cynomolgus Monkeys |

**Authors**: *Pradeep Bista, Jou-Ku Chung, Rafif Dagher, Charles Omer, Sachin Chandran, Andrew Nichols | Astria Therapeutics, Boston MA USA*

**BACKGROUND**: Inhibition of plasma kallikrein activity is a validated mechanism for prevention of hereditary angioedema (HAE)
- High potency and long duration of action are key drivers of prophylactic efficacy
- STAR-0215 is a novel, potent, and selective long-acting monoclonal antibody plasma kallikrein inhibitor for the potential treatment of HAE

## 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 a patent application directed to STAR-0215. If granted, the patent would expire in 2042, excluding any potential patent term extension*

## STAR-0215 is a Novel, Potent, Selective, and Long-Acting Monoclonal Antibody Inhibitor of Plasma Kallikrein

| $K_D$/SPR (nM) | EC50 plasma kallikrein inhibition (PFR-AMC substrate) (nM) | EC90 plasma kallikrein inhibition (HMWK substrate) (nM) |
|---|---|---|
| 1.1 | 0.3 | 30 |

| $IC_{50}$ [M] | Trypsin | Hepsin | Thrombin |
|---|---|---|---|
| Gabexate mesylate (positive control) | $2.23 \times 10^{-9}$ | $5.10 \times 10^{-8}$ | $8.37 \times 10^{-7}$ |
| STAR-0215 | n.d. (>1 µM) | n.d. (>1 µM) | n.d. (>1 µM) |

| | STAR-0215 **(YTE)** | STAR-0213 **(non-YTE)** |
|---|---|---|
| $T_{1/2}$ (days) | 33.6 ± 8.3 | 10.9 ± 0.4 |

Mean +/- SD | Cynomolgus monkeys dosed i.v. with antibodies

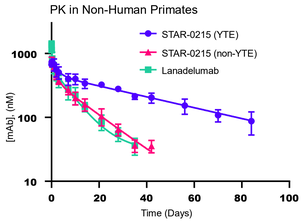
**POTENT**
STAR-0215 has nM potency for functional inhibition of plasma kallikrein and does not bind pre-kallikrein

**SELECTIVE**
STAR-0215 was also fully inactive against 16 additional proteases related to plasma kallikrein. No binding to ~6,000 cell surface expressed proteins

**LONG-ACTING**
YTE-modification in the Fc domain of STAR-0215 enhances pH-dependent FcRn binding, thereby improving the circulating half-life

*Please also see our ePoster #001263 to learn more about STAR-0215*

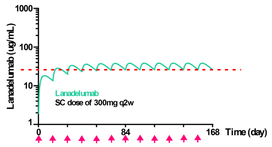
## STAR-0215 Has Shown Substantially Prolonged Plasma Half-Life Compared to Lanadelumab in Non-Human Primates



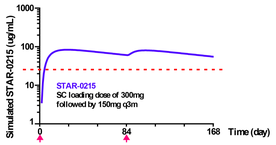

**STAR-0215 engineered with YTE half-life extension technology**
- Enhanced FcRn binding translated to a more than three-fold increase in plasma half-life with STAR-0215 compared to an antibody without YTE modifications
- Half-life of mAbs with similar half-life extension technology
  - Non-human primates: 20 – 40 days
  - Humans: 70 – 120 days

| 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) |

## Human PK Modeling Suggests STAR-0215 is Anticipated to Achieve and Maintain Target Exposure with a Once Every 3 Month Dosing Frequency

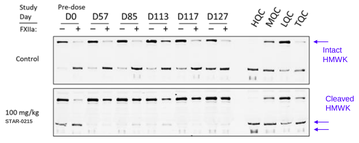



- With a 300 mg every other week dosing regimen of lanadelumab, steady state was achieved after 5 doses and reduced HAE attack frequency to <0.25 attacks/month. Dashed line represents the exposure required to inhibit circulating plasma kallikrein in HAE corresponding with attack-rate suppression (Wang, 2020)




- Minimal physiologically based PK (mPBPK) modeling predicts STAR-0215 can achieve exposures to reach this level with only 4 doses per year (versus 24 doses per year with lanadelumab) with potential to rapidly reach steady state using an initial loading dose

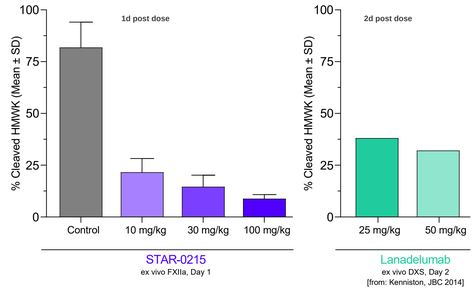
## STAR-0215 Inhibits Plasma Kallikrein Mediated Cleavage of HMWK in Cynomolgus Monkeys




- Western Blot method to specifically detect intact and cleaved HMWK (endogenous plasma kallikrein substrate)
- Plasma samples were collected from animals subcutaneously dosed with STAR-0215 and treated ex vivo with 10nM FXIIa to simulate activation of contact pathway

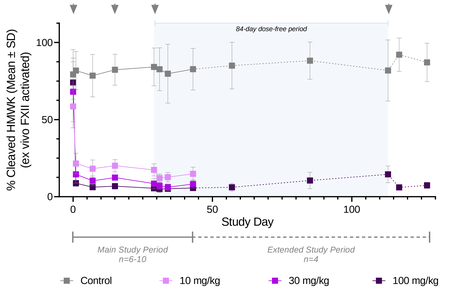
*HQC, MQC, LQC: High, Medium, and Low QC samples with approximately 99, 67 and 18% cleaved HMWK*
*TQC: treatment QC is FXIIa treated LQC sample*

## STAR-0215 Demonstrates Rapid Inhibition of Plasma Kallikrein After Subcutaneous Administration in Monkeys




- Strong inhibition is apparent rapidly after subcutaneous dose
- In cynomolgus monkeys, greater maximal reduction in cleaved HMWK was achieved with a lower-dose of STAR-0215 compared to lanadelumab

## In Cynomolgus Monkeys, Functional Inhibition of Plasma Kallikrein by STAR-0215 is Durable




- Inhibition of HMWK cleavage was rapid (within one day after subcutaneous dose administration)
- Inhibition was sustained throughout an 84-day dose-free period in the extended portion of the study
- In cynomolgus monkeys, these data confirm the long-half life of STAR-0215, and demonstrate prolonged pharmacological activity of STAR-0215 in circulation

**SUMMARY**: STAR-0215 rapidly and durably inhibits functional plasma kallikrein activity when dosed subcutaneously in cynomolgus monkeys
- PD data supports the potential of STAR-0215 to be dosed once every 3 months or longer in humans
- STAR-0215 is in development as a treatment for HAE and is planned to enter clinical trials in 2022

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