Evaluate Vantage

June 01, 2016

Therapy focus – Strimvelis approval could rejuvenate gene therapy arena

Madeleine Armstrong

Investors in gene therapy companies are no doubt hoping that European approval of GlaxoSmithKline's Strimvelis could breathe new life into the space. The field has had several scientific setbacks with failures from the likes of Celladon and Avalanche, as well as the commercial disappointment of Uniqure's Glybera.

But an analysis of the field shows that some green shoots are already evident, with a surprising number of projects in phase II and III (see table below). The next up for approval is likely Spark Therapeutics' SPK-RPE65, which the company hopes to file with the FDA by the end of the year in the genetic eye disease Leber congenital amaurosis.

If all goes well it looks set to become the first gene therapy in the US, addressing a market that could be worth over $500m according to Leerink analysts. Spark expects to file SPK-RPE65 in Europe in early 2017.

Pricey

Getting approval looks like an easier hurdle to clear than convincing healthcare systems to pay for what can be prohibitively expensive therapies – just ask Uniqure. Only one patient in Europe shelled out for Glybera, and last year the company scrapped its plans to pursue US approval (*UniQure pivots to pipeline while Glybera sputters, December 1, 2015*).

Glaxo has so far refused to disclose exactly how much Strimvelis will cost, although the UK-based company has previously said its price tag should be significantly lower than Glybera's $1m.

But Glaxo and other gene therapy developers will undoubtedly push the benefits of their products – one is that they hold the promise of a one-time treatment, which could save costs further down the line.

Strimvelis has the go-ahead for severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), also known as "bubble boy" disease because patients need to live in a sterile environment to protect them from infections. The disorder affects around 15 children per year, so is unlikely to be a big earner for Glaxo.

But this is not stopping the company from pushing on with other gene therapy candidates and it has another rare disease in its sights: Wiskott-Aldrich syndrome (WAS), which it plans to target with GSK2696275 (*ASH – Glaxo scores with second rare disease gene therapy, December 5, 2015*).

Bright Spark

Spark appears to be the most active player in late-stage gene therapy development – as well as the aforementioned SPK-RPE65 it is also has two phase II candidates: SPK-CHM in another eye disorder, choroideraemia, and SPK-FIX in haemophilia B.

The group will present data on SPK-FIX, also known as SPK-9001 and partnered with Pfizer, at the European Hematology Association meeting on June 11 – at first glance it appears to have outperformed Uniqure's haemophilia B contender AMT-060 (*EHA preview – First blood for Spark, May 20, 2016*).

Haemophilia B is an area of stiff competition for gene therapy, with four candidates in phase II that aim to enable patients to produce factor IX, the blood-clotting protein that is missing or defective in the disease.

The most advanced is Baxalta's BAX 335, which is due to start phase III this year – however, the project seems to have stagnated, perhaps as Shire's purchase of its originator goes through.

Selected gene therapies in phase II and III development				
Product	**Company**	**Indication**	**Status**	**Trial details**
Glybera	Uniqure	Familial lipoprotein lipase deficiency	Approved in EU 2012	-
Strimvelis	GlaxoSmithKline	ADA-SCID	Approved in EU; US filing expected 2017	-
SPK-RPE65	Spark Therapeutics	Leber congenital amaurosis	Filings expected 2016/17	NCT00999609
Lenti-D	Bluebird Bio	Childhood cerebral adrenoleukodystrophy	Phase III	NCT01896102
Ad-RTS-hIL-12	Ziopharm Oncology	Breast cancer, melanoma	Phase II	NCT02423902
GSK2696275	GlaxoSmithKline	Wiskott-Aldrich syndrome	Phase II	-
LentiGlobin BB305	Bluebird Bio	Beta-thalassemia, sickle cell disease	Phase II	NCT01745120; NCT02151526; NCT02140554
SPK-CHM	Spark Therapeutics	Choroideraemia	Phase II	NCT02341807
BAX 335	Baxalta	Haemophilia B	Phase II	NCT01687608
SPK-FIX/ SPK-9001	Spark Therapeutics/ Pfizer	Haemophilia B	Phase II	NCT02484092
AMT-060/ AAV5-hFIX	Uniqure/Chiesi	Haemophilia B	Phase II	NCT02396342
DTX101	Dimension Therapeutics	Haemophilia B	Phase II	NCT02618915
BMN 270	BioMarin	Haemophilia A	Phase II	NCT02576795
AAV-CNGB3	Applied Genetic Technologies	Achromatopsia	Phase II	NCT02599922
AMT-110	Uniqure	Sanfilippo syndrome	Phase II	-
CGF166	Novartis	Hearing loss	Phase II	NCT02132130

Haemophilia A is around four times more common but so far only BioMarin's BMN 270 has made it to phase II, with the company reporting preliminary data in April. Spark also has a project here, known as SPK-FVIII, but it is still at the preclinical stage.

Bluebird's wings clipped

Bluebird Bio is another hot name in gene therapy and has two products in late-stage development. Lenti-D, the most advanced, is expected to get the go-ahead in 2018 for childhood cerebral adrenoleukodystrophy.

But it is Lentiglobin, in phase II for beta-thalassaemia and sickle cell disease, which should be the bigger moneyspinner: *EvaluatePharma* sellside consensus predicts revenues of $824m by 2022.

After initial high expectations things have not gone smoothly for Bluebird, which was hammered after presenting disappointing Lentiglobin results in both sickle cell disease and the severe beta-0/beta-0 form of beta-thalassaemia at last year's ASH meeting.

New data with Lentiglobin in both indications are expected at ASH 2016. Bluebird also plans to start a potentially pivotal study, HGB-207, in non-beta-0/beta-0 transfusion-dependent thalassaemia in the second half of this year.

While Glaxo’s Strimvelis is the poster child for gene therapy for now, it should soon be joined by other new products. After several false dawns, the gene therapy resurgence might finally be back on.

To contact the writer of this story email Madeleine Armstrong in London at madeleinea@epvantage.com or follow @medtech_ma on Twitter