Evaluate Vantage

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Sarepta contains UK study halt, for now

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Sarepta made a neat transition from its marketed Duchenne muscular dystrophy drug, Exondys 51, to developing what could be an even better asset, golodirsen. But there could be trouble ahead: treatment at UK sites involved in the latter's pivotal trial has just been halted, *EP Vantage* has learned.

The reason for what Sarepta says is a temporary stop in dosing is "one serious adverse event that could possibly be related to the investigational drug product", the company confirmed. A direct causal connection has not been made, however, and there are reasons to believe that the hold might not last long.

For one, safety data from all patients in Essence, the study in question, have been reviewed by an independent monitoring committee, which deemed that dosing could continue for all subjects, Sarepta told *EP Vantage*. The group has not issued a formal statement about the hold, which seems to have occurred last week, implying that this was not a material event.

Volatility

But this does not mean that investors can rule out the possibility of a more serious problem, and there could be stock volatility, especially in the current jittery markets. Yesterday Sarepta was off 6% on a dismal day in which the Nasdaq biotech index fell 4%.

EP Vantage became aware of the UK halt after seeing posts on Facebook from the parent of a child enrolled into Essence. "My son was due his biopsy and first dose of 45 skip [in] Essence last week. They have temporarily stopped dosing in the UK ... I understand due to rhabdomyolysis side effects," the parent wrote.

Rhabdomyolysis is the breakdown of damaged skeletal muscle, causing muscle pain. Investors with long memories will recall that Bayer's cholesterol-lowerer Baycol was pulled from the market in 2001 owing to reports of this side effect.

However, the risk-benefit of a mass-market drug can hardly be compared to that of one targeting a rare disease. Sarepta said the adverse event observed was consistent with those seen in patients with Duchenne; there have also been case reports of anaesthetic-induced rhabdomyolysis in Duchenne children.

Two treatments

Should the side effect be deemed to be treatment-related it will be vital to specify to which treatment. The placebo-controlled Essence trial actually comprises two separate active arms: one in subjects amenable to exon 53 skipping, given golodirsen, and another in exon 45 patients, given the follow-on project SRP-4045 (*Sarepta hopes to pull off the same trick twice, September 6, 2017*).

Essence is under way at 51 locations, according to Clinicaltrials.gov, in the US, Israel and eight European countries. In the UK the four enrolling centres are Leeds Teaching Hospitals NHS Trust, Alder Hey Children's Hospital, Great Ormond Street Hospital and Royal Victoria Infirmary.

Sarepta said the MHRA ordered all UK centres to halt dosing because of "UK-specific stopping rules", and it is submitting an amendment to the regulator that, if approved, could cause UK dosing to be reinitiated. The study remains blinded.

Study	Detail	Trial ID
Essence	Double-blind, 126 subjects given golodirsen, SRP-4045 or placebo.	NCT02500381

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