

An Update on Scholar Rock's Progress in SMA

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Introduction

Currently approved SMN treatments* have helped those living with SMA by slowing motor neuron degeneration, however muscle atrophy and associated weakness remains a continued challenge for many.

Scholar Rock is researching apitegromab, which aims to address muscle atrophy and associated weakness in SMA. After several years of clinical studies, Scholar Rock is anticipating having phase 3 clinical study results in 2024.

Apitegromab is an investigational treatment and the efficacy and safety have not been evaluated by the U.S. Food and Drug Administration (FDA). If successful, Scholar Rock intends to submit an application to the FDA for approval.

The Role Of Muscle In SMA

SMA affects both nerves and muscles

- Current approved treatments target motor neurons, slowing further motor neuron deterioration.
- Motor neurons are nerve cells that connect to and communicate with skeletal muscle, letting them know when to contract.
- The goal of Scholar Rock's approach is to strengthen the muscle component.
- This approach presents an opportunity to increase muscle mass, with the aim of improving motor function.

Increasing muscle mass in SMA may support many different activities:

- Muscle Fatigue**
Withstand activities for longer like writing their notes at university or typing on a phone or computer
- Hand Control**
Drinking a glass of water, operating a wheelchair, pressing an elevator button
- Muscle Tone**
Sitting, turning sides in bed, lifting a blanket
- Chewing**
Being able to eat different and tougher foods
- Transfers**
Going from bed to the bathroom, wheelchair to toilet, etc.

Where We Were

PHASE I

STATUS Complete

WHO PARTICIPATED?

Healthy volunteers (Volunteers not living with SMA)

WHAT WAS THE GOAL?

Safety and how the body responds to apitegromab

PHASE 2: TOPAZ STUDY

STATUS Complete

WHO PARTICIPATED?

Type 2 & Type 3 SMA split into three groups:

- 1 Type 3, ambulatory*, ages 5-21 years
- 2 Types 2 & 3, nonambulatory*, ages 5-21 years, who started an SMN therapy at or after age 5
- 3 Type 2, nonambulatory, age 2 years or older, who started SMN therapy before age 5

WHAT WAS THE GOAL?

Safety and effectiveness of apitegromab in Type 2 and 3 SMA

Where We Are

PHASE 3: SAPPHIRE TRIAL

STATUS Ongoing topline results expected in Q4, 2024

WHO IS PARTICIPATING?

Types 2 & 3 SMA nonambulatory*, divided into two groups:

- 1 Those aged 2 – 12, in people using SMN therapy
- 2 Those aged 13 – 21, in people using SMN therapy

WHAT IS THE GOAL?

Compare the effect of apitegromab with placebo*. Gather additional data to support an application to the Food and Drug Administration (FDA) for approval.

ONYX OPEN-LABEL EXTENSION STUDY

STATUS Ongoing

WHO IS PARTICIPATING?

Participants who have completed the TOPAZ or SAPPHIRE study had the opportunity to enroll

WHAT IS THE GOAL?

Long-term safety of apitegromab

What We're Looking Forward To

SAPPHIRE STUDY INITIAL RESULTS (2024)

STATUS We anticipate having a readout of initial study data this year.

Exploring apitegromab in other SMA populations such as ambulatory SMA and younger people living with SMA.

A Potential Approach to Supporting Muscle in SMA



Myostatin is a protein that every person has in their body, including those living with SMA. It regulates the breakdown of muscle, as part of a natural system that regulates muscle growth. **Preventing the activation** of myostatin reduces this breakdown and can increase the size of skeletal muscle throughout the body.

Reducing myostatin activation, in addition to addressing SMN deficiency, may be an approach that leads to increased muscle mass and improved motor function in those living with SMA. This is the approach used by apitegromab, which is currently under investigation.

DEFINITIONS*

SMN treatments include Spinraza, Evrysdi, and Zolgensma.

Nonambulatory: for the purposes of our studies, we have defined nonambulatory as the inability to walk more than 10 steps without assistance.

Ambulatory: for the purposes of our studies, we have defined ambulatory as the ability to walk more than 10 steps without assistance.

Placebo: a substance that has no therapeutic effect, used as a control in testing new drugs.