Scholar Rock Announces Publication of Comprehensive Pharmacological Study of SRK-015, a Novel Inhibitor of Myostatin Activation, Supporting the Treatment of Muscle Atrophy Disorders

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Preclinical data in Scientific Reports demonstrate localization and selectivity of action supporting novel therapeutic approach

CAMBRIDGE, Mass., February 2, 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 "Blocking extracellular activation of myostatin as a strategy for treating muscle wasting," in *Scientific Reports*, the peer-reviewed, open-access journal published by *Nature*.

The preclinical research published today by Scholar Rock researchers demonstrates that inhibiting the activation of the latent precursor form of myostatin using monoclonal antibodies offers a potentially superior approach to address this important therapeutic target. The research shows that:

- The predominant form of myostatin in muscle is the precursor form.
- The precursor of myostatin is localized to the extracellular matrix, coating individual muscle fibers.
- SRK-015, Scholar Rock's lead drug candidate, binds to the myostatin precursor with exquisite selectivity, avoiding binding to closely related protein growth factors.
- By binding with high affinity to the myostatin precursor, SRK-015 blocks activation of myostatin, thereby blocking atrophy and promoting increased muscle mass and strength in preclinical models.

Myostatin is a key signaling protein that negatively regulates muscle mass and function. Inhibiting myostatin signaling therefore has the potential to address a wide range of muscle disorders. Traditional approaches, directly targeting myostatin or its receptor on muscle cells, have yielded only limited success in treating muscle wasting disorders. Furthermore, selectivity challenges could limit the broad applicability of these approaches for the treatment of many neuromuscular diseases.

"The results of this study demonstrate the power of focusing therapeutic intervention in growth factor signaling one step upstream of the signaling event," said Alan J. Buckler, Ph.D., Chief Scientific Officer of Scholar Rock. "By understanding the processing and release of growth factors in the tissue microenvironment, we see a vast opportunity to improve therapeutic outcomes in many severe diseases with serious unmet medical needs. We are particularly excited to further our understanding of myostatin's role as we begin clinical trials of SRK-015 in the coming months."

SRK-015 is initially being developed and investigated 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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