OliverWyman

UNLEASHING SUCCESS

Closing the commercial viability gap in cell and gene therapy

INTRODUCTION

Cell and gene therapies (CGTs) have the potential to revolutionize the treatment landscape and even cure previously incurable diseases. Optimism surrounding these innovative therapies is propelling a 46% compound annual growth rate over the next five years, bringing total the global market size to nearly $37 billion.[1]

Yet given the high cost of the drugs, combined with smaller population sizes, early innovators still face significant issues securing reimbursement from payers which limits their ability to recoup investments. Ongoing funding challenges for health systems around the globe could further tighten reimbursement and add pressure to lower prices.

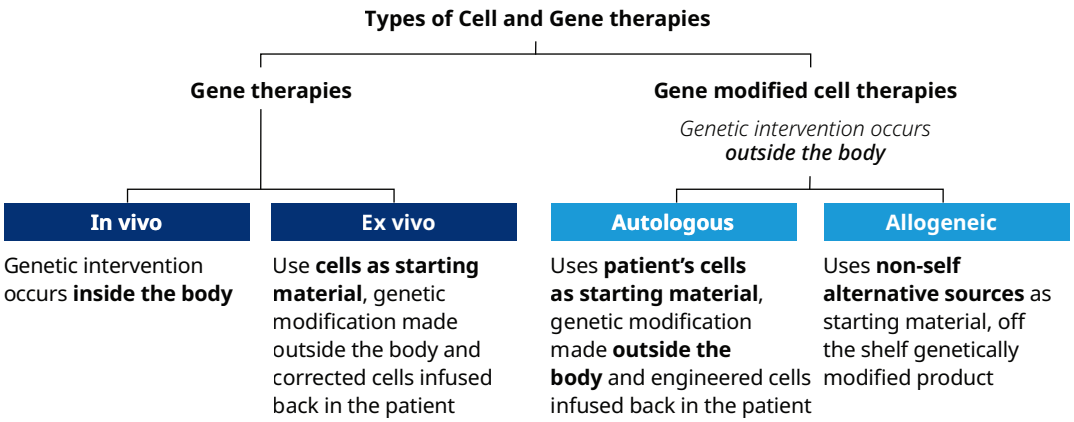
At the same time, manufacturing and quality processes remain immature and non-standardized with low automation and high material cost, resulting in margin levels that test the commercial viability of the new product classes — both in cell and gene therapies.

Closing the commercial viability gap will be a key priority to successfully give large patient populations access to the great potential these therapies can bring. This report details steps organizations can take to make greater progress on pricing and bring the cost of goods down to viable levels.

FROM SCIENCE FICTION TO BLOCKBUSTER DRUGS

Cell and gene therapy refers to the introduction, removal, or change in the content of a person's genetic code to treat or cure a disease. This is achieved by either directly injecting genetic material into their bodies or using modified cells and (re)inserting those as the therapy (Exhibit 1). What was once an unimaginable leap in science has now become a reality for many patients.

Exhibit 1: Cell and Gene therapy taxonomy

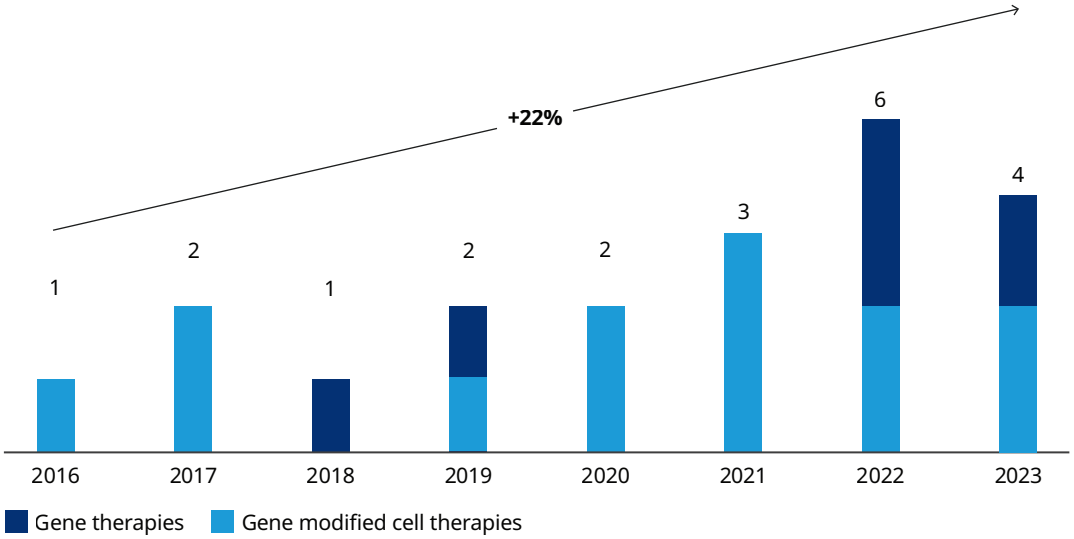


Source: Oliver Wyman analysis

1 EvaluatePharma

Cell and gene therapies started getting regulatory approval in the mid-2010s. Since then, the number of annual approvals has been mounting, reaching 21 total approvals in the US and Europe as of early April 2024. Not only has the volume of therapies increased, but there have been many technological advancements within the therapies such as the approval of Casgevy in December 2023 which is the first therapy approved using CRISPR gene editing (Exhibit 2).

Exhibit 2: Count of CGT approvals in Europe or the US per year and recent approval highlights

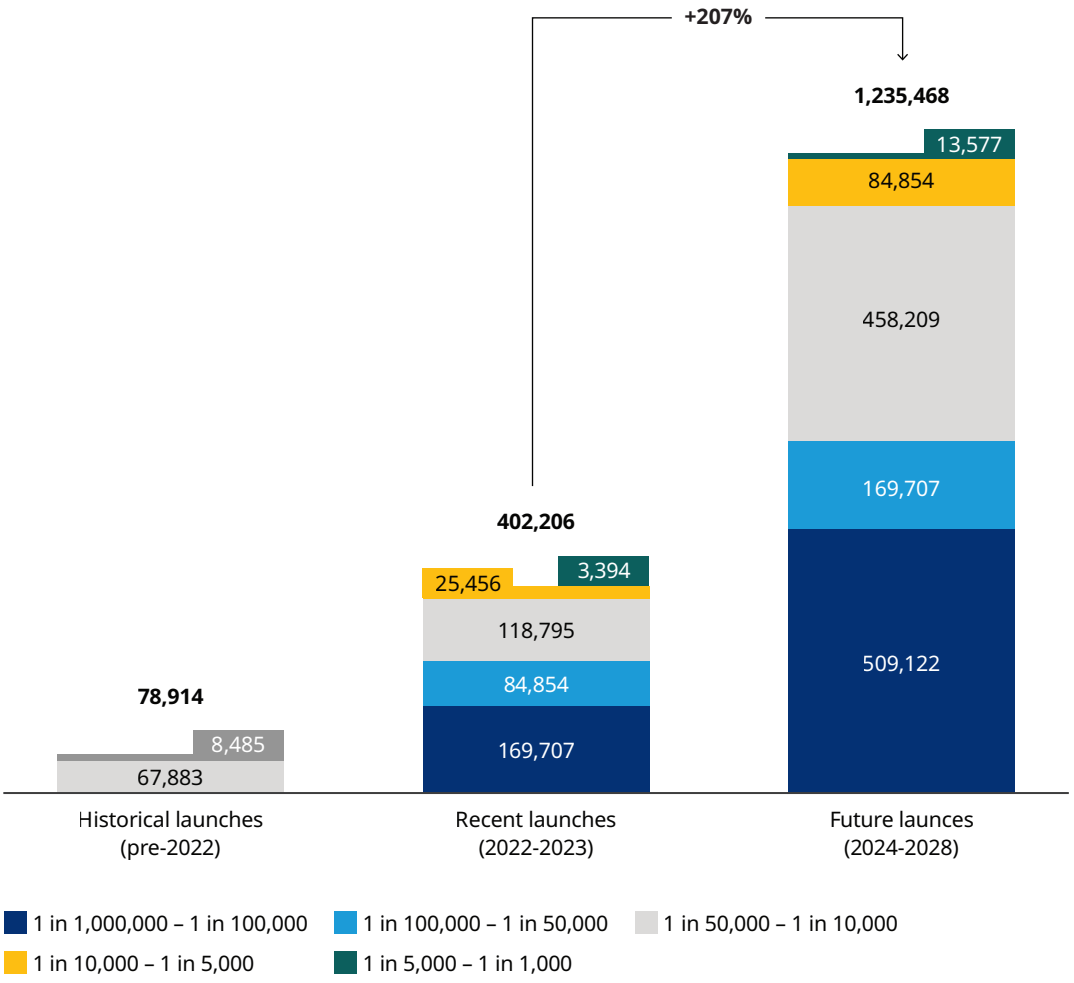


Approval Date		Therapy	Manufacturer	Recent approval breakthroughs
2023	December	Casgevy	Vertex	First ever **CRISPR/Cas9 based** gene editing therapy approved indicated for sickle cell disease and transfusion-dependent beta thalassemia
	June	Elevidys	Sarepta	First adenoviral vector-based gene therapy approved **for Duchenne muscular dystrophy**
	May	Vyjuvek	Krystal	First **Multidose & topical gene therapy** — delivers COL7A1 gene via modified HSV to treat dystrophic epidermolysis bullosa
2022	December	Ebvallo	Atara Bio	First **allogenic T-cell immunotherapy** approved — indicated for Epstein-Barr virus positive post-transplant lymphoproliferative disease
		Adstiladrin	Ferring pharmaceuticals	First adenoviral vector-based gene therapy approved for **solid tumours-** indicated for BCG unresponsive non-muscle invasive bladder cancer

Source: Oliver Wyman analysis

To date, two CGTs which have reached blockbuster status, Zolgensma and Yescarta. This will likely increase to six by 2028. Taking late-stage pipeline candidates into account, the potential addressable patient population magnitude is forecasted to increase by more than 207% by 2028. This is driven by both a larger volume of CGTs entering the market and expansion into such larger indications as systemic lupus erythematosus (Exhibit 3). As a result, CGTs are becoming a common therapeutic class with applications across millions of patients globally, expanding beyond the traditional utilization for ultra rare diseases.

Exhibit 3: Cumulative total addressable patient population based on approved/ pipeline therapies in the US and EU. Magnitude of total addressable patient population categorized by therapy indication incidence rane



Source: Evaluate Pharma, Oliver Wyman Analysis

Still, the commercial viability of CGTs remains uncertain. Securing reimbursement and improving operating margins are both looming challenges ahead for sustaining the future of CGT's commercial success.

SECURING CGT REIMBURSEMENT

Despite the scientific success and advancements, most CGTs have fallen behind analysts' revenue forecasts. Reasons for the shortcomings include:

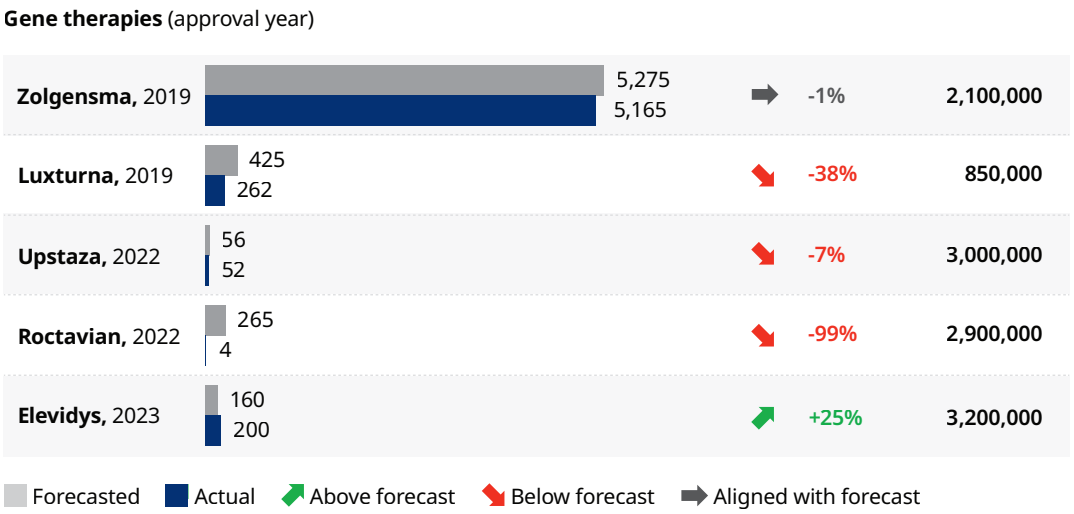
1. **Approval delays:** For example, Roctavian was initially rejected in 2020; the Food and Drug Administration then added a three month delay in 2023 to review additional data before granting final approval in June of that
2. **Supply constraints:** Yescarta and Kymriah and other CAR-T therapies, for instance, have been thwarted by supply chain and manufacturing challenges
3. **Reimbursement:** Unfavorable reimbursement forced Bluebirdbio to pull Zynteglo out of the EU and consequently suspension of all European operations and withdrawal of their initial CGT product, Skysona, as well

The most striking shortcoming came this February when BioMarin announced its 2023 revenues for Roctavian at $3.5 million, far below their internal target of $50 million-$150 million for 2023 (Exhibit 4).

Exhibit 4: Worldwide cumulative actual vs analyst forecasted sales at time of regulatory approval ($ million, launch date to 2023) and average US list prices

Launch date to 2023[1], worldwide sales, in $ million

Cell therapies (approval year)		Forecast vs. actuals	List price
Yescarta, 2017	4,206 / 3,145	-25%	373,000
Kymriah, 2017	2,541 / 1,975	-22%	475,000
Abecma, 2021	775 / 1,024	+32%	420,000
Tecartus, 2020	700 / 889	+27%	373,000
Carvykti, 2022	496 / 603	+22%	465,000

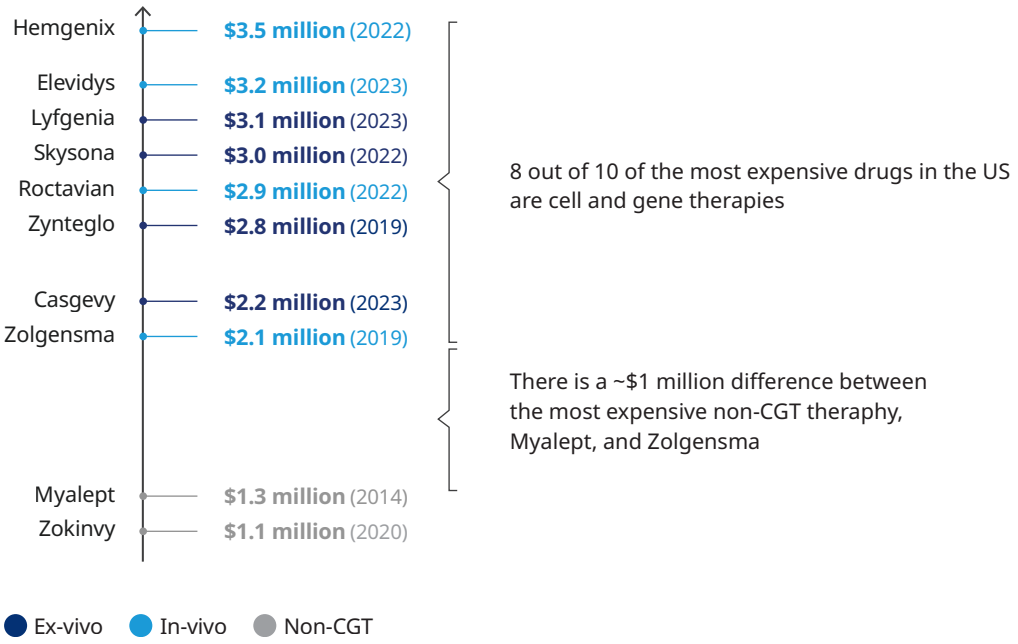


1. 2022 for Kymriah and Yescarta; due to earlier launches forecasts only available until 2022 at time of launch. Luxturna and Upstaza actual sales includes 2023 estimate due to lack of actual data.

Source: Evaluate Pharma, Oliver Wyman Analysis

Beyond the extenuating circumstances mentioned above, price remains the one universal challenge impeding the widescale adoption of CGTs. It seems every year, a new CGT hits the most expensive drug record (Exhibit 5). The skyrocketing prices of CGTs, which accrue at once due to the one-off nature of CGTs, place immense pressure on payers making reimbursement securement challenging. As CGTs move into the mainstream treatment landscape, the need to commercialize via a sustainable model will be necessary.

Exhibit 5: Top 10 most expensive drugs in the US, list price (approval year)[1]



1. Based on yearly per patient cost.

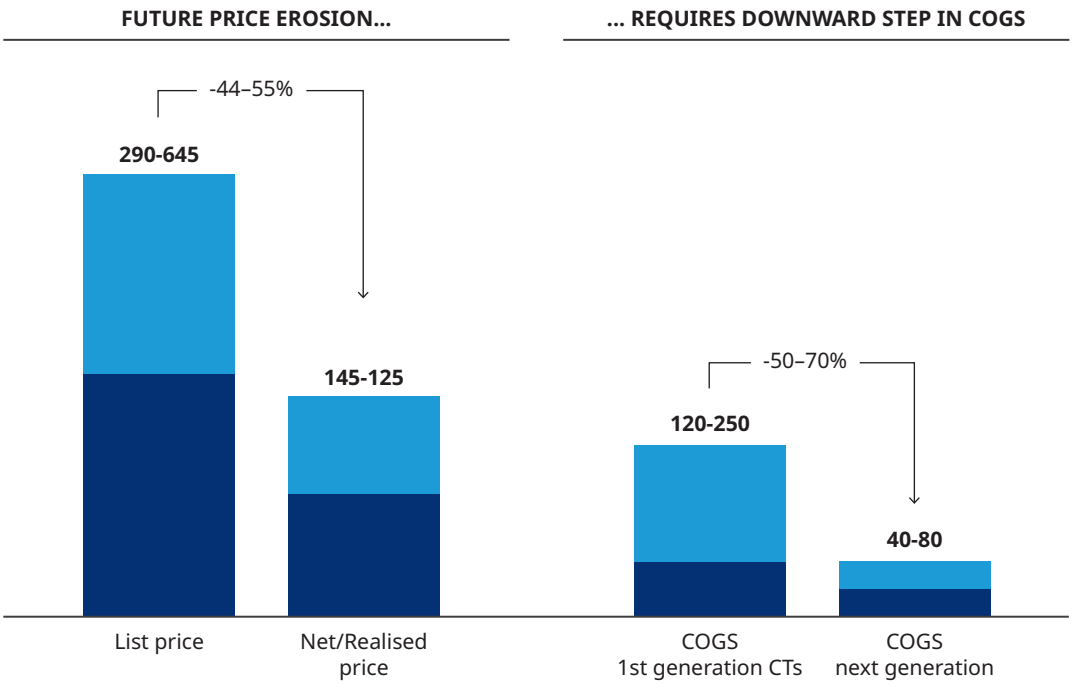
Source: Oliver Wyman Analysis

Outcome-based agreements (OBAs) have been explored as a potential vehicle to secure CGT reimbursement while providing affordability relief to payers. However, the OBA landscape remains patchy with agreements being reached at individual product-country levels but have not yet achieved coverage on a widescale basis. Furthermore, there have been stark discrepancies across countries' readiness and willingness to adopt OBAs. European countries, particularly Italy, have been early adopters of OBAs even outside of CGTs. Change may be coming in the US in 2025 when the Centers for Medicare and Medicaid Services launches a pilot program testing a new access model for sickle cell disease under Medicaid. More than 100,000 people in the US, most of whom are Black, have the genetic disorder. CMS will support states in negotiating and executing OBAs. Fostering collaboration across stakeholders, including setting up the necessary infrastructure to enable OBA like patient data registries will be the key to reliably securing CGT reimbursement in the future.

IMPROVING OPERATING MODELS

Another barrier to CGTs achieving sustainable commercial success is the slim operating margins. Cell therapy commercial viability largely depends on reducing manufacturing costs through COGS optimization. For instance, autologous CAR-Ts have dominated the gene modified cell therapy market but unless the costs are reduced by at least 50%, therapies are unlikely to be commercially viable and their growth potential will be limited [Exhibit 6]. Allogeneic cell therapies have been explored as a more cost-efficient off-the-shelf alternative. Nonetheless, allogenic therapies are not truly scalable either and only represent about 25% of gene modified cell therapies in the pipeline. Therefore, autologous cell therapies are here to stay and the need for improved manufacturing via personnel, capital and material cost optimization throughout the value chain cannot be ignored.

Exhibit 6: Autologous CAR-T price erosion and future required reduction in COGS
Cell therapy commercial viability cliff — Autologous CAR-Ts, in thousands, $



Source: Oliver Wyman benchmarking

In contrast, the main challenge facing gene therapies is recuperating large R&D capital expenditures from small patient populations. Gene therapies are highly complex with long lead times rendering them expensive investments. Meanwhile, gene therapies are typically indicated for rare diseases, meaning patient populations are small and often hard to identify. Furthermore, given the curative nature of gene therapies, the total addressable patient population declines with every patient treated. Manufacturers therefore are at an increased risk of not making a return on their investments. The most predominant bottleneck in improving development cost effectiveness lies in improving viral vector manufacturing techniques.

The scientific and clinical progress of CGTs has accelerated tremendously in the last decade, however manufacturing technologies need to advance at an equal, if not quicker, pace and to avoid falling short of commercial success.

Oliver Wyman is a global leader in management consulting. With offices in more than 70 cities across 30 countries, Oliver Wyman combines deep industry knowledge with specialized expertise in strategy, operations, risk management, and organization transformation. The firm has 7,000 professionals around the world who work with clients to optimize their business, improve their operations and risk profile, and accelerate their organizational performance to seize the most attractive opportunities.

For more information, please contact the marketing department by phone at one of the following locations:

Americas	Europe	Asia Pacific	India, Middle East & Africa
+1 212 541 8100	+44 20 7333 8333	+65 6510 9700	+971 (0) 4 425 7000

AUTHORS

Marie-Lyn Horlacher
Partner
marielyn.horlacher@oliverwyman.com

Oliver Eitelwein
Partner
oliver.eitelwein@oliverwyman.com

Laura Jochem
Engagement Manager
laura.jochem@oliverwyman.com

Allegra Hohn Honari
Associate
allegra.hohnhonari@oliverwyman.com