Evaluate Vantage

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GenVec failure highlights gene therapy risks

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The failure of GenVec's TNFerade is yet another demonstration of just how tricky the field of gene therapy is proving to be. The novel agent, one of the few remaining late stage gene therapies, now joins a growing list of clinical disappointments or failures that also recently claimed Ark Therapeutics' Cerepro.

News that the group and an independent Data Safety Monitoring Board decided that the pancreatic cancer product had failed to demonstrate clear clinical effectiveness caused shares in GenVec to plummet by 73% in early trading today to just 76 cents.

However, despite TNFerade being the group's most advanced product, accounting for almost all of its value, the very wounded GenVec may be able to limp on given the now fortuitous looking fundraising it completed in January that netted $28m. This should provide the company with a reasonable cushion out to at least 2012 if some of the $11m cash that the group reported for the end of 2009 is included. But given that the next products in the pipeline consist of two phase II treatments and five in phase I which will take several years to move through the clinic, the group looks set to spend considerable time in the investment wilderness as shareholder interest falls away.

Diminishing returns

A large axe will now have to be taken to costs to preserve the cash the group has, despite the fact that many of the earlier stage products GenVec has are subsidised by grants; the January share sale is likely to be the last fundraising the group will be able to conduct until any other product starts to show results.

The relatively robust phase III trial, which recruited 330 patients for two years, means it looks very likely that development of TNFerade in pancreatic cancer will be scrapped. Hopes had been high for the product in this particularly tricky to treat cancer indication given the positive results from the first interim look at the data last year that showed patients had a 25% reduced chance of dying when on TNFerade when compared with standard treatment at the 18-month mark. This difference, however, fell to just 8% in this second look at the trial data over the 24-month mark, making it unapprovable for a BLA.

This dwindling of efficacy was also mirrored in the survival benefit offered by the product, which uses an adenovector to carry a gene for tumour necrosis factor-alpha (TNFa) directly into tumours. As the months went on the trial showed an increasingly slender difference in survival rates for those on TNFerade and the standard of care treatment. At 12 months 39.9% of TNFerade patients were alive compared with 22.5% in the control arm. But at 24 months the survival rates in the control arm had overtaken those in the treatment arm.

Smaller field

So with this latest set back to the late-stage gene therapy pipeline, is seems likely Epeius Biotechnologies' Rexin-G will remain the sole marketed product for the time being. There is little information on this agent, which is only approved in the Philippines for the rather vague indication of 'treatment of solid tumours'.

TNFerade has also been studied in head and neck cancer and although at this point it is not clear whether the product will be scrapped in entirety, the prognosis does not look good. However, the failure in pancreatic cancer will not inspire any further confidence in a therapy area that is already dogged by not only the lack of a credible approved champion, but one that is viewed as difficult because of the high regulatory and safety hurdles placed on it by regulators, as well as the technical challenges (*Therapeutic focus - Gene therapy looking for a new hero, December 22, 2009*).

Investors have also shied away from the area due to the anticipated high cost of these drugs, that could make reimbursement a challenge. Analysts also seem reluctant to spend too much time on predicting the success of gene therapy products and as such there are still only a handful that currently have sales forecasts, despite the fact that there are over five products worldwide that have been filed and are awaiting regulatory decisions.

This rather short list includes Daiichi Sankyo and Sosei's HGF DNA Plasmid, which has been filed in Japan to treat peripheral vascular disease, and is still awaiting a decision despite submitting its application back in

March 2008. Sanofi-Aventis’ Phase III candidate, XRP0038, is another rare beast with forecasts and is expecting data by the end of the year in critical limb ischaemia.

However, while the sector desperately needs some good news, given the track record of gene therapy products and given Daiichi’s seeming hold up in trying to get its candidate past regulators it is unlikely the industry will witness an approval any time soon.