FROM PIPELINE TO PRICING & REIMBURSEMENT: ECONOMIC IMPACT AND ACCESS CHALLENGES OF UPCOMING GENE THERAPIES

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BACKGROUND/INTRODUCTION

- It is without doubt an exciting time for gene therapies. 2023 set the record for the highest annual number of gene therapies approved by the FDA and EMA and expectations for the coming years remain high.[1]
- Rare indications still dominate the pipeline, with an ever-increasing price- Lenmeldy recently launched at $4.25m in the US- posing ongoing affordability and access challenges.[2]
- However, the emergence of gene therapies targeting more prevalent conditions such as diabetes and Parkinson's disease, alongside technological advancements (e.g. gene editing and re-dosing) could shift the gene therapy reimbursement and pricing expectations.
- Despite the promise of these developments, the growing pipeline of gene therapies raises questions about long-term funding sustainability. If targeting more common diseases becomes the norm, it could exacerbate financial pressures on healthcare systems.

OBJECTIVE(S)

- The objective of this poster is to review gene therapy pipeline developments in the previous 12 months, and draw out key themes emerging, considering implication for pricing & reimbursement.

METHODS

- Cogentia analysed 126 gene therapies currently in clinical development, exploring developments & news flow in the past 12 months.
- Publicly available sources were analysed, including clinicaltrials.gov, and grey literature to establish developments in the previous 12 months.
- Each gene therapy was then categorised as follows:
  - Positive development
  - Limited/no development
  - Negative development
- Qualitative mixed methods were used to draw out key themes emerging, considering both the manufacturer and the payer perspective.
- The definition of gene therapy was limited to in-vivo or ex-vivo insertion of a gene, and did not include cell therapies, or gene editing therapies.

RESULTS

Results of the analysis are presented in Table 2 and Figure 1. Some of the key emerging themes in the gene therapy pipeline are described below:

- **De-prioritisation of products due to competitive dynamics**
  - **Case study: SPK-8016 and BAY 2599023** for haemophilia A have both been discontinued by their manufacturers (Roche and Bayer, respectively). It is likely that commercial assessments of BioMarin's Roctavian and a highly competitive landscape resulted in the conclusion that the competitive landscape in haemophilia A was no longer supportive of development
- **Targeting more prevalent indications.** Of the gene therapies included in this analysis, 22% targeted prevalent diseases (defined as >50/100,000), a 7.1% increase from our previous analysis. This is reflective of a trend in the pipeline to targeting more prevalent indications
  - **Case study: Prevail Therapeutic's PR001 for Parkinson's disease (PD) with GBA1 mutations.** PD is a prevalent disorder affecting 1-2/1000 people[3] and approximately 5% of PD patients carry a GBA1 mutation.[4] Over 20 gene therapy trials have been in PD completed so far.[5]

Table 1: Number of investigational drugs that fit into each category

Pipeline developments in past 12 months	Number (n=126)
Positive development	58
Limited/no development	42
Negative development	26

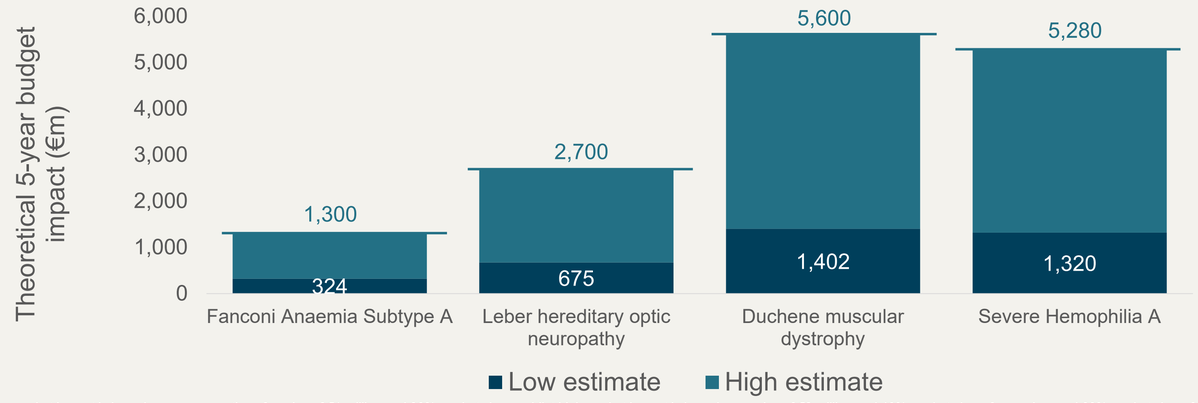
- 12/31 gene therapies at Phase 3 or 2/3 produced positive developments, potentially owing to the reduced risk as molecules progress through the clinic.

Table 2: Analysis of 5 near-term gene therapies using a framework to predict pricing & reimbursement success

Product	Disease area	Prevalence	Age in clinical trials (years)	Disease burden	Direct treatment costs	Current treatment options	Cost of comparator per patient per year*	Successful analogue
RPL102	Fanconi Anaemia Subtype A	1-5/1,000,000	3-7	Characterised by physical abnormalities, bone marrow failure, and increased risk for malignancy.	€60-€80k per year for HSCT	HSCT, androgrens	€60-€80k for HSCT	N/A
Lumevoq	Leber hereditary optic neuropathy	>10/100,000	15-17	LHON typically initiates painlessly in one eye, progressing to the second eye within a year, leading to profound visual impairment, colour vision deficits, and central scotomas.	€70-€80k with Raxone treatment + BSC vision aids	Raxone, BST	€70-€80k	Raxone has achieved mixed reimbursement in Europe
Fordadistrogene movaparvovec	Duchene muscular dystrophy	5/100,000	4-7	Rapidly progressive, lethal neuro muscular disorder. Life expectancy <30 years	Ranging from €20k-50k per year as disease progresses	Corticosteroids, Translarna, Exondys 51, Vyondys 53	€150k-300k, some patients only	Translarna has achieved mixed reimbursement in Europe
Giroctocogene fitelparvovec	Severe Hemophilia A	5/100,000	18+	Life expectancy around normal with extensive treatments	BioMarin put the cost of lifetime treatment at $25m (US costs)	Factor VIII, Hemlibra	€400k-600k	Hemlibra has achieved broad reimbursement in Europe
Isaralgagene civaparvovec	Fabry disease	1/1,000,000	16-50	Type 1 leads to excruciating pain in extremities and progressive renal insufficiency. Life expectancy 58-75 years	~€140kper year, including hospital admissions, surgery, diagnostic imaging, ERT	Fabrazyme, Galafold, Elfabrio	€100k-€200k	Galafold has achieved broad reimbursement in Europe

Ratings relate to impact on likelihood of positive P&R and commercialisation. Ratings span dark green (highly favourable) to orange (likely to prove challenging). As an example, a treatment for a disease with a reasonable prevalence, early treatment with potential to accrue a lifetime of benefits, high disease burden, large cost offsets in resource use & comparator, and a successful analogue is well set for success. BSC, best supportive care; HSCT, Haematopoietic stem cell transplant; HCP, healthcare professional; LHON, Leber's hereditary optic neuropathy.

Figure 1: Theoretical 5-year European budget impact of five gene therapies in late-stage development



Low market impact is based on an assumption of a price of €1 million and 30% market share, whilst high market impact is based on a price of €2 million and 40% market share for ex-vivo, and 60% market share for in-vivo, gene therapies. Estimates are based on the EU eligible patient population pool at 5 years post product launch. All indications shown had one-time administration gene therapies in late-stage development with expected launch date between 2024-2026. Indications were selected on the basis that they had one of more gene therapies in late-stage development with the potential to launch in the near-term defined as 2024-2026.

DISCUSSION

- Our analysis provides an in-depth review of gene therapy developments, to better contextualise the excitement growing around gene therapy as a modality, as well as a commercial assessment of close to launch indications.
- Figure 1 shows budget impact will remain a key concern for near launch gene therapies, especially those targeting more prevalent indications.

CONCLUSIONS

- There have been significant developments in the gene therapy pipeline in the previous 12 months. By analysing the news flow & clinicaltrials.gov, this poster presents a mixed picture, with roughly as many positive as negative updates
- Negative updates included 12 projects that were discontinued not due to their clinical profile, but instead due to re-prioritisation of funding following acquisitions by big pharma as commercial opportunities are re-assessed as well as manufacturing challenges and biotech liquidations.
- Key themes include a shift towards targeting more prevalent indications, a desire for improved safety and administration regimes, and the de-prioritisation of assets due to competitive dynamics. Analysis of five near-term gene therapies supports the hypothesis that budget impact issues will continue to be of concern to payers, which in turn may support restricted recommendations.
- It is our view that beyond the clinical profile, challenges faced by gene therapies can often be anticipated with prior planning, and an early market access strategy is critical to avoid withdrawal, either in late-stage trials or after reaching the market.

1. https://www.pharmaceutical-technology.com/features/whats-next-for-aav-gene-therapies-in-2024/
2. https://www.bloomberg.com/news/articles/2024-03-20/world-s-most-expensive-drug-is-now-4-25-million-gene-therapy
3. Epidemiology of Parkinson's disease – PubMed
4. https://www.ncbi.nlm.nih.gov/books/NBK536716/#:~:text=Mutation%20in%20the%20GBA1%20gene,1%25%20of%20the%20healthy%20population.
5. https://www.clinicaltrials.gov/search?cond=Parkinsons%20Disease&term=Gene%20therapy&aggFilters=status:com%20act