Evaluate Vantage

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The picture worsens for Astellas’s gene therapy

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Astellas insists that it remains committed to developing its gene therapy for the rare childhood disease X-linked myotubular myopathy after the fourth death in the project’s phase 2 trial. News that the patient was sick with liver enzyme elevations caused the Aspiro trial, assessing AT132, to be halted at the start of the month; the patient died on September 9. In the meantime the FDA placed the study on formal clinical hold. This patient was on the low dose in the trial, dashing hopes that reducing the dose could reduce the risk – the three earlier deaths had all occurred in the high-dose group. Astellas says the cause of death is not yet confirmed. The choice of viral vector for the gene therapy is perhaps not at fault: AAV8 is used by a handful of other gene therapies, and no deaths have been reported in the clinical trials of these agents. Astellas has another AAV8-based gene therapy in the clinic, AMT845 for Pompe disease. This was, like AT132, obtained via the Audentes acquisition in 2019. If ’132 has to be abandoned, ’845 will be the only clinical-stage asset Astellas has to show for the $3bn Audentes deal.

Selected AAV8-based gene therapies

Product	Company	Indication	Status	2026e sales ($m)
Fidanacogene elaparvovec	Pfizer	Haemophilia B	Benegene-2, ph3, data expected 2022	405
RGX-314	Regenxbio/ Abbvie	Wet AMD and diabetic retinopathy	Wet AMD: Atmosphere, ph3, data due 2023 and Aaviate, ph2, data imminent; DR: Altitude, ph2, data 2021	0
AT-132	Astellas	X-linked myotubular myopathy	Aspiro, ph2, on clinical hold	0
DTX401	Ultragenyx	Glycogen storage disease type Ia	Unnamed ph1/2 trial, data expected 2021	270
AMT845	Astellas	Pompe disease	Fortis, ph1, data expected 2022	0

AMD=age-related macular degeneration; DR=diabetic retinopathy. Source: Evaluate Pharma & company websites.