Evaluate Vantage

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ICNMD 2022 – still unclear whether Sarepta can accelerate

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New data with SRP-9001 look decent, but filing plans remain uncertain.

Sarepta today added weight to its goal of getting the nod for its Duchenne muscular dystrophy gene therapy SRP-9001, with an ostensibly positive data drop. However, the company still cannot say whether it will seek accelerated approval for the project, or whether it will need to await data from the placebo-controlled Embark study, due next year.

Investors, perhaps hoping for more clarity on this point, pushed Sarepta's stock down 2% this morning. They might also have been spooked by a new adverse event of myocarditis – a problem that has hit Pfizer's rival DMD gene therapy.

Questions about these two issues dominated a conference call today. On the issue of accelerated approval, Sarepta execs would only say that the group was in discussions with the FDA, and should get some guidance in the "not-too-distant future".

For now, the base-case is that Embark will be needed for approval. And the FDA might well want placebo-controlled data: the results presented today came from three studies that compared SRP-9001-treated patients with matched external controls.

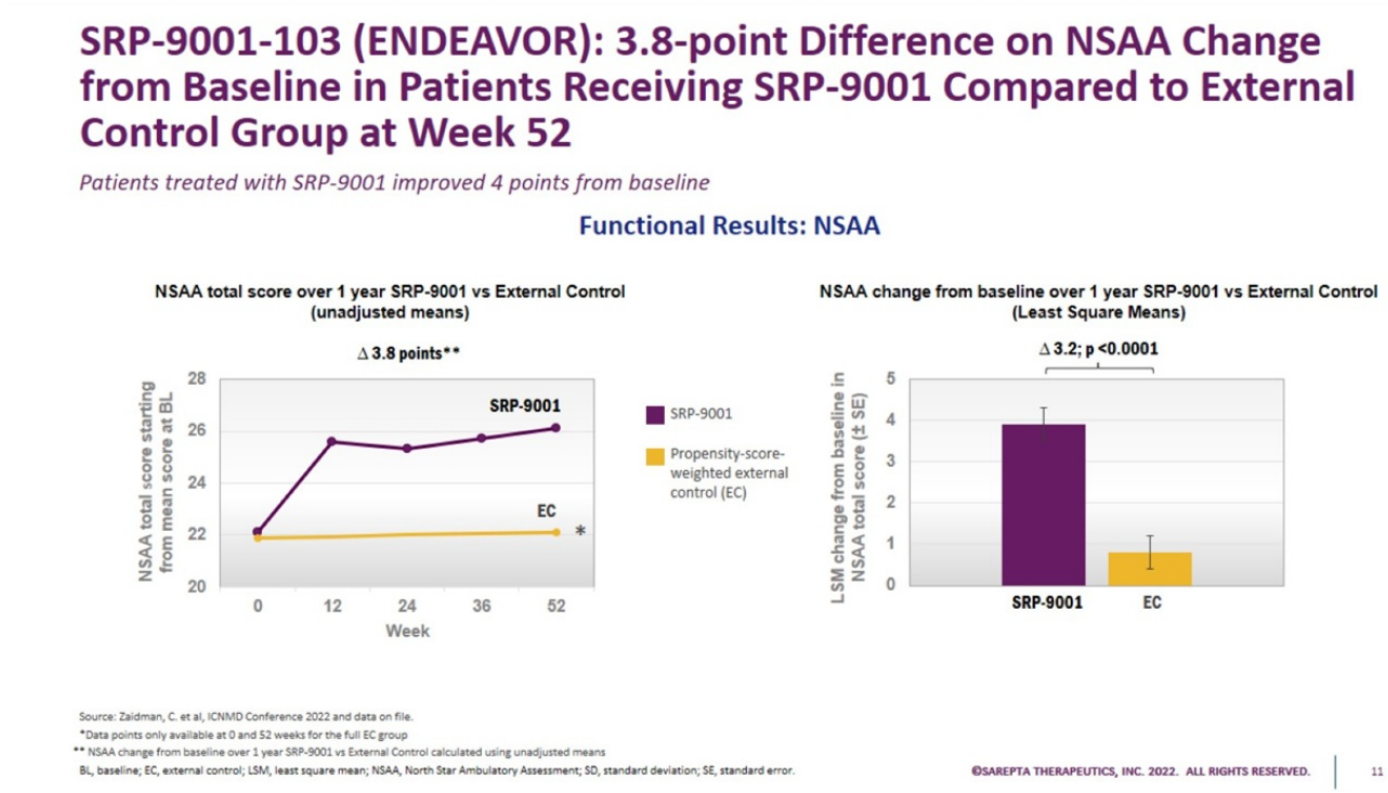
Still, as previously noted, such analyses were prespecified and the external controls, who came from three separate studies, were rigorously matched to study participants, according to Sarepta.

The FDA might also have been burned by Sarepta's previous reluctance to follow through on confirmatory studies, but this looks unlikely to be an issue this time given that Embark is already under way.

Commercial grade

The most relevant of the results presented today by Sarepta and its partner Roche probably come from Study-103, also known as Endeavor, which uses commercial-grade SRP-9001. The data came at the International Congress on Neuromuscular Diseases in Brussels.

Among 20 patients there was a 3.8-point improvement in North Star Ambulatory Assessment (NSAA) score at one year versus external controls.



Source: Company presentation

This looks better than the two-point improvement reported in part 2 of Study-102, which uses clinical-grade product, in January (*JP Morgan 2022 – Sarepta gets another bite at the gene therapy cherry, January 11, 2022)*. However, the placebo-controlled first part of that study failed, providing another reason for caution.

As for the case of myocarditis – inflammation of heart tissue – this was seen in an 11-year-old boy in Study-103. He had no symptoms of cardiac dysfunction, but raised troponin levels were detected when he was hospitalised for nausea and vomiting. He has since returned to normal.

Pfizer's gene therapy, fordadistrogene movaparvovec, has also been linked with myocarditis, and the phase 3 trial of that project was later put on hold after a patient death. That hold has since been lifted, but the new protocol includes a seven-day hospitalisation period to enable close monitoring.

Pfizer also excluded patients with certain mutations – the theory was that gene transfer could spur an immune response in patients who had not previously been exposed to dystrophin.

Sarepta execs said today that there was no evidence that the myocarditis case seen in its trial was immune related.

Regarding other adverse events, nausea and vomiting were seen in 50-60% of patients across Study-103, Study-102 and the four-patient Study-101. Sarepta execs stressed that there was no complement activation, an issue that has been seen with both Pfizer's project and Solid Biosciences' SGT-001.

Sarepta's trials with SRP-9001			
Trial	**ID**	**Details**	**Note**
Study-101	NCT03375164	4 pts, clinical grade product	
Study-102	NCT03769116	41 pts, clinical grade product	Placebo-controlled part 1 failed; in part 2 pts originally on placebo crossed over to therapy
Study-103 (Endeavor)	NCT04626674	38 pts, commercial grade product, single arm	
Embark	NCT05096221	120 pts, commercial grade product, placebo controlled	Enrolment due to complete mid-2022; data due mid-2023
Source: Evaluate Pharma & clinicaltrials.gov.			

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