Evaluate Vantage

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Tiny populations up the ante for gene therapy pricing

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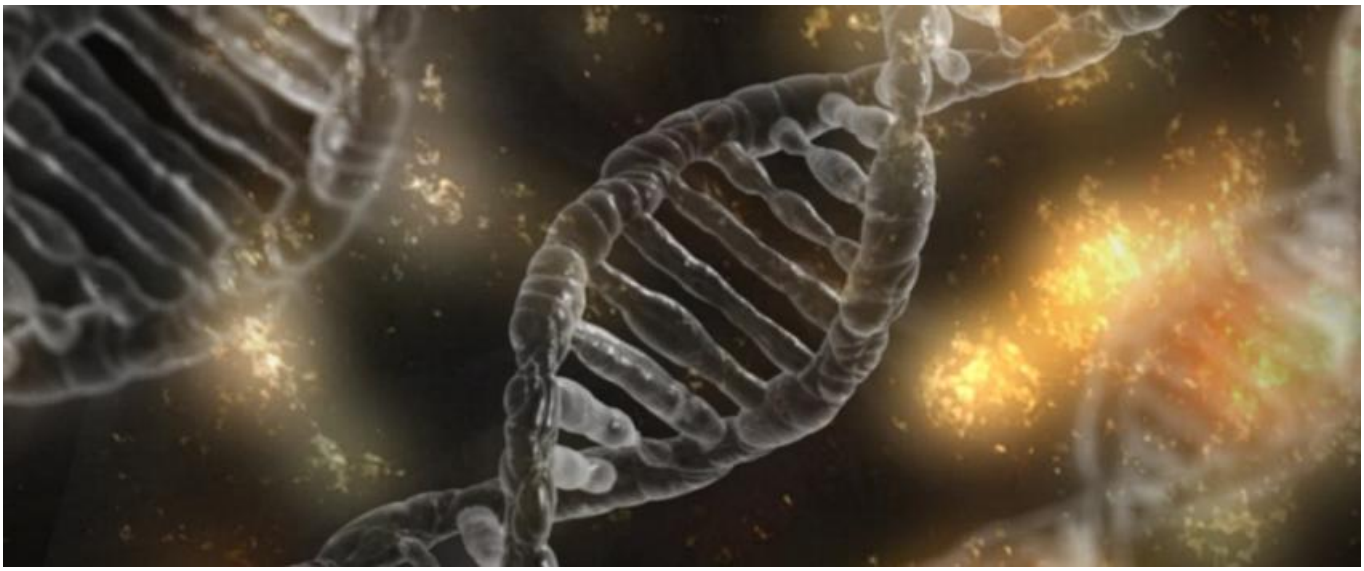

Digging into the sales forecasts for gene therapies shows just how low their penetration is expected to be. Could biopharma come to regret its high-price, low-volume strategy?

Enthusiasm for gene therapy is running high, with investors piling into companies like Sarepta, Solid Biosciences, Uniqure and Homology Medicine, which have made one-time cures central to their development strategies. Sales of these therapies are forecast to hit $14.6bn in 2024, representing 1.2% of all global pharmaceutical revenues.

This is a remarkable figure when considering that the diseases these specific therapies have been designed to treat afflict only 0.02% of the US and EU population. Diving further into the sellside figures reveals that these huge forecast numbers are based on the assumption that only a fraction of addressable patients will benefit.

Most gene therapies are expected to cost around $1m; indeed, it could be argued that a lower price might allow greater penetration than the high-price, low-volume strategy that manufacturers have chosen so far. Such a shift seems highly unlikely, however, and a look at how current sales forecasts reflect the expected uptake is illuminating.

For this analysis, Vantage looked at development-stage gene therapies forecast to be the top 10 sellers in 2024, and tried to determine how many patients could be eligible for treatment, to analyse sales and NPV per patient.

This is a simplistic approach, but the numbers can serve as signposts as to sellside expectations about utilisation. And it shows that, assuming an admittedly unrealistic 100% penetration, the *EvaluatePharma* 2024 consensus forecasts come nowhere near the $1m per patient prediction made by many observers.

Gene therapy patients and sales					
Project	**Company**	**Indication**	**Addressable patients in 2018**	**2024e sales ($m)**	**Sales/patient ($)**
Lentiglobin	Bluebird Bio	Beta-thalassaemia	16,200	528	32,592
		Sickle cell disease	11,804	1,466	124,195
AAVrh74.MHCK7.Micro-Dystrophin	Sarepta Therapeutics	Duchenne muscular dystrophy	17,503	1,659	94,783
SGT-001	Solid Biosciences	Duchenne muscular dystrophy	17,503	1,589	90,784
AVXS-101	Novartis	Spinal muscular atrophy	3,710	1,420	382,749
Valoctocogene roxaparvovec	Biomarin	Haemophilia A	29,133	1,210	41,533
AMT-061	Uniqure	Haemophilia B	11,437	770	67,325
SPK-8011	Spark Therapeutics	Haemophilia A	29,133	458	15,721
HMI-102	Homology Medicines	Phenylketonuria	35,000	362	10,343
SPK-7001	Spark Therapeutics	Choroideremia	16,810	353	20,999
ABO-102	Abeona Therapeutics	Mucopolysaccharidosis III	1,094	343	313,528

**Counts DMD and haempohilia A patients once. Source: EvaluatePharma.*

Of course, penetration of any therapy into a given disease area is never 100%. But even at 50% some of these numbers remain far from the million-dollar mark. Diving into individual sellside models shows that in some disease areas, like sickle cell and beta thalassaemia for example, analysts expect penetration in the single digits.

With as many as 60 gene therapies set for approval in the next six years companies will be walking a tightrope to try to maximise their returns while ensuring that projects are actually used in the clinic.

Gene therapy has the promise to be a life-changing technology for patients with rare diseases, but price, access and reimbursement have created a great deal of uncertainty about its ultimate commercial promise.

A $1m question

Another conundrum for gene therapy developers is the "Harvoni problem" – that is, functional cures for what once were intractable illnesses could make these treatments nearly obsolete over time.

This is apparent with Novartis's SMA treatment AVXS-101, now branded Zolgensma, for which the sellside is already forecasting a peak by 2023. Certainly, if all prevalent cases are cured a replacement rate of 400 new US patients a year would not sustain an annual sales forecast of $1.4bn.

Zolgensma is the standout on both analyses, logging per-patient sales of $383,000 and NPV of $1.8m. The treatment, which targets the survival of motor neuron 1 gene, needs to perform at least that well to justify the $8.7bn the Swiss group spent to acquire its originator, Avexis (*How many million-dollar drugs can health systems tolerate?, November 6, 2018*).

The most obvious conclusion from this analysis is that there remains much uncertainty about gene therapy, perhaps more than the sellside lets on even as it confidently attaches a $10bn combined consensus to the 10 projects listed above.

Gene therapy is in its commercial infancy, and the expected launch of Zolgensma in May should help the sector understand such matters as patient uptake and the prices insurers are willing to pay. Novartis has

suggested that a $4m-a-patient price could be justified even as it attested that it would never do such a thing.

It is clear that very few patients will be expected actually to receive a gene therapy. If those already low numbers prove too ambitious, industry could find its high-price, low-volume strategy even harder to defend.

Gene therapy value		
Project	**NPV ($m)**	**NPV/patient ($)**
Lentiglobin	6,509	232,431
AAVrh74.MHCK7.Micro-Dystrophin	1,227	70,102
SGT-001	4,296	245,443
AVXS-101	6,603	1,779,784
Valoctocogene roxaparvovec	4,310	147,942
AMT-061	1,931	168,837
SPK-8011	1,419	48,707
HMI-102	1,475	42,142
SPK-7001	831	49,434
ABO-102	116	106,032
Totals	*28,717*	*avg 289,085*

Methodology for the above analysis:

Determining the prevalence of these genetic diseases is difficult, and required subjective judgements about which patients would be eligible.

For example, with Lentiglobin Bluebird Bio is targeting a subgroup of beta-thalassaemia patients with transfusion-dependent disease, and this analysis used the patient numbers for beta-thalassaemia major, the most severe form that causes anaemia and enlarged liver and spleen, as a proxy.

In sickle cell disease our number was based on the 5.2% of patients who experience three to 10 vaso-occlusive crises per year, which fits with the clinical trial inclusion criteria of four in the previous 24 months.

For Duchenne muscular dystrophy the number was based on the normal incidence rate through age 12, at which point many patients lose the ability to walk. In haemophilia A the eligible population was based on the share considered severe, which is the patient population Biomarin is enrolling into its trials of valoctocogene roxaparvovec (valrox).