Evaluate Vantage

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Fulcrum’s biopsy conundrum

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Fulcrum’s shares tanked 48% yesterday after its lead project, losmapimod, faltered at an interim look in a progressive neuromuscular disorder, and further data next year need to impress to keep the project from the scrapheap. Biopsy results from the phase IIb Redux4 trial in 29 patients with facioscapulohumeral muscular dystrophy (FSHD) showed no separation from placebo at 16 weeks in DUX4-driven gene expression, and while a reduction in expression was hoped for in fact an increase was seen. FSHD is a caused by aberrant expression of DUX4 in skeletal muscle, leading to muscle death. Fulcrum was keen to point out that gene expression varies significantly throughout a patient's muscles, and in biopsies with high levels of DUX4 at baseline there were signs of a reduction. Data on 80 patients are due in the first quarter of 2021, and will include full-body MRI results, which Leerink analysts believe could capture losmapimod's impact across the body. Functional data are due in the second quarter. There are no disease-modifying treatments for FSHD, and for now Fulcrum has the lead project.

Redux4 interim results – change from baseline in DUX4 activity				
	All subjects		**Highest expressing muscle biopsies**	
	Sample size	**Fold change**	**Sample size**	**Fold change**
Losmapimod	15	3.7	3	-38.0
Placebo	14	2.8	5	-5.4
Source: company press release.				