Myostatin is a protein that prevents muscle growth

Mutations that prevent myostatin from functioning result in larger muscles in multiple species, including humans.

Animals that lack myostatin appear healthy; there have been no observed pathologies of other organ systems in the absence of myostatin.

This suggests that using a drug to prevent myostatin from functioning could be an effective way to increase muscle growth and strength in patients with SMA.

Myostatin inhibition has the potential to improve muscle function in SMA

- Myostatin inhibition preferentially affects Type II (fast twitch) muscle fibers. Fast twitch muscle is critical for short duration, power driven movements, such as rising to a standing position and lifting objects from the floor.
- In SMA, fast-twitch muscle is often atrophied.
- Myostatin inhibition alone (e.g. in ambulatory type III patients) or in combination with any SMN splice modulator (e.g. in Type II and non-ambulatory type III patients) may provide benefits to SMA patients.

TRADITIONAL APPROACHES

Specificity for myostatin is difficult to achieve.

Most mature myostatin inhibitors can also inhibit other proteins

Antibodies to the receptor inhibit signaling of multiple proteins

Inhibitors can distinguish between myostatin and related proteins.

Some of these proteins are very similar to myostatin, so not all myostatin inhibitors can distinguish between myostatin and related proteins.

If a drug blocks multiple family members, there may be unwanted side effects.

Most myostatin inhibitors also target related proteins

Safety concerns raised by lack of myostatin selectivity

Myostatin is part of a large family of 33 related proteins which have a wide range of biological functions.

Some of these proteins are very similar to myostatin, so not all myostatin inhibitors can distinguish between myostatin and related proteins.

If a drug blocks multiple family members, there may be unwanted side effects.

There is an unmet medical need for a muscle therapy in SMA

SMN upregulators are having important impacts on neuromuscular function in SMA patients.

SMN upregulators work mainly by preventing further loss of motor neurons.

But SMN upregulators have less effect on muscle atrophy that is already present in patients.

Muscle function in a mouse model of SMA is improved upon inhibition of Myostatin activation

Inhibition of Myostatin improves muscle mass and strength in healthy mice

Muscle weight

Contractile force

Muscle fiber size

Overview of mouse model of SMA

SMA mice are engineered with the same genetic make-up as human SMA Type I/II patients

Age of mice

1 day

24 days

52 days

SRK-015 specifically inhibits myostatin activation

SRK-015 binding to myostatin and related proteins

SRK-015 Offers Therapeutic Potential for SMA

SRK-015 is a specific inhibitor of Myostatin activation.

The specificity of SRK-015 for myostatin makes it particularly suited to investigation in pediatric indications.

The lack of binding to related family members may reduce the potential for unwanted side effects that may occur with less specific drugs.

Scholar Rock has demonstrated that inhibition of myostatin activation is effective at increasing muscle mass and strength in multiple pre-clinical models, including a mouse model of SMA.

We anticipate SRK-015 to enter clinical trials ~mid-2018 in Type II and non-ambulatory Type III in combination with an SMN splice modulator.

Ambulatory Type III as a monotherapy.

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