Scholar Rock and Collaborators at Harvard Medical School and Northeastern University Elucidate Molecular Basis of Myostatin Activation – a Key Physiological Process in Muscle Health

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Data provide foundational understanding for novel approach to the treatment of muscle atrophy disorders

CAMBRIDGE, Mass., January 23, 2018 – Scholar Rock, a biotechnology company focused on discovering and developing drugs that selectively target growth factors in the disease microenvironment, today announced the publication of "Tolloid cleavage activates latent GDF8 by priming the pro-complex for dissociation" in *The EMBO Journal* in collaboration with the laboratories of Prof. Timothy Springer (Dept. of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, and Boston Children's Hospital) and Prof. John R. Engen (Dept. of Chemistry and Chemical Biology, Northeastern University).

Myostatin (also known as GDF8) is a key signaling protein that contributes to the regulation of muscle mass and function. Initially produced by muscle in a latent inactive form, myostatin can be activated under certain conditions by sequential enzymatic steps. For the first time, the new study provides an understanding at the molecular level of the structural changes that take place in the protein during this activation process, and the central role of the tolloid enzyme in generating active myostatin. Insight into the activation mechanism of myostatin and other related proteins is central to the drug discovery platform established at Scholar Rock for the development of novel therapies for the treatment of many severe diseases.

"Deploying deep structural understanding of growth factors and their activation is opening a profound new way to intervene in human disease," said Alan J. Buckler, Ph.D., Chief Scientific Officer of Scholar Rock. "SRK-015, our clinical candidate for the treatment of muscle atrophy and wasting disorders, exemplifies the strong potential of targeting specific structural states of myostatin with the objective of providing superior therapeutic outcomes."

The proprietary therapeutic antibody, SRK-015, was discovered and designed by Scholar Rock to selectively and locally target the latent form of myostatin with the ability to specifically block its intramuscular activation. In a variety of preclinical models of muscle atrophy, SRK-015 has demonstrated improvement in muscle function. SRK-015 is initially being developed by Scholar Rock for the improvement of muscle strength and function in patients with Spinal Muscular Atrophy (SMA) with the treatment of additional neuromuscular diseases to follow.

About SRK-015
SRK-015 is a selective and local inhibitor of the supracellular activation of latent myostatin. Myostatin, a member of the TGF-beta 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 that will evaluate the potential to improve muscle strength and motor function in patients with Spinal Muscular Atrophy (SMA). Scholar Rock plans to develop SRK-015 both in SMA patients who are on therapies aimed at upregulating the expression of SMN and as monotherapy in certain subpopulations of SMA patients. SRK-015 is an investigational drug candidate. The effectiveness and safety of SRK-015 have not been established and SRK-015 has not been approved by the FDA or any other regulatory agency.

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 SMN, 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 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 modulating supracellular activation. With our proprietary technology, we are developing novel medicines aimed at achieving 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.

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