Evaluate Vantage

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Freeline’s Fabry data fall short

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Freeline Therapeutics has followed 4D Molecular and Sangamo with data on a Fabry disease gene therapy candidate. But the results with FLT190, in just two patients, have failed to hit the heights reached by the other groups’ projects. True, FLT190 was dosed much lower than both 4D’s 4D-310 and Sangamo’s ST-920, a fact that could explain why Freeline only saw subtherapeutic and near-normal levels of alpha-galactosidase A (AGA), the enzyme that is missing in Fabry patients. But both patients treated with the lowest FLT190 dose showed signs of myocarditis, raising questions about whether Freeline will be able to dose any higher. The group described these cases as “mild” and “transient”, adding that Fabry patients have underlying cardiac disease, which might have predisposed them to this issue. But the development has scuppered Freeline’s plans to move to a higher dose, $1.5x10^{12}$vg/kg, at least for now; the Marvel-1 trial’s data-monitoring committee has recommended that the company treat another patient at the lowest dose to investigate this finding further.

The Fabry gene therapy data so far

Project	Company	Trial	N	Dose(s)	AGA activity
FLT190	Freeline Therapeutics	Marvel-1	2	$7.5x10^{11}$vg/kg (lowest dose)	0.8-1.3 (subtherapeutic) & 3.9nmol/hr/ml (near normal)*
ST-920	Sangamo Therapeutics	Staar	4	$0.5x10^{13}$ & $1x10^{13}$vg/kg (low & mid dose)	2-15-fold above mean normal (5.70nmol/h/ml)
4D-310	4D Molecular Therapeutics	NCT04519749	3	$1x10^{13}$vg/kg (lowest dose)	248.1, 5.7 & 209.3nmol/hr/ml**

*Note: all studies ph1/2; *both pts experienced myocarditis; **one case of atypical haemolytic uremic syndrome; AGA=alpha-galactosidase A. Source: company releases.*