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Sarepta loses its Momentum

Elizabeth Cairns

A clinical hold for the company's Exondys 51 follow-on adds further pressure on the forthcoming gene therapy readouts.

Low magnesium levels had already been flagged as an adverse event with Sarepta's SRP-5051, a next-gen exon skipper pegged as Exondys 51's replacement. So professions of surprise from analysts that a serious case of hypomagnesemia has prompted the FDA to halt a phase 2 trial ring somewhat hollow.

At least '5051 is not where major expectations lie for Sarepta, as shown by investors shrugging off the clinical hold and the stock edging higher this morning. Much more attention is on SRP-9001, the gene therapy that is, like '5051, in development for Duchenne muscular dystrophy, and on which crucial data are looming.

The clinical hold concerns a patient in part B of the Momentum trial who had just moved to a higher dose of the SRP-5051. Sarepta believes the peptide part of the molecule, which is responsible for getting it into cells, is the cause of the hypomagnesemia, though the group is still unsure of the exact mechanism.

The trial's monitoring plan will now be altered, such as by proactively identifying patients sensitive to hypomagnesemia ahead of dose-escalation. The company insists that the trial will complete enrolment by the end of the year as scheduled.

Still, if the clinical hold is not resolved soon, it is likely that the remaining subjects will come from Momentum's EU and Canadian sites, which are not on clinical hold. There is thus a risk in terms of geographic representation, although the FDA has not specified a minimum number of US patients.

Two weeks' time

A more important catalyst for the company is on the horizon, however: new data on its Duchenne gene therapy SRP-9001 is expected on July 7 at the ICNMD Conference. This will include: one-year data from patients dosed with commercial-grade material in Study 103; four-year results from Study 101, which includes older patients; and an analysis of data across 4-7 year olds who received the target dose of '9001.

Sarepta has previously noted that this latter dataset could support an accelerated approval, though their base case expectation is to file on results of the phase 3 Embark trial, probably in the second half of 2023.

Expectations here are feverish – *Evaluate Pharma* forecasts sales of $1.1bn for '9001 in 2028, $230m of which will accrue to Sarepta's partner, Roche. Following a sizeable mishap with this project 18 months ago and an attempt at reanimating it, the new data will have to be pretty convincing.

Clinical trials of SRP-9001			
Status	**Trial**	**N**	**PCD**
Phase 1	Endeavor, aka 103 (NCT04626674)	38	Oct 2022
Phase 1/2	101 (NCT03375164)	4	Apr 2023
Phase 2	102 (NCT03769116); placebo-controlled	41	Dec 2020
Phase 3	Embark, aka 301 (NCT05096221), placebo-controlled	120	Oct 2023
PCD = primary completion date. Source: Evaluate Pharma.			