Evaluate Vantage

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Nightstar becomes nightmare, but Biogen has bigger fish to fry

Jacob Plieth

A second clinical failure means that Biogen threw away $877m, but this sum will today be seen as little more than a rounding error.

It is just as well that Aduhelm was approved, adding $18bn to Biogen's market cap, or the group's business development decisions would now be coming under fire. Yesterday's failure of the second of two gene therapies Biogen got from Nightstar has rendered that $877m acquisition, done in 2019, worthless.

$877m is chump change against what analysts think Aduhelm will sell, and today's disappointing depression data for the Sage-originated zuranolone similarly pale into insignificance for Biogen. But the failure shows how difficult targeting eye diseases with gene therapy is proving to be, and vindicates Nightstar's decision to sell itself at a seemingly undemanding valuation.

The Nightstar deal was priced 14% lower than where the target's stock had been trading just six months previously (*Nightstar gives Biogen a cheap way to expand in gene therapy, March 4, 2019*). Thus the sale looked questionable, but it was accepted as a compromise between the peak of investor euphoria and a realistic minimum necessary to get a deal done.

Flattering

Reality has turned out far more flattering for those managing the sale of Nightstar, which effectively had two R&D assets. The first of those, BIIB112 for X-linked retinitis pigmentosa, failed in its phase 1/2 Xirius study last month.

Yesterday came news that the second, BIIB111 for the rare inherited retinal disease choroideremia, was also going nowhere. The phase 3 Star trial failed its primary endpoint, which had aimed to show that BIIB111 could improve best corrected visual acuity at 12 months by 15 letters or more versus control. Biogen added that key secondary measures were also missed.

Neither BIIB111, known under the INN timrepigene emparvovec, nor BIIB112 (cotoretigene toliparvovec) had carried significant sellside consensus forecasts, and their failures do not move the needle in terms of Biogen's investment case. This is especially true now that in Aduhelm Biogen has a potential Alzheimer's disease blockbuster on its hands.

Tough

Still, it will not go unnoticed that eye diseases are proving tough for gene therapy. The recent setback for Adverum's ADVM-022 concerned not lack of efficacy but a toxicity scare, while Regenxbio's RGX-314, like ADVM-022 a gene therapy for wet AMD, spent time on clinical hold.

Investor confidence is waning fast, something the Nightstar disappointments will do nothing to help. For instance Applied Genetic Technologies, a major player in gene therapies for rare ocular disorders, is today worth under $200m; its lead asset, AGTC-501, has failed to excite.

AGTC-501 is about to start a pivotal trial in X-linked retinitis pigmentosa, as is Meiragtx's Johnson & Johnson-partnered MGT009. 4D Molecular is also active in X-linked retinitis pigmentosa and wet AMD, and is worth $780m, down 20% this year.

In choroideremia Roche is developing two gene therapies: 4D-110, licensed from 4D Molecular, and RG6367, acquired along with Spark in 2019. BIIB111's failure leaves the way clear for these, now biopharma's most advanced choroideremia gene therapies; the former's phase 1 trial should read out next year, but the latter hardly appears in sellside models any more.