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ANALYSIS OF THE PREVALENCE OF DISEASE AREAS IN THE GENE THERAPY PIPELINE: FROM ULTRA-RARE TO PREVALENT

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INTRODUCTION

- The volume of gene therapies in development has risen sharply over the last decade with the FDA anticipating that 10–20 cell and gene therapies will be approved per year by 2025[1,2]
- The high price of gene therapies is based on anticipated long-term benefits, benefits which at launch are often subject to significant uncertainty
- Prevalence is a major driver of budget impact
- High prevalence targets for upcoming gene therapy drugs could therefore lead to high budget impact scenarios – leading to challenges around sustainability and affordability
- Similarly ultra-low prevalence diseases may be so rare as to fail to provide a viable market for the drug, leaving manufacturers without a payoff for their investment

OBJECTIVE

- To examine the prevalence of the diseases targeted by gene therapies currently in the development pipeline
- To draw conclusions regarding the rationale for their selection and speculate on possible outcomes and downstream impacts

METHODS

Figure 1 Methods overview

98 gene therapies (targeting 62 unique diseases) in development were extracted from clinicaltrials.gov (Phase I – III)

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10 intentionally diverse popular gene therapy disease areas selected

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Prevalence of target diseases identified via Orphanet and therapies grouped by disease prevalence

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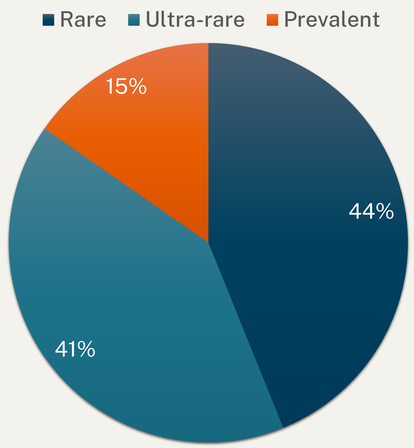
Ultra-rare[1] (<2/100,000) | Rare (≤50[2] ≥2/100,000) | Prevalent[3] (>50/100,000)

RESULTS

Figure 2 Percentages of gene therapy assets in development targeting rare, ultra-rare and prevalent diseases



Percentages relate to the prevalence of diseases targeted by gene therapy manufacturers. Prevalent diseases are significantly less popular than rare and ultra-rare targets

- Of the 98 gene therapy assets analysed, 44% targeted rare diseases (**Figure 2**)
- 41% of disease areas were classed as ultra-rare, whilst 15% were classed as prevalent conditions
- The prevalent conditions almost exclusively fell under the therapy areas of neurology and ophthalmology (**Table 1**), with therapies targeting Parkinson's disease and AMD accounting for over half of the prevalent category (data not shown)
- Ultra-rare conditions were most typically metabolic or neurological, with a number of the lysosomal storage disorders fitting into this category

Table 1 Pivot table showing prevalence breakdown for each disease area

THERAPY AREA	PREVALENT	RARE	ULTRA-RARE	TOTAL
Cardiology	3	0	0	3
Dermatology	0	0	2	2
Endocrinology	0	1	0	1
Haematology	0	8	2	10
Immunology	0	1	5	6
Metabolic	0	11	17	28
Musculoskeletal	1	4	4	9
Neurology	7	2	8	17
Ophthalmology	4	16	2	22
TOTAL	**15**	**43**	**40**	**98**

DISCUSSION

- Despite the challenges of launching a high-cost gene therapy to either significant or very small patient populations, 56% of therapies fall into prevalent or ultra-rare categories
- Identifying and treating sufficient patients to deliver commercially viable returns is challenging in ultra-rare indications. This is demonstrated by uniQure's Glybera which was withdrawn from the European market in 2017 due to limited usage[6]
- Conversely, the prohibitively high budget impact of gene therapies in more prevalent indications such as Parkinson's may make such gene therapies unaffordable for payers, perhaps forcing manufacturers to compromise heavily on price
- Commercial rationale for the high number of rare targets may be due to the favourable balance between budget impact and customer base
- Other factors including scientific rationale and clinical need play a major role in selection of disease targets and the composition of the gene therapy pipeline
- Pricing and budget impact issues need to be addressed to ensure a sustainable solution given the relatively high number of prevalent disease targets in the current pipeline

CONCLUSIONS

- Rare diseases are targeted by nearly half of the current gene therapy assets in development
- Rare diseases are an attractive compromise of a small but viable population size which avoids an overly large budget impact for payers while allowing manufacturers a competitive price
- Previous examples demonstrate the challenges of launching in ultra-rare diseases where low patient numbers can be prohibitive
- Solutions are required to balance reasonable returns on investment with affordability of innovative treatments for payers
- When pooled together, the high number of gene therapies in development represent a future challenge for the market

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