Clinical Development of SRK-015, a Fully Human Anti-proMyostatin Monoclonal Antibody, for the Treatment of Later-Onset Spinal Muscular Atrophy

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SRK-015 is a fully human anti-proMyostatin monoclonal antibody (mAb) that selectively binds to pro- and latent myostatin with high affinity, inhibiting the proMyostatin activity of the growth factor and, therefore, preventing myostatinmediated muscle loss. Preclinical studies demonstrated selective inhibition of myostatin activation, effectively increasing muscle mass and function in a SMA mouse model. The structural basis for SRK-015 binding to pro-Myostatin will be presented. No toxicologically significant findings were observed for SRK-015 in rats and non-human primates. A Phase 1 healthy volunteer study demonstrated a favorable safety profile of SRK-015 administered intravenously (IV) at all doses tested. The ongoing Phase 2 study evaluates the safety and efficacy of SRK-015 dosed IV every four weeks over a 12-month treatment period. Three distinct parallel cohorts were enrolled. Cohort 1 enrolled 23 patients (5–21 years old) with ambulatory Type 3 SMA and were treated with 20 mg/kg of SRK-015 as monotherapy or in combination with an approved SMN up regulator. The primary objectives are to assess safety and the mean change from baseline in the Revised Hammersmith Scale (RHS). Cohort 2 enrolled 15 patients (5–21 years old) with Type 2 or non-ambulatory Type 3 SMA who were already treated with an approved SMN up regulator and were treated with 20 mg/kg of SRK-015. Cohort 3 enrolled 20 patients with Type 2 SMA, who were at least 3 years of age and initiated treatment with an approved SMN up regulator before enrollment. Patients were randomized 1:1 to either 2 mg/kg or 20 mg/kg of SRK-015. For Cohort 2 and Cohort 3, the primary objectives are to assess safety and the mean change from baseline in Hammersmith Functional Motor Scale Expanded (HFMSE). Demographics and baseline characteristics will be provided.

SRK-015: A Fully Human Antibody that Blocks Cleavage of the Myostatin Prodomain

Abstract
SRK-015 is an investigational drug candidate being developed and studied for SMA and other indications. The effectiveness and safety of SRK-015 have not been established and SRK-015 has not been approved by the FDA or other regulatory agency.

Selecting of 20 mg/kg of SRK-015 as the first dose
• Initial administration: 20 mg/kg followed by 20 mg/kg monthly IV for 12 months
• No dose interruptions in Cohort 2

Key Results
• SRK-015 was well-tolerated with no apparent safety signals
• No dose-limiting toxicities identified up to highest evaluated dose of 30 mg/kg in both SAD & MAD
• No discontinuations due to treatment-related adverse events (AEs)
• No treatment-related serious adverse events (SAEs) or deaths
• No hypersensitivity reactions
• PK/Rx results informed Phase 2 dosing regimen

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References

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