A phase 1a/b open label study of SAT-3247 in healthy volunteers and adult patients with Duchenne muscular dystrophy

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BACKGROUND

- Duchenne muscular dystrophy (DMD) is an X-linked recessive neuromuscular disorder caused by mutations in the dystrophin gene
- While existing therapies represent meaningful advances in Duchenne muscular dystrophy, there remains a significant unmet medical need, underscoring the importance of continued innovation to address gaps in treatment across the full disease spectrum
- Loss of dystrophin signalling disrupts skeletal muscle repair and regeneration, leading to progressive muscle loss
- SAT-3247 is an oral small molecule inhibitor of AAK1 designed to restore this required signaling in a dystrophin independent fashion, enhancing repair and regeneration of damaged skeletal muscle
- Preclinical studies have shown that SAT-3247 increases progenitor cell counts, improves muscle pathology, and improves functional muscle strength in Mdx mouse and canine models of DMD

How SAT-3247 Works:
Supporting the Body's Muscle Repair and Regeneration Process

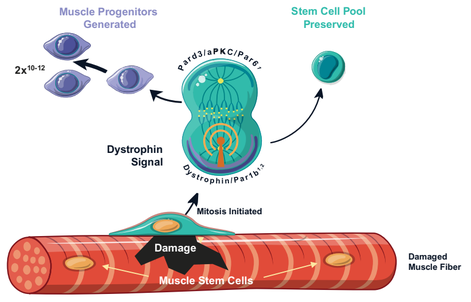
THE PROBLEM

In Duchenne muscular dystrophy, muscles are damaged faster than the body can repair them. Over time, this imbalance leads to a steady decline in muscle strength and function.

HEALTHY MUSCLE REPAIR

In healthy muscle, stem cells respond to damage by dividing in a balanced way — some become new muscle cells to repair tissue, while others stay as stem cells to support future repair. This balance is essential for ongoing muscle health and is illustrated below.

Dystrophin 'signal' present: Repair and regeneration occurs

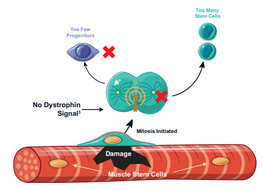


1. *Pard3, APKC, Par6, and Par1b form the Par Polarity Complex*
2. *Dystrophin phosphorylates Par1b to establish the basal pole of the cell and release Pard3 et al to form the apical pole*
3. *Absent Dystrophin, phosphorylation of Par1b does not occur, polarity is impaired and the balance of stem cells to progenitors is distorted*

THE BREAKDOWN

Dystrophin 'signal' absent: Repair and regeneration impaired

Satellos discovered that in Duchenne, this balance is upset as the process breaks down. Stem cells simply don't divide the way they should. As a result, the body can't keep up with the damage, and muscle regeneration slows down significantly.



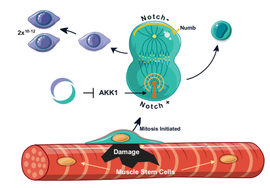
THE INSIGHT

Research at Satellos uncovered an important reason why this process breaks down: A critical signal that muscle stem cells rely upon is missing. In healthy muscle, this signal is normally provided by a protein called dystrophin. Without it, as occurs in Duchenne, stem cells lose their ability to divide properly.

THE APPROACH

Missing 'signal'replaced: repair and regeneration occures

Satellos identified an alternative way to provide this needed signal — independent of dystrophin. Doing so can help restore balance in how muscle stem cells divide. SAT-3247 is an oral investigational treatment designed to temporarily block a protein called AAK1. In this way, SAT-3247 helps support a more balanced stem cell response to muscle damage, enabling repair and regeneration.



1. *Notch signaling is a conserved pathway that regulates cell proliferation, cell fate, and differentiation.*
2. *Inhibiting AAK1 establishes a notch gradient across the satellite cell, via Numb inhibition at the apical pole, restoring appropriate cell division*

THE GOAL

Our goal is to restore the body's natural ability to regenerate muscle — from within.

In Duchenne, where muscle repair is disrupted, we aim to restart the cycle of muscle growth and renewal.

SAT-3247-CL-101

TRIAL OVERVIEW

Ph 1a: Healthy Volunteers (n=72)			Ph 1b: DMD Adults
Part A: SAD* Study	Part B: MAD* Study	Part C: Food Effect Study	Part D: 28-day, Open-Label Study
▪ 10 - 400 mg ▪ 5 cohorts of 8 ▪ Single dose / 1 day	▪ 60 - 240 mg ▪ 4 cohorts of 8 ▪ Single dose / 7 days	▪ 150 mg ▪ 1 cohort of 8 ▪ Single dose / 1 day	▪ 60 mg daily dose, weekdays only for 4 weeks ▪ 5 patients enrolled and completed ▪ Age range 20 – 27, all on steroids

SAT-3247 was safe and well tolerated across Ph 1a & 1b studies with a desirable PK profile

Endpoints

Primary (Ph 1a & 1b): Incidence and severity of TEAEs

Secondary (Ph 1a & 1b): Pharmacokinetic exposure (PK)

Exploratory (Ph 1b only): Grip/pinch strength, upper body effort, lung function (FVC), serum markers

**SAD: single ascending dose; *MAD: multiple ascending dose. Part C utilized select participants from Part A*

KEY DEMOGRAPHICS

Characteristic	Part A/C (n=40)	Part B (n=32)	Part D (n=5)
Age at screening (years)			
Mean	33.2	37.5	23.4
SD	12.7	15.1	2.7
Min, Max	20, 65	18, 64	20, 27
Sex at birth n (%)			
Female	23 (57.5)	7 (21.9)	0
Male	17 (42.5)	25 (78.1)	5 (100)
Weight at screening (kg)			
Mean	74.39	76.98	51.72
SD	15.23	13.89	12.19
Min, Max	47.6, 107.1	50.6, 105.3	36.3, 65.3
Concomitant steroid use n(%)	N/A	N/A	5 (100)

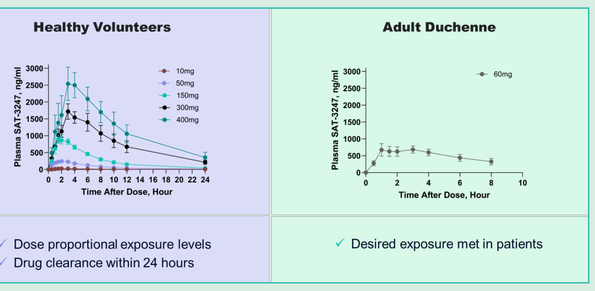
Part C demographics are not displayed, as participants in Part C were a subset of those who completed Part A

SAFETY SUMMARY

AE Category	Part A (n=30)	Part B (n=24)	Part C (n=12)	Part D (n=5)
Any TEAE	9	18	4	4
Any related TEAE	1[a]	2[b]	0	2[d]
Any serious TEAE	0	0	0	2
Any related serious TEAE	0	0	0	0
Any TEAE leading to withdrawal	0	1[c]	0	0
Any TEAE leading to death	0	0	0	0

[a] Mild nausea/abdominal pain (resolved)
[b] Mild somnolence (resolved), mild abdominal pain (resolved)
[c] Covid-19 (unrelated, resolved)
[d] Mild nausea (resolved), elevated ALT ((ref range (5, 40) – baseline(29), day 28(47) - resolved))

PHARMACOKINETIC PROFILING



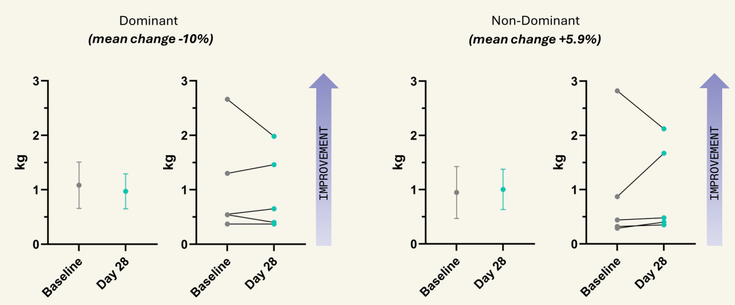
SYDE DEVICE DATA AT DAY 28

Participant	Maximum Effort	Mean_norm_gyr_99	Vertical Amplitude	Movement Duration
112-001	-2.11	2.08	2.25	-6.93
112-003	13.98	3.51	-3.18	-3.55
112-008	-10.66	-1.94	-3.58	-5.65
112-009	17.34	1.19	0.49	6.31
112-010	-16.71	0.12	-6.01	-5.13

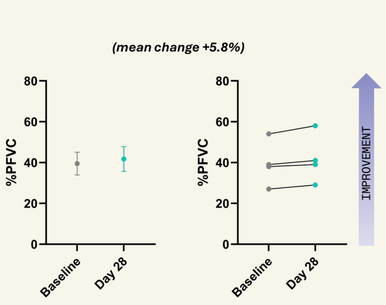
(% Change from baseline)

No consistent trend of benefit across participants with Syde or Maximum Pinch Strength assessments

MAXIMUM PINCH STRENGTH



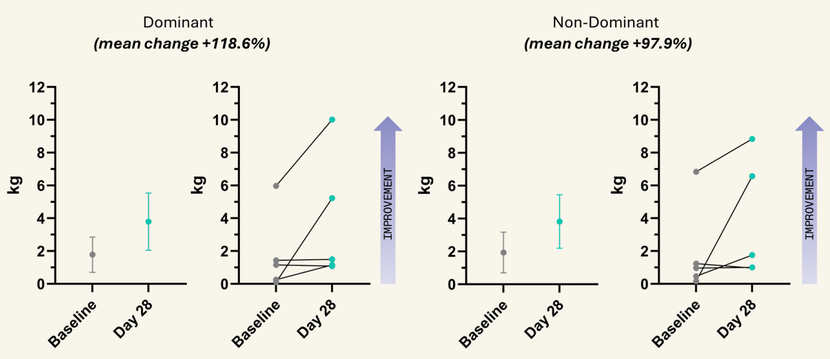
% PREDICTED FORCED VITAL CAPACITY*



**N=4 participants, 1 participant unable to perform final measurement*

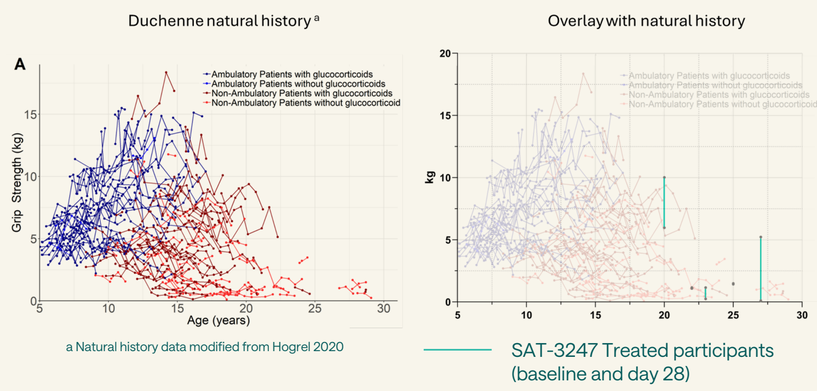
Approximately 5% benefit observed in % Predicted FVC; Consistent benefit observed across all 4 participants

MAXIMUM GRIP STRENGTH



Near doubling in grip strength across 5 participants in dominant and non-dominant hand

MAXIMUM GRIP STRENGTH VS NATURAL HISTORY

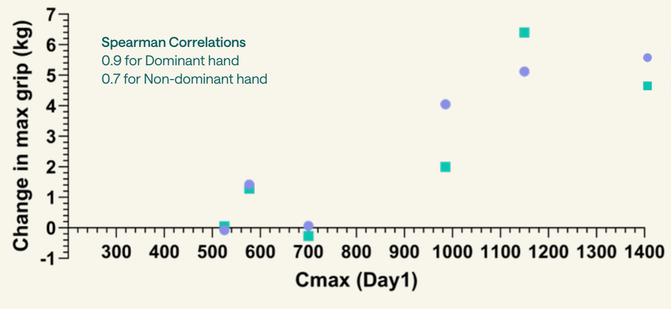


a Natural history data modified from Hogrel 2020

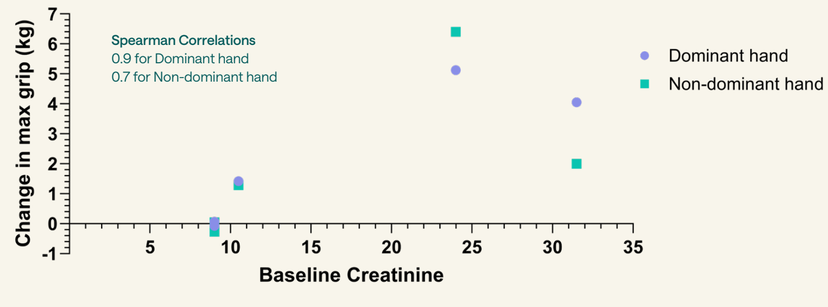
SAT-3247 Treated participants (baseline and day 28)

Improvement with SAT-3247 beyond what is reported for natural history

MAXIMUM GRIP STRENGTH VS CMAX



MAXIMUM GRIP STRENGTH VS BASELINE CREATININE



Greatest improvement in grip strength occurred in participants with highest Cmax on Day 1; Greatest improvement in grip strength occurred in participants with highest baseline creatinine (surrogate marker for muscle mass)

CONCLUSIONS AND NEXT STEPS

- SAT-3247 was safe and well tolerated across all parts of the study, with a consistent AE profile between healthy volunteers and adult participants with Duchenne
- SAT-3247 exposure levels were consistent between healthy volunteers and adult participants with Duchenne and were in line with predictions based upon preclinical data.
- Adult Duchenne participants who received SAT-3247 over a 28-day period demonstrated apparent increases in grip strength that warrant future follow-up
- Participants studied in SAT-3247-CL-101 are now eligible to enroll in an 11-month follow-up study to assess long-term safety, tolerability, and exploratory efficacy of SAT-3247
- See Poster 411P for more details on the long-term follow-up study SAT-3247 LT-001, and SAT-3247-CL-201, a global RCT that will assess SAT-3247 in pediatric ambulatory Duchenne patients