Evaluate Vantage

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Gene therapy suffers another blow as Temusi crashes out

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Gene therapy has suffered another disappointment. Temusi, the Vical candidate partnered with Sanofi-Aventis that aimed to regrow arteries in patients with critical limb ischaemia (CLI), failed to prevent amputation or death when compared to placebo over 12 months of follow-up in a phase III trial.

The likely loss of Temusi caused Vical's shares to fall 32% Wednesday to a 12-month low of $2.62, amid disappointment that the company's most advanced product, partnered with a major global company, has failed to live up to its promise. Vical will lose out on milestones and royalties on sales projected at $115m in 2016, making its loss a significant blow.

No better on amputations or death

Temusi, also known as NV1FGF, is a DNA vaccine encoded for fibrolast growth factor-1 (FGF-1), a protein thought to stimulate the growth of blood vessels. Vical’s technology constructs plasmids containing the DNA used in the therapy – in the case of Temusi, FGF-1.

The Sanofi-led pivotal Tamaris trial enrolled 525 patients who received an intramuscular injection of Temusi or placebo every two weeks over a six week period. The primary endpoints were time to amputation of the treated limb or death – 30% of CLI patients would have a limb amputated within a year and 25% die. Temusi failed to demonstrate significant improvements in either goal.

This failure follows a phase II trial in 107 people that found no statistically significant improvement in the percentage of patients with complete healing of leg ulcers when compared with placebo, its primary endpoint. It did detect significant improvement in the risk of amputations and a combined measure of amputation and death when compared to placebo. The findings were interesting enough to proceed to a phase III trial.

Citi analysts now anticipate the programme will be cancelled, although full results will be detailed at the American Heart Association meeting in November.

Blues in gene therapy

This represents a setback not only for Vical and Sanofi but also for gene therapy, a space that despite great promise has experienced little success (*Therapeutic focus - Will hopes evaporate as gene therapy pipeline flows?,August 25, 2010*). Temusi is one of six gene therapy candidates in phase III, a list that includes Allovectin-7, a cancer vaccine that is now Vical’s most valuable pipeline asset.

Vical is an important player in the space, with three of the 11 products in late and mid-stage development. It retains US marketing rights to Allovectin-7 and has partnered it with AnGes MG in Japan and key Asian countries, with Eczacibasi Ilac Pazarlama in Turkey and Northern Cyprus, and with Teva in Israel.

Analysts have enough confidence in Allovectin-7 to start forecasting sales, with Rodman & Renshaw projecting the melanoma vaccine will earn $58.9m for Vical in 2014 and Needham expects $146m by 2015. However, in the risky area of gene therapy, and with one product having already failed a late-stage trial, Allovectin-7 will now be viewed as even more high-risk.

As if to underscore the risk, AnGes last week announced it has withdrawn the other Vical-developed treatment for peripheral vascular disease, Collategene, from the Japanese approval queue, where it had been since 2008. AnGes cited the need for more data and said it is preparing a global phase III trial. The company has received a special protocol assessment for the trial and fast track designation from the FDA.

Gene therapy has delivered very little on its promise so far. As Vical is a significant player and two of its products have experienced setbacks this month, what remaining faith there is in the space must be very shaken indeed.