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Solid stumble sets up Sarepta

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The most surprising thing about Solid Biosciences' latest setback and subsequent crash is that investors had driven stock up to such dizzy heights in the first place. The warning signs had been there, with the departure of a high-profile board member and a partial clinical hold on the company's lead asset, the Duchenne muscular dystrophy gene therapy, SGT-001.

But Solid still managed to price its initial public offering in January, at only a small discount, and had been firmly in the black until the full clinical hold was disclosed last night. Any idea that this might make investors more cautious about DMD gene therapy seems to be unfounded, with the news already being seen as a positive for other players including Sarepta (see table below). The question of what might finally burst the current biotech bubble remains.

The good times appear to be over for Solid, at least until it can resume its phase I/II Ignite DMD trial, an outcome that is far from certain based on the limited information available. The company's shares plunged 63% this morning, with investors no doubt wishing they had heeded the earlier red flags.

But other companies profited from Solid's misfortune; notably Sarepta was up 2% this morning, with bulls keen to point out the differences between that company's two clinical-stage DMD projects and SGT-001. Sarepta expects first-in-human data with its two projects in mid-2018.

DMD gene therapy pipeline

Project	Company	Pharma class	Trial(s)	Status
Phase I/II				
AAV1-Follistatin	Milo Biotechnology	Myostatin inhibitor	NCT02354781	Completed Nov 2017
Micro-dystrophin gene therapy project	Sarepta	Micro-dystrophin gene therapy	NCT03375164	Preliminary data due mid-2018
GALGT2 gene therapy project	Sarepta	GalNAc transferase gene therapy	NCT03333590	Preliminary data due mid-2018
SGT-001	Solid Biosciences	Micro-dystrophin gene therapy	Ignite DMD, NCT03368742	On hold
Phase I				
PF-06939926	Pfizer	Muscular dystrophy gene therapy	NCT03362502	Primary completion Jul 2024

Source: EvaluatePharma.

But this is still a risky sector, as demonstrated amply by Solid. The full clinical hold of the Ignite DMD trial was triggered after the first patient given SGT-001, at 5x1013vg/kg, was found to have a decreased platelet count and evidence of complement activation.

The patient later recovered, but the development is particularly worrying as it involved a low dose of SGT-001. This had not been covered by the previous partial hold, which had prohibited the company from dosing above 5x1013vg/kg (*DMD-day for investors, January 26, 2018*).

At the time, Solid said that the partial hold had been put in place because its manufacturing capabilities did not meet FDA requirements for the higher doses; in February the company was close to resolving these, according to Leerink analysts.

It is unclear what triggered the latest adverse event, although it is possible that it could be related to the viral vector or a contaminant, given Solid's previous manufacturing problems.

Avexis readacross

If it is the vector this could be bad news for Avexis, whose AVXS-101, in phase III for spinal muscular atrophy, uses the same AAV9 vector as SGT-001.

William Blair analysts played down any read-across to Avexis's project, pointing out that, although the study of AVXS-101 uses a higher dose per kilogram, patients are smaller than the non-ambulatory DMD subject who received SGT-001, making the actual dose of AVXS-101 lower. Still, Avexis's stock was down 2% this morning.

Meanwhile, Sarepta's DMD gene therapy projects use a different vector, and this is one factor boosting the confidence of that company's investors this morning.

Both of the group's clinical-stage gene therapy assets, one targeting micro-dystrophin and the other targeting GALGT2, use the RH74 vector, which is related to AAV8. So far, two patients had been dosed in the micro-dystrophin programme, with a third due to be dosed this month, a spokesperson for Sarepta told *EP Vantage*.

He added that Sarepta's project was being dosed at 2x1014vg/kg, a fourfold increase over Solid's starting dose, with no adverse reactions seen to date. Separately, a UK clinical hold on Sarepta's non-gene therapy asset golodirsen was lifted last week, the company confirmed yesterday, which might also have contributed to its stock rising.

These factors appear to have saved Sarepta from getting caught up in Solid's woes. But the latest crash is a reminder of how quickly high-risk projects can go wrong, even in a bull market.

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