SCHOLAR ROCK

Scholar Rock to Develop SRK-015 to Improve Muscle Function in Patients with Spinal Muscular Atrophy

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First data on inhibition of myostatin activation in a preclinical model of SMA to be highlighted at the Cure SMA Annual Conference

Treatment with SRK-015 resulted in significantly increased muscle strength in a genetic model of SMA

CAMBRIDGE, Mass., June 28, 2017 – Scholar Rock, a biotechnology company focused on discovering and developing drugs that selectively target growth factors in the disease microenvironment, announced today that SRK-015, the company's lead clinical candidate, will be developed for the improvement of muscle strength and function in patients with Spinal Muscular Atrophy (SMA). SRK-015 is a highly selective inhibitor of the supracellular activation of myostatin. SMA is a rare, and often fatal, genetic disorder that dramatically impacts neuromuscular function. This announcement coincides with the presentation of data for SRK-015 in preclinical studies, including a genetic model of SMA, being presented at the Cure SMA Annual Conference on June 29-July 2, 2017 in Orlando, Florida.

"We are excited to advance SRK-015 toward clinical testing in SMA patients based on the data we are presenting at the Cure SMA Annual Conference, and bolstered by our emerging translational insights into myostatin biology, neuromuscular pathology, and the unique pharmacology of SRK-015," said Nagesh Mahanthappa, PhD, President and Chief Executive Officer of Scholar Rock. "We see the development of SRK-015 in SMA as an important step towards demonstrating the broad therapeutic potential of targeting the supracellular activation of protein growth factors to treat a wide range of human diseases."

Scholar Rock plans to develop SRK-015 both in combination with therapies aimed at correcting the underlying genetic defect in SMA and as monotherapy in patients with certain subtypes of SMA. Scholar Rock has demonstrated that SRK-015 selectively binds to the latent forms of myostatin, inhibiting activation while avoiding interaction with other closely related members of the TGFβ superfamily that may lead to unintended adverse effects.

Scholar Rock is reporting results for the first time on the potential efficacy of SRK-015 in SMA in an oral presentation at the Cure SMA Annual Conference. Highlights of the preclinical studies include:

- SRK-015 specifically targets the activation of latent forms of myostatin and does not inhibit GDF11 or Activin A, proteins that are structurally similar to myostatin but implicated in regulating a wide range of biological processes beyond muscle biology.
- SRK-015 substantially increases lean body mass in non-human primates, with a particularly notable effect on muscles with a high proportion of fast-twitch fibers, a muscle fiber type that is particularly affected in SMA.
- In a mouse model of SMA, inhibition of myostatin activation, in combination with a 'corrector' therapy that targets the underlying genetic defect, significantly improved the strength of the gastrocnemius relative to treatment with 'corrector' therapy alone.

"We are encouraged by the preclinical data emerging on SRK-015, including the effects upon fast-twitch muscle fibers that are particularly relevant for SMA as well as its selectivity profile, which may be very important when considering chronic therapy in children," said Karen S. Chen, PhD, Chief Scientific Officer of the SMA Foundation and a co-author of the study being presented at the Cure SMA Annual Conference. "We are hopeful these exciting preclinical results will translate into clinical benefit for patients. The SMA community has seen tremendous progress with therapies to address the loss of motor neurons, which begin to address the unmet medical need in SMA. The development of therapies like SRK-015 that directly tackle muscle atrophy by itself or in combination with SMN-upregulating therapies is now the next frontier."

About SMA

Spinal Muscular Atrophy (SMA) is a rare, and often fatal, genetic disorder that affects approximately 1 in every 10,000 births. This disease is due to defects in the SMN1 gene that produces a protein important for the survival and function of lower motor neurons. Deterioration and loss of lower motor neurons that innervate skeletal muscle lead to significant muscle atrophy, particularly in fast-twitch fibers. Muscle weakness is the most common and prominent feature of SMA, leaving many patients suffering from difficulty in performing many basic motor functions. While there has been meaningful progress in the development of therapeutics that address the underlying SMA genetic defect, there continues to be a high unmet need for therapeutics that directly address muscle atrophy. Directly targeting the weakening of skeletal muscle may lead to improvements in muscle strength and motor function that could positively impact patients with SMA.

About SRK-015

SRK-015 is a selective and local inhibitor of the activation of latent myostatin. Myostatin, a member of the TGFβ superfamily of growth factors that is expressed primarily in skeletal muscle cells, is a genetically validated target that regulates muscle mass. Scholar Rock is actively working to advance SRK-015 into clinical trials to improve muscle strength and motor function in patients with Spinal Muscular Atrophy (SMA). Scholar Rock plans to develop SRK-015 both in combination with therapies aimed at correcting the underlying genetic defect and as monotherapy in certain subpopulations of SMA patients. SRK-015 is an investigational drug candidate. The effectiveness and safety of SRK-015 has not been established and SRK-015 has not been approved by the FDA or any other regulatory agency.

About Scholar Rock

Scholar Rock is discovering and developing a pipeline of innovative new medicines to treat a range of serious diseases in which growth factors play a fundamental role, including neuromuscular diseases, cancer and fibrosis. By focusing on newly elucidated biology of growth factor activation, Scholar Rock has developed insights which allow us to selectively target growth factors in the disease microenvironment – through the mechanism of supracellular activation. With our proprietary technology, we are developing novel medicines designed to achieve therapeutic effects specifically at the source of disease to deliver new solutions for patients. Scholar Rock is led by a highly-experienced management team of leaders who have built successful biotechnology companies, and is backed by leading investors.