

Considerations for a pathway to commercializing gene therapies for ultra-rare diseases

Part 1

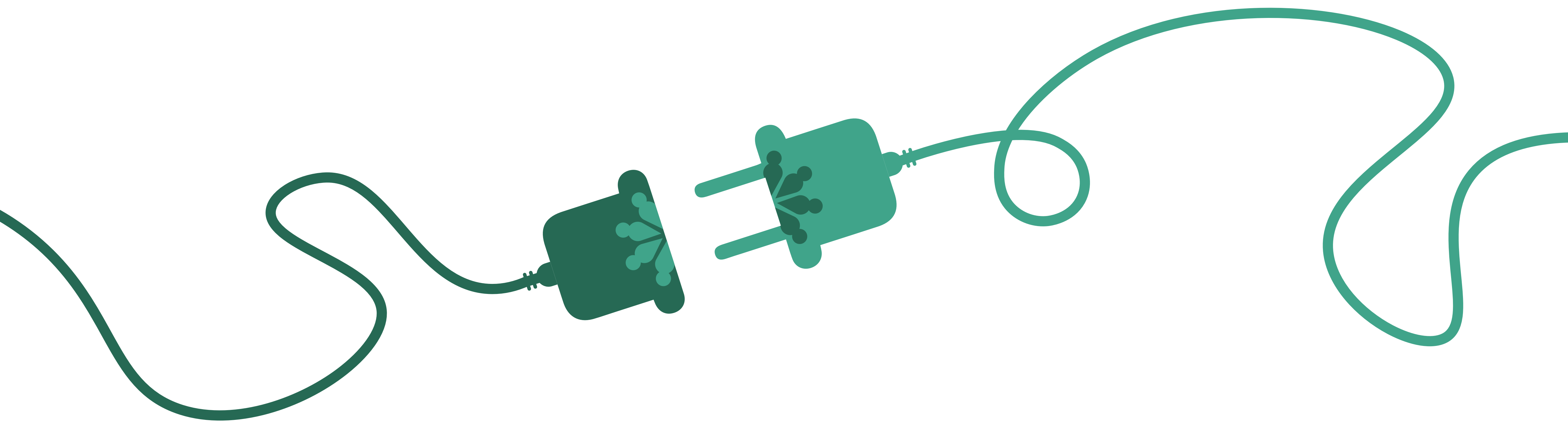
2025



THINK GLOBAL

Over 8000 genetic rare diseases have been identified globally, yet the current therapeutic landscape indicates that **only 5%** of these conditions currently have FDA-approved treatments^[1].





Over the last decade, many small biotech companies began developing new gene therapy-based treatments for ultra-rare diseases.

However, bringing these treatments to patients has been a significant challenge due to:

1

The high pre-clinical and clinical development costs

2

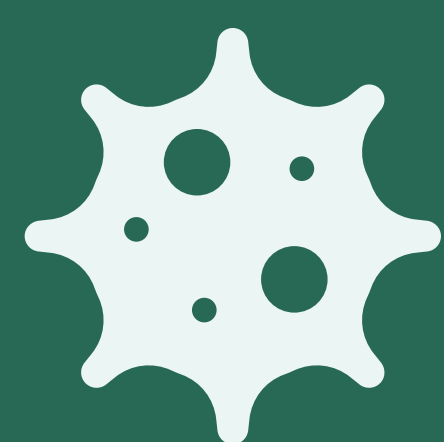
An inherent restriction to a single indication

3

Limited opportunity for label expansion post-commercialization

These confounding factors coalesce into negative net present value calculations that discourage many companies from continuing ultra-rare disease programs.

Between 2021 and 2023, **over fifty** rare disease programs were either shelved or abandoned altogether^[2].



8000

Genetic rare diseases have been identified globally



95%

Of genetic rare diseases currently have no FDA-approved treatments



>50

Rare disease programs shelved or abandoned between 2021-2023

**Where does this
leave the remaining
ultra-rare disease
programs?**



CLIMBING OUT OF THE “VALLEY OF DEATH”

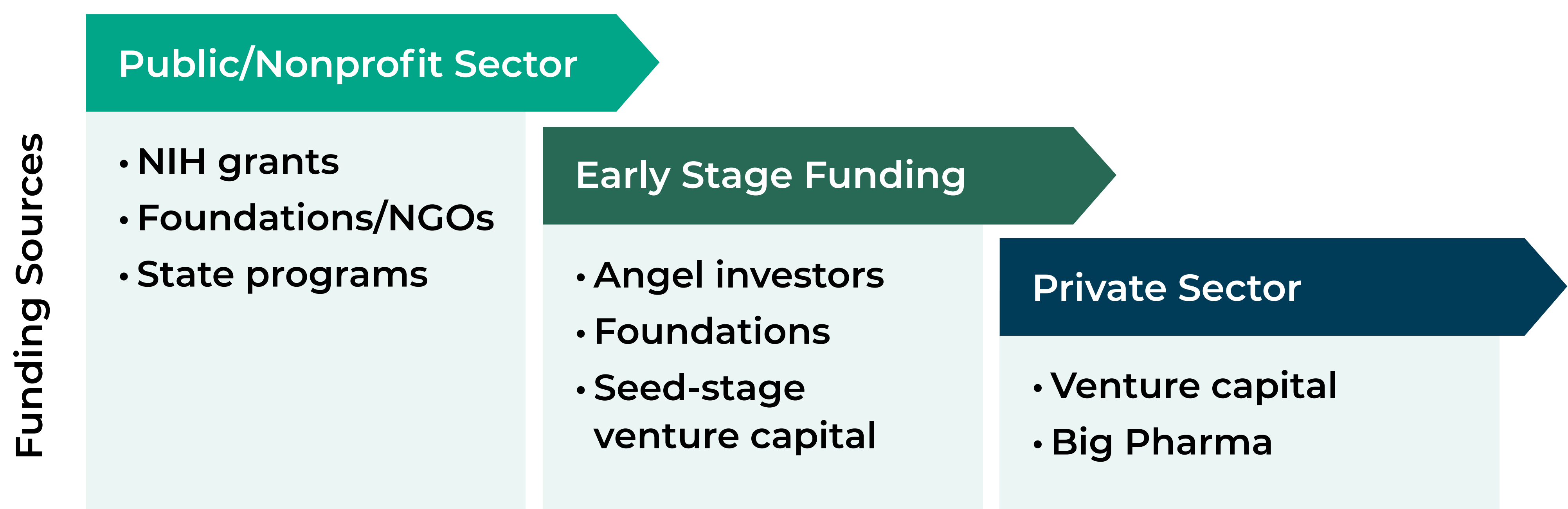
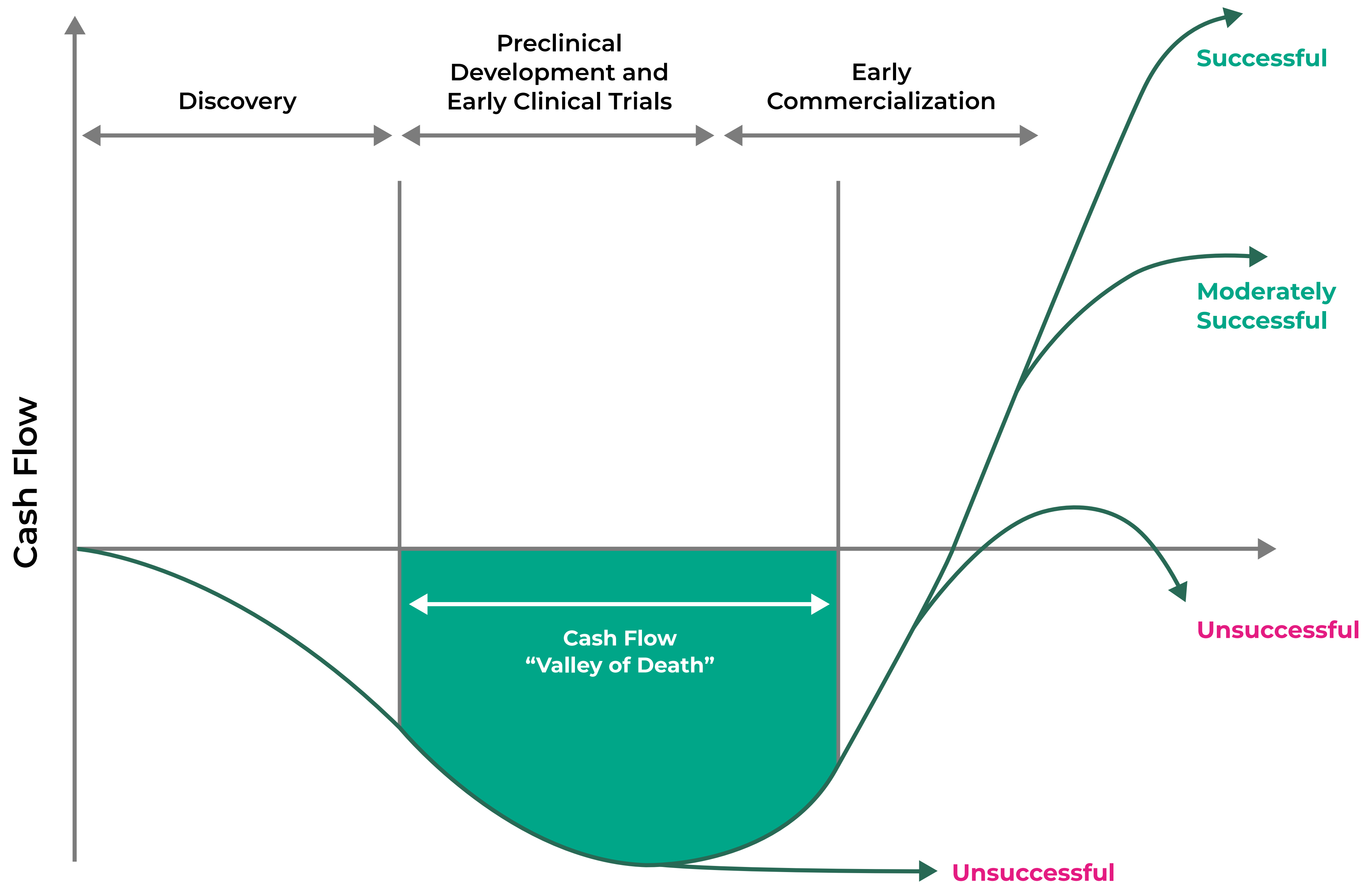
First, let’s acknowledge **the problem.**

The funds required to bring ultra-rare therapies through development phase are being allocated elsewhere.



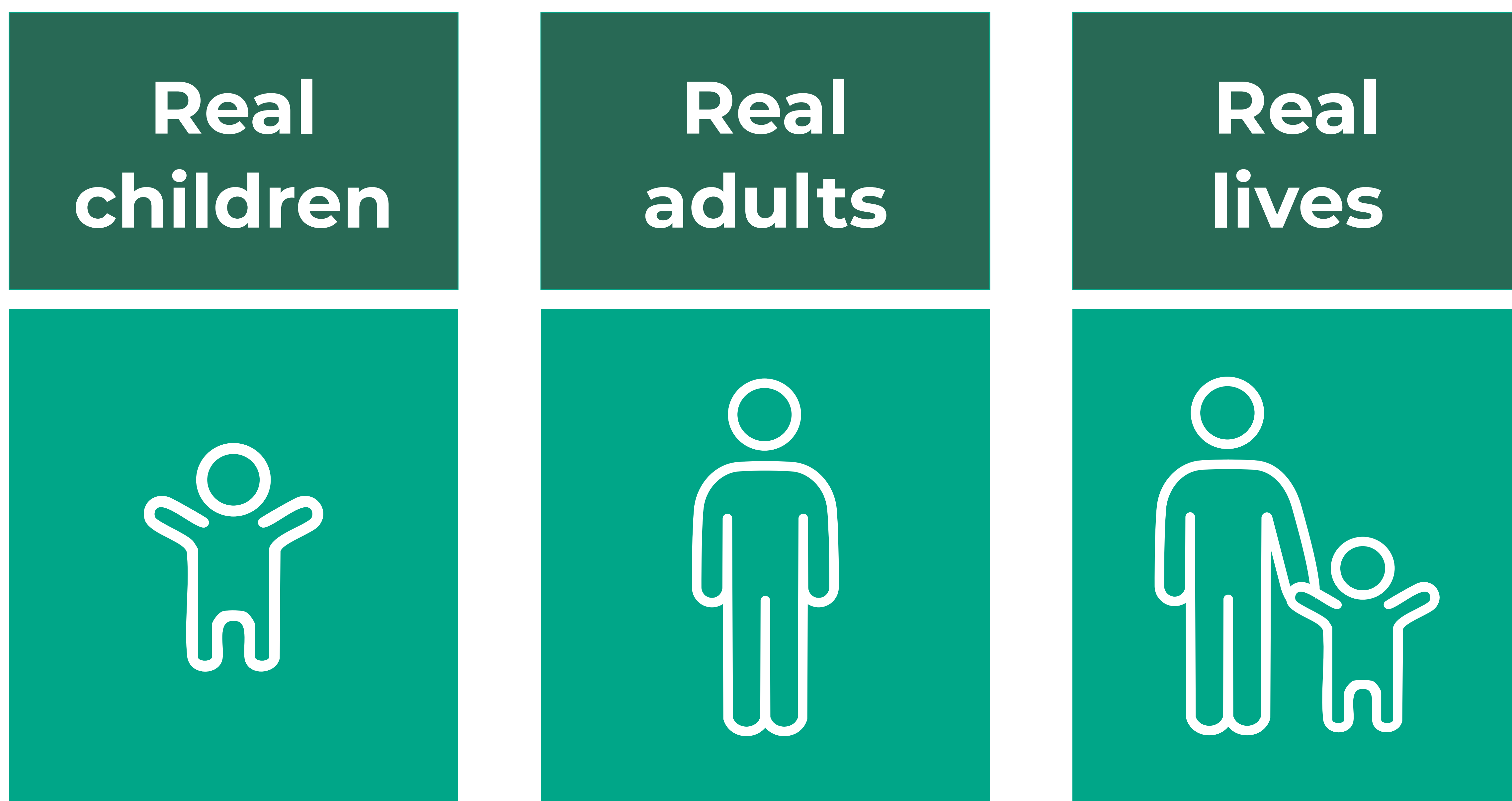
This leads to the so-called cash flow **“Valley of Death”** in the development of ultra-rare disease gene therapies.

“VALLEY OF DEATH” FOR ULTRA RARE DISEASE GENE THERAPY COMMERCIALIZATION^[3]



⚠ Traditional investment sources for gene therapy development and commercialization, such as Big Pharma and venture capital, are no longer as willing to fund these programs as they have in past years.

Patient groups, academia, and foundations can only do so much to fill the valley.



Yet, millions of real lives remain at stake with **little to no** treatment alternatives.

**So where does
this leave us?**



**At TKD Solutions,
we believe that
a multifaceted
approach will be
required to climb
out of this valley.**



IN RESPONSE

We will be writing a series of reports that bring forth opportunities for true collaboration across **development, supply chain, CMC, and regulatory pathways** to develop risk-appropriate solutions that will rein in costs, reduce development timelines, and establish more robust platform approaches that are specifically designed for ultra-rare disease programs.

^[1] Berry, Diane et al, Ensuring patient access to gene therapies for rare diseases: Navigating reimbursement and coverage challenges, Molecular Therapy Methods & Clinical Development, Volume 33, Issue 1, 101403

^[2] Yingling N, Sena-Esteves M, Gray-Edwards HL. A Paradox of the Field's Own Success: Unintended Challenges in Bringing Cutting-Edge Science from the Bench to the Market. Hum Gene Ther. 2024 Feb;35(3-4):83-88. doi: 10.1089/hum.2023.29264.nyi. PMID: 38381466.

^[3] Steinmetz, Karen & Edward, Spack. (2009). The basics of preclinical drug development for neurodegenerative disease indications. BMC neurology. 9 Suppl 1. S2. 10.1186/1471-2377-9-S1-S2.



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