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

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**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**

- Potency
  - STAR-0215 has nm potency for functional inhibition of plasma kallikrein and does not bind pre-kallikrein
- Selectivity
  - STAR-0215 was also fully inactive against 18 additional proteases related to plasma kallikrein. No binding to ~6,000 other cell-surface proteins
- Long-acting
  - Western blot method to specifically detect intact and cleaved HMWK (endogenous plasma kallikrein substrate)
  - Plasma samples were collected from animals treated ex vivo with 10nM FXIIa to simulate activation of contact pathway

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

** POTENT **

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<th>Control</th>
<th>10 mg/kg</th>
<th>30 mg/kg</th>
<th>100 mg/kg</th>
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<td>1.3</td>
<td>3.0</td>
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**SELECTIVE **

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**LONG-ACTING **

- Western blot method to specifically detect intact and cleaved HMWK (endogenous plasma kallikrein substrate)
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**STAR-0215 Has Show 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

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

- Minimal physiologically based PK (PBPK) 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 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