

Another Fabry flop, courtesy of 4D



[Madeleine Armstrong](#)

Amid a [narrowing pipeline of gene therapy candidates for Fabry disease](#), new doubts are creeping in about one of the contenders, 4D Molecular's 4D-310. An update yesterday detailed three cases of atypical haemolytic uremic syndrome (aHUS) among six patients who have received the project so far - one of which was classified as grade four. This adverse event was seen in one patient in the initial [data drop in 2021](#). 4D is now pausing enrolment into its current studies, although a pivotal trial is being planned. The group will also abandon the corticosteroid regimen it has been using for immunosuppression, in favour of a rituximab-sirolimus regimen that it hopes will prevent aHUS. In addition, 4D reported intriguing cardiac efficacy data from three patients in the phase 1/2 US Inlaxa study, but this was clearly not enough to reassure investors, who sent the group's stock down 10% yesterday. More details on 4D-310's efficacy and safety will be presented at the World Symposium in February. This meeting is also set to feature further results on Sangamo's ST-920, which currently looks like the Fabry gene therapy project to beat - although the bar is low.

The Fabry gene therapy data so far

Project	Company	Trial	Dose(s)	AGA activity	Note
4D-310	4D Molecular	Inlaxa & Asia-Pacific trial	1x10 ¹³ vg/kg (lowest dose)	Feb 2022: 10 to 14-fold of mean normal in 2 pts; Jan 2023: cardiac data in 3 US pts	Three cases of aHUS across 6 pts in US & Asia-Pacific trials; enrolment paused
ST-920	Sangamo	Staar	0.5x10 ¹³ , 1x10 ¹³ , 3x10 ¹³ & 5x10 ¹³ vg/kg	Oct 2022: 2 to 30-fold of mean normal in 9 pts; 4 pts withdrawn from ERT	Study now in dose-expansion phase
FLT190	Freeline	Marvel-1	7.5x10 ¹¹ vg/kg (lowest dose)	Nov 2021: subtherapeutic & near normal in 2 pts*; Nov 2022: levels "sustained" for 1-3yrs	Dosing in 2nd cohort (1.5x10 ¹² vg/kg) began Sep 2022

*Note: all studies ph1/2; *both pts experienced myocarditis; AGA=alpha-galactosidase A; ERT=enzyme-replacement therapy. Source: company releases.*

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