Evaluate Vantage

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Therapeutic focus - Will hopes evaporate as gene therapy pipeline flows?

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As faith begins to build in the area, the gene therapy community is looking forward to a rather dynamic period in the coming months. Some pivotal points are on the horizon as the first approvals are sought, key data from a number of programmes are expected, and some earlier-stage research reaches milestones.

Two candidates are vying to be the first gene therapy to receive approval in major markets, Glybera in Europe and Collategene in Japan, and the outcome of the race is anyone's guess (*EP Vantage Interview - AMT hoping to pop the cork with Glybera approval, August 25, 2010*). After the setbacks of Ark Therapeutics' Cerepro failure last year, GenVec's scrapping of phase III pancreatic trials of TNFerade in March, and with investors and analysts still not wholly convinced of the future for such therapies, some really good news is needed (*Gene therapy players sensing light at the end of the tunnel, August 25, 2010*).

Selected gene late stage gene therapy candidates						
	Product	**Company**	**Therapeutic Subcategory**	**Pharmacological Class**	**Indication Summary**	**2016 sales ($m)**
Filed	Collategene (HGF DNA Plasmid; DS-992)	Daiichi Sankyo / Vical / Sosei / AnGes MG	Cerebral & peripheral vasotherapeutics	Hepatocyte growth factor (HGF) gene therapy	Peripheral vascular disease (PVD) [Filed]; Coronary artery disease (CAD) [Phase I]	33
	Glybera	Amsterdam Molecular Therapeutics	Anti-hyperlipidaemics	Lipoprotein lipase gene therapy	Hyperlipidaemia [Filed]; Pancreatitis [Phase I]; Liver disorders [Pre-clinical]; General cardiovascular indications [Pre-clinical]	-
Phase III	Temusi	Sanofi-Aventis / Vical	Cerebral & peripheral vasotherapeutics	Fibroblast growth factor (FGF) gene therapy	Peripheral vascular disease (PVD) [Phase III]; Intermittent claudication [Phase II]	110
	Allovectin-7	AnGes MG / Teva Pharmaceutical Industries / Vical	Other cytostatics	HLA-B7 gene therapy	Melanoma [Phase III]; Head & neck cancers [Abandoned - Unclassified]	64
	Cerepro	Ark Therapeutics	Other cytostatics	HSV tk gene therapy	Glioma [Phase III]	26
	Generx	Bayer / Cardium Therapeutics	Cardiac therapy	Fibroblast growth factor (FGF) gene therapy	Angina, chronic stable [Phase III]	-
	Amolimogene	Eisai	Anti-virals	Anti-human papillomavirus (HPV) agent	Cervical dysplasia [Phase III]	-
	TNFerade	Asahi Kasei / GenVec	Other cytostatics	TNFa gene therapy	Pancreatic cancer [Phase III]; Head & neck cancers [Phase II]; Melanoma [Phase II]; Colorectal cancer [Phase II]; Soft tissue sarcoma [Phase II]; Oesophageal cancer [Phase II]	-
Phase II	Trinam	Ark Therapeutics / Crucell	Other cardiovasculars	VEGF gene therapy	General cardiovascular indications [Phase II]	118
	ProSavin	Oxford BioMedica	Anti-Parkinson's agents	Dopamine gene therapy	Parkinson's disease [Phase II]	-
	AAV-RPE65	Targeted Genetics	Eye preparations	RPE65 gene therapy	General eye disorders [Phase II]	

Vying with Vical

First, Daiichi Sankyo, Vical and AnGes are eagerly awaiting an approval decision in Japan for Collategene for peripheral vascular disease (PVD), expected during the second half of the year. Collategene is a DNA plasmid-based gene therapy encoding hepatocyte growth factor (HGF), designed to stimulate blood vessel growth to supply blood to ischemic limbs.

Vical, whose technology is licensed for use in many late-stage gene therapy products, commented recently that Japanese regulatory authorities have kept rather quiet after a phase III trial was stopped early. Analysts have speculated that an immediate but restricted launch might be expected, which has happened before when a Japanese phase III trial was cut short.

AnGes plans to start another Japanese peripheral artery disease (PAD) study if approval is granted, assuming it can securing extra funding.

Vical also expects pivotal data for Temusi (NV1FGF; XRP0038) to be presented by partner Sanofi-Aventis at the American Heart Association (AHA) conference in November in Chicago. Temusi is a gene therapy, similar to Collategene in that it is pro-angiogenic, ie. designed to promote blood vessel growth in ischemic areas, but encoding the fibroblast growth factor (FGF) gene. The agent was being studied in the Tamaris phase III trial in critical limb ischemia patients, against placebo.

Staying with Vical, which seems to have the all-encompassing position in the late-stage gene therapy world, the company hopes to report topline survival data on Allovectin-7, its gene-based immunotherapy for stage III/IV melanoma, in the first quarter of 2011. Vical bosses say that data collection for the candidate is one of the company's top priorities; 12-month follow-up study data should also be available by February, with full results by mid-year.

Waiting in the wings

Among the other candidates in phase III, amolimogene is a DNA vaccine intended as a therapeutic approach to cervical dysplasia by attacking human papilloma virus infections. Eisai acquired the vaccine with its 2008 purchase of MGI Pharma. It is undergoing a phase II/III trial in the US, which was scheduled to finish in December 2009. Eisai's most recent mention of the vaccine is in its 2010 annual report.

In the developmental ranks, Oxford BioMedica has also said that it expects all four of its ocular gene therapies to have entered clinical trials by the end of next year, with RetinoStat expected to enter the clinic by the end of 2010.

Some slim chances

Even though GenVec scrapped a phase III trial of TNFerade in locally advanced pancreatic cancer after an interim analysis demonstrated no improvement in overall survival over standard of care, it has not formally scrapped the treatment (*GenVec failure highlights gene therapy risks, March 30, 2010*). Since the announcement, the Maryland company has entered into a strategic review, and with three years' worth of cash on hand one cannot necessarily count them out, or the treatment.

Indeed, the one company making a forecast on GenVec, Roth Capital Partners, still includes a forecast of $122m in royalties in 2016 based on its potential in oesophageal and head and neck cancers.

A plethora of candidates are in phase II, too many to include in an article here. However, one candidate EvaluatePharma has highlighted as scheduled to report data in the middle of next year is Ark Therapeutics' Trinam, a treatment using the vascular endothelial growth factor gene to prevent re-blockage of blood vessels after vascular surgery.

Given Ark's treacherous financial state – the UK company had just £4.5m ($7m) in cash as of June 30 – Trinam may be its last bid for glory.