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ANALYSIS OF THE THERAPY AREAS TARGETED BY GENE THERAPY MANUFACTURERS IN CLINICAL TRIALS

Mark Orchard[1], David Alderson[1]

[1]Cogentia Healthcare Consulting, Cambridge, United Kingdom

Contact the authors via cogentia.co.uk/contact

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BACKGROUND/INTRODUCTION

- In the last 25 years, the composition of top five therapy areas has changed dramatically (1)
  - Top five therapy areas in 1995 were cardiovascular, anti-ulcerants, mental health and cholesterol, representing 53% of the spending, and decreasing to 6% in 2020
  - Top five therapy area in 2020 are Oncology, Immunology, anti-diabetics, anti-coagulants and HIV anti-virals representing 62% of the spending, and growing from 11% in 1995
- The first approval of a gene therapy was in 2012 in Europe and 2018 in the US, with Glybera and Luxturna, respectively, achieving that landmark (2,3)
- There are signs that the rate of gene therapy approvals is set to accelerate, and in fact the FDA predicts that by 2025 they will be approving 10–20 cell and gene therapies a year, with them consequently hiring an additional 50 clinical trial reviewers in preparation (4,5)
- The evaluation of the sustainability of the gene therapy pipeline should include the market potential (size, competition, and so on) for each disease and the evolution of the gene-therapy market dynamics

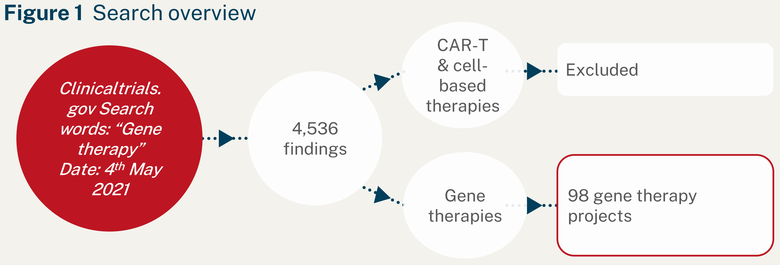
OBJECTIVE

- To analyse the therapy areas being targeted with gene therapies and consider whether this focus is sustainable

METHODS

- Search for 'gene therapy' in clinical development Phase I–III clinical trials on ClinicalTrials.gov on 04 May 2021
- This study considered gene therapy specifically, and so CAR-T and other cell-based therapies were not included
- The diseases being targeted were then categorised into their respective therapy areas
- Analysis of the therapy areas was undertaken to assess for trends. We also considered sustainability by looking at density of competition

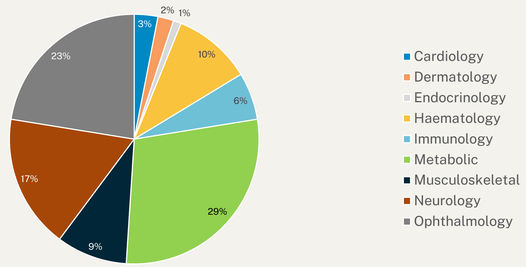
Figure 1 Search overview



RESULTS

- The 98 gene therapy projects in clinical trials, targets 59 diseases. The most commonly targeted therapy areas were in order: metabolic disorders (29%), ophthalmology (22%), and neurology (17%) (**Figure 2**)
- Lysosomal storage disorders in particular were found to be a common target for gene therapy manufacturers (>12 projects)

Figure 2 Distribution of gene therapy projects undergoing clinical trials by therapy area



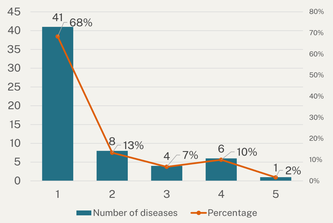
- The specific disease areas that appear most frequently in the gene therapy pipeline included retinitis pigmentosa, Duchenne muscular dystrophy, and haemophilia A

Table 1 Type of diseases targeted by the ongoing gene-therapy projects in clinical trials

Type of disease	#	%
Prevalent disease	10	17%
Rare disease	16	27%
Ultra-rare disease	33	56%

Definitions: prevalence ultra-rare < 1 in 50,000 people; prevalence rare disease: >1 in 50,000 and < 5 in 10,000 people; prevalence prevalent disease > 5 in 10,000 people.

Figure 3 Number of disease with competing gene therapy projects



- Most diseases targeted by gene therapy projects are ultra-rare (56%) and rare (27%), with only 17% being a prevalent disease (**Table 1**)
- 11 diseases (19%) present three or more competing project in clinical trials. (**Figure 3**). All of them are presented in **Table 2**
- 73% of the highly competed diseases correspond to rare diseases, where the largest prevalence correspond to 1 to 5 patients every 10,000 population for Fabry Disease (**Table 2**)
- Two ultra-rare diseases, GM1 Gangliosidosis and Choroideremia, have three competing assets in clinical trials (**Table 2**)

Table 2 Diseases with more than three gene therapy projects

Therapy Area	Disease	# Assets	Prevalence	Type of disease
Haematology	Haemophilia A	5	1 in 5,000 to 1 in 10,000 males	rare disease
Metabolic	Fabry disease	4	1 to 5 in 10,000	rare disease
Neurology	Parkinson's disease	4	1 in 350 people	prevalent
Ophthalmology	Achromatopsia	4	1 in 30,000 people	rare disease
Ophthalmology	Retinitis Pigmentosa	4	1 in 3,500 to 4,000 people	rare disease
Ophthalmology	X-linked retinitis pigmentosa	4	1 in 26,200 males and 1 in 18,000 of females	rare disease
Musculoskeletal	Duchenne muscular dystrophy	4	1 in 3,500 male births	rare disease
Haematology	Haemophilia B	3	1 in 35,000 to 1 in 50,000	rare disease
Metabolic	GM1 gangliosidosis	3	1 in 100,000 to 200,000 new-borns	ultra-rare disease
Metabolic	Pompe Disease	3	1 in 40,000 people	rare disease
Ophthalmology	Choroideremia	3	1 in 50,000 to 100,000 people	ultra-rare disease

Definitions: prevalence ultra-rare < 1 in 50,000 people; prevalence rare disease: >1 in 50,000 and < 5 in 10,000 people; prevalence prevalent disease > 5 in 10,000 people.

DISCUSSION

- Gene therapy projects target a wide range of disease prevalence, biggest proportion of ultra-rare diseases, but also a small fraction of prevalent ones with a high number of potential patients
- Ultra-rare diseases from a Payer perspective have a small budget impact; and from a manufacturing perspective represent a challenge to secure the return on investment. Particularly in highly competitive diseases like GM1 Gangliosidosis and Chroideremia
- Prevalent diseases are attractive to manufacturers due to the revenue potential; but for Payers they result in high budget impact, so it will be relevant to understand how uncertainty factors into the price
- Rare diseases sit in the middle between manufacturers and Payers interests, potentially explaining the fact that 50% (8 out of 16) of them are in the highly competitive disease group

CONCLUSIONS

- There are many projects in the clinic for gene therapy, with a wide range of disease prevalence. It is wrong to assume that gene therapies are just for ultra-rare diseases
- The most common therapy areas are Metabolic disease, Ophthalmology and Neurology, including diseases like: Fabry disease, Parkinson's disease, and Retinitis Pigmentosa
- Further research is needed to understand the elements to build an investment rationale in gene therapy. Some of them might be prevalence of the disease and how this affects budget impact, competition and patient commercial availability particularly in ultra-rare diseases

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