



▶ Pharma's Transformation towards Next-Generation Therapeutics

How to overcome novel challenges by reshaping
operating models



INSIGHTS

//01

Next-generation therapeutics (NGT) hold the promise of treating previously untreatable diseases and represent the biggest hope in the fight against cancer.

//02

17 out of the 20 top pharmaceutical companies already have next-generation therapeutics in their pipelines, with US companies taking the lead in the market.

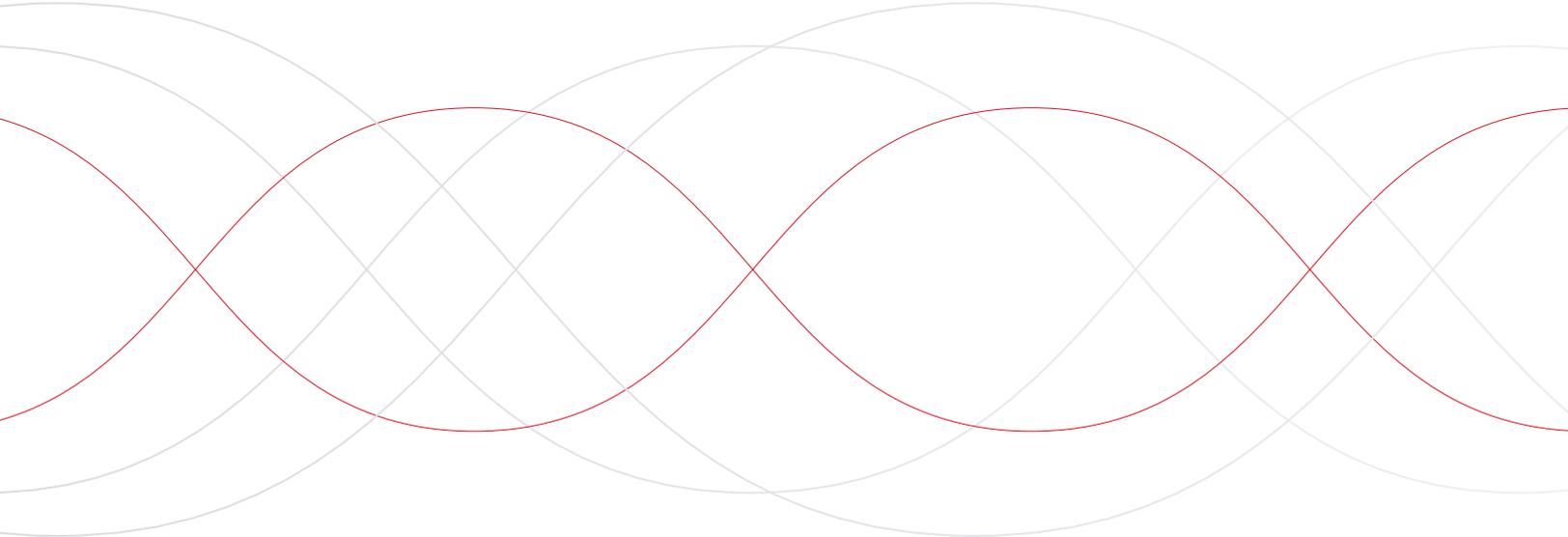
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Seven imperatives should be followed to adjust operating models in order to meet the specific demands of NGTs and succeed in the future.



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This paper is aimed at pharma and Contract Development and Manufacturing Organization (CDMO) executive level and strategy departments.

Innovation plays a pivotal role in most industries. In the pharmaceutical industry, however, it has the potential to both save and enhance millions of lives. As the sector undergoes continuous transformation, it is possible to categorize the most groundbreaking innovations in distinct waves. The preceding wave was predominantly centered around biologics, such as antibodies, while the current wave is bringing up new therapeutic modalities called “next-generation therapeutics” or NGTs. “We are entering a new frontier in medical innovation [...]” said then-FDA commissioner Scott Gottlieb in 2017, when Novartis’ Kymriah became the first officially approved therapy with genetically modified cells (CAR T-cell therapy) in the US.¹ These new entities are achieving commercial maturity and reaching the market at an accelerated pace.



This strategy paper aims to provide information on the latest developments around next-generation therapeutics by offering fresh perspectives on their market and commercial dynamics as well as their scientific specialties. The paper puts an

emphasis on the NGT value chain, and the respective challenges from research and development to market launch and roll-out of the product. Additionally, Porsche Consulting identified seven essential strategic imperatives for overcoming these challenges and mastering this new and innovative class of drugs.



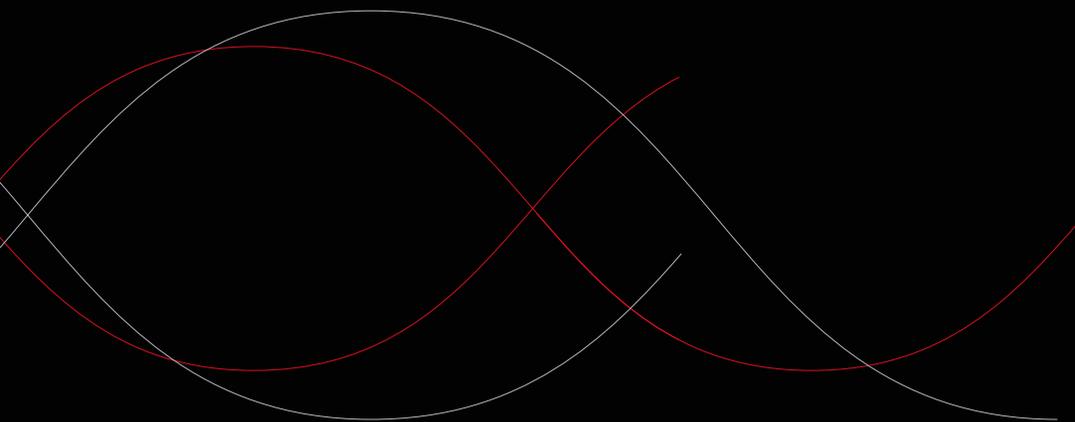
Driven by market trends like the looming patent cliff and scientific advancements such as the mRNA proof of concept, NGTs are playing an increasingly important role in the pipelines and portfolios of leading pharmaceutical companies. In particular, mRNA-enabled therapies gained worldwide attention when Pfizer/BioNTech and Moderna succeeded in using the technology for the fast development of highly effective COVID-19 vaccines. The relative novelty and complexity associated with the development, supply chain, and commercialization of NGTs, however, is putting the industry’s established operating model to the test. At the same time, the therapeutic and commercial opportunities create a significantly attractive growth potential for pharma companies. In order to leverage the growth potential, pharma companies need to reshape their business models and ride the second wave of pharmaceutical innovation.

Introduction

Numerous lifesaving drugs, improving the health and quality of life for hundreds of millions of people worldwide, represent the significant level of innovation achieved in the last decades. Aided by technological innovation and medical breakthroughs, the number of newly discovered compounds and therapeutics is steadily growing, with the USA as global leader in drug research and development. Although it is becoming increasingly complex and expensive to develop new medical products, the number of new chemical and biological entities introduced by US companies has jumped by 80 percent in recent years, from 88 to 159 in the period from 2012–2016 to 2017–2021.²

This can be seen as a sign of the pharmaceutical industry's innovation firepower, which has the highest R&D intensity of all sectors, at 12.4 percent of net sales.² The outlook into the future of health becomes even more promising with the advent of

next-generation therapeutics (NGTs). These new types of therapeutics hold the promise of treating previously untreatable diseases and represent the biggest hope in the fight against cancer. With the FDA approval of Novartis' cell therapy Kymriah in 2017, a new milestone in medical innovation has been reached and a variety of NGTs have followed ever since—most prominently Pfizer/BioNTech's mRNA vaccine Comirnaty, which has catapulted the small German biotechnology company into the ranks of Big Pharma with annual revenue of € 17.3 B in 2022.³ And there is yet more to come: as a recent example, in June 2023, the German pharmaceutical company Bayer announced first positive clinical trial results of a novel cell therapy for Parkinson's disease. Although there have only been positive results from Phase 1 so far, the development of a successful therapy for Parkinson's disease could generate billions in revenue.⁴

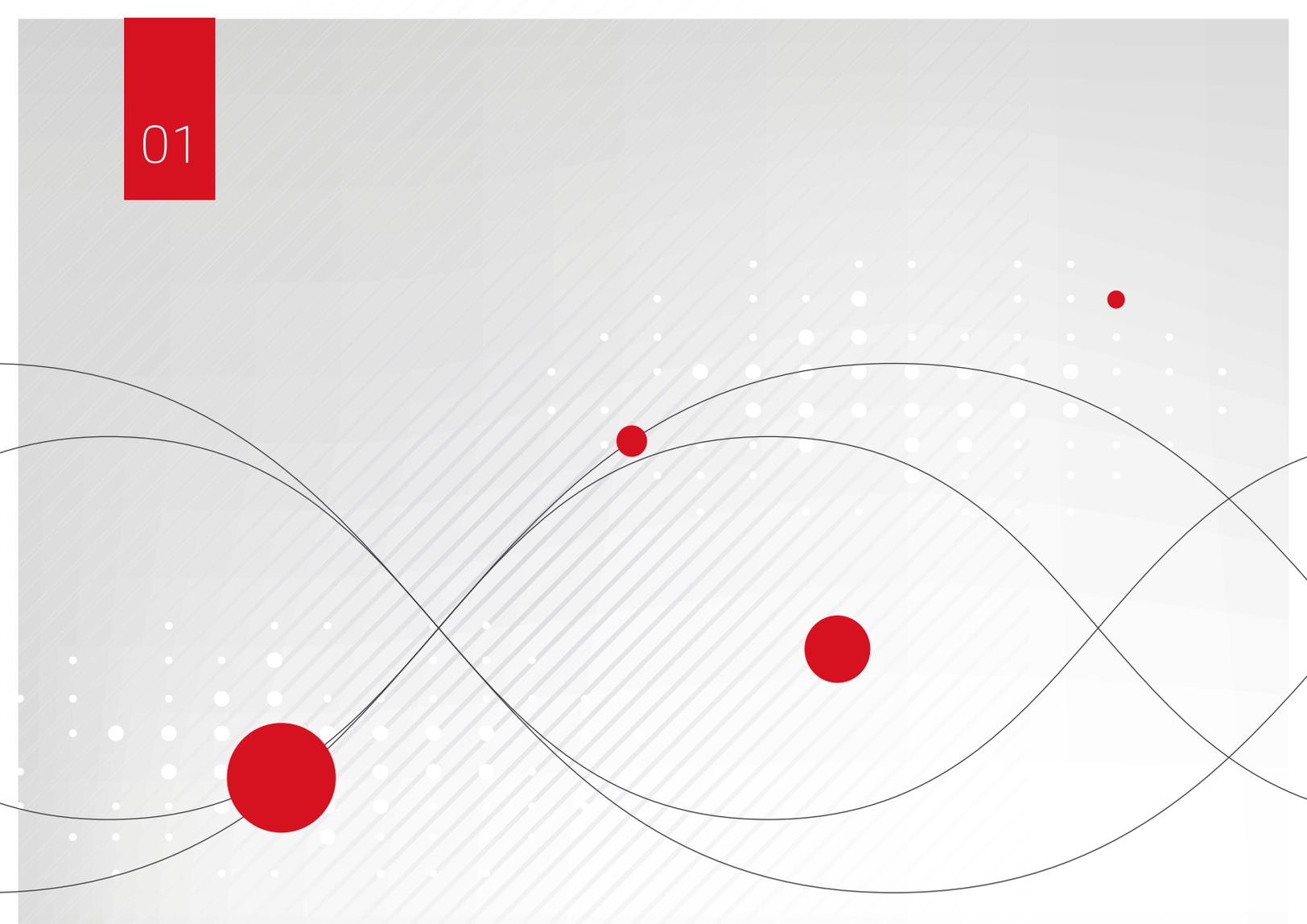


Industry revolution:

Analogy between the automotive and pharmaceutical industries

Both sectors are currently undergoing a paradigm shift driven by technological innovation to address major challenges, such as climate change and global health. The automotive industry is transitioning towards the electrification of cars, while the pharmaceutical industry is moving towards next-generation therapeutics. Both industries are receiving strong backing from regulatory forces—the car industry is heavily subsidized through initiatives like the Inflation Reduction Act and the European Green Deal; the pharmaceutical industry has received billions in funding to develop COVID-19 vaccines and enjoys ongoing support through initiatives like the Cancer Moonshot and Mission Cancer.

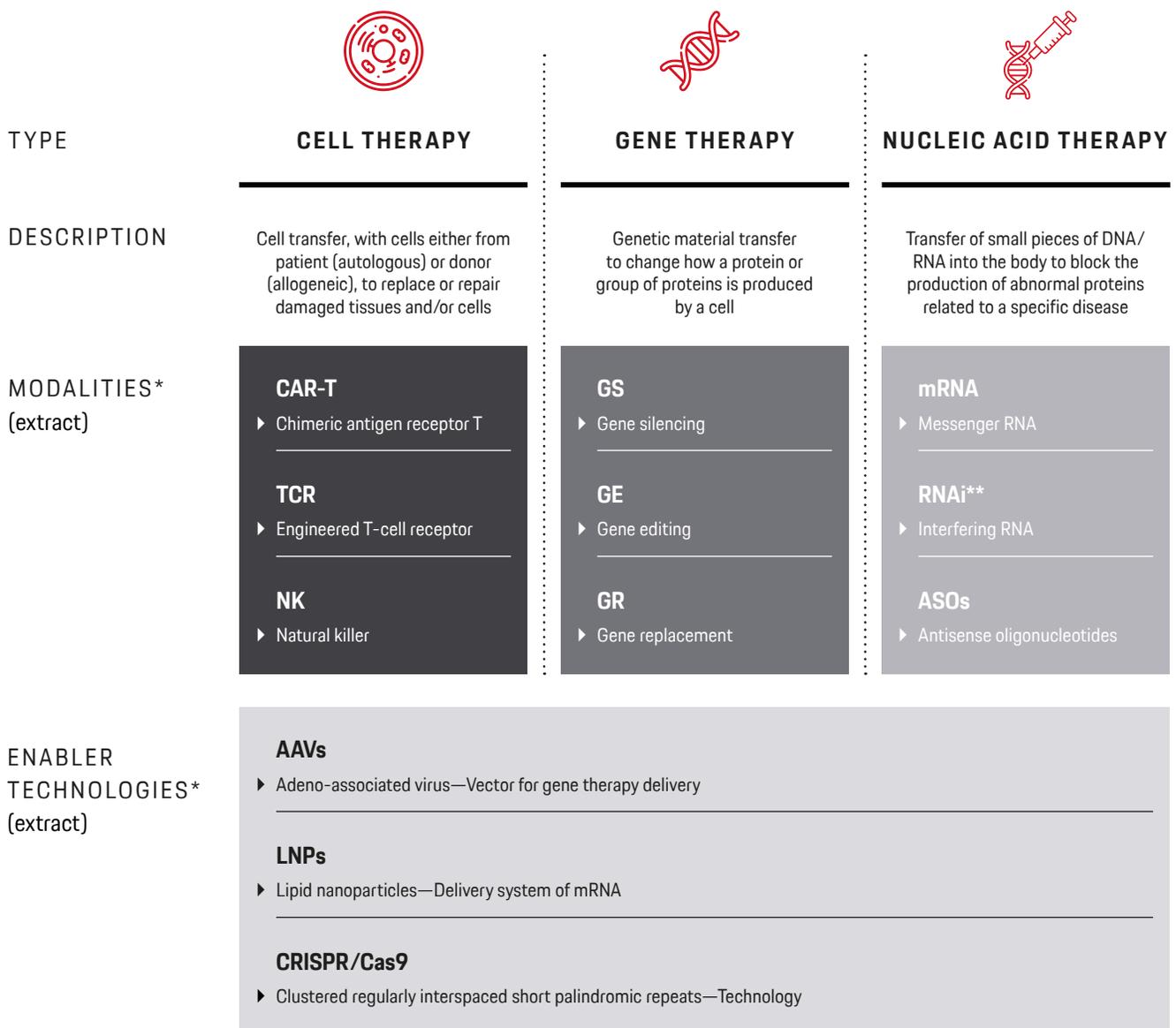
While there are differences between the two industries, such as technological maturity and pace of consumer adoption/patient access, some learnings from the automotive industry can be nicely applied to the pharmaceutical industry, whose players have yet to bridge key hurdles in the development and commercialization of next-generation therapeutics.

An abstract graphic featuring several overlapping, thin black circles of varying sizes. Four prominent red circles of different diameters are scattered across the composition. The background is a light gray with a subtle pattern of fine, parallel lines and a cluster of small white dots in the upper right quadrant.

NGT TYPES, MODALITIES, AND ENABLER TECHNOLOGIES

The development of NGTs can be traced back to the late 1970s, when the discovery of recombinant DNA technology paved the way for the biotechnology industry. Ever since, groundbreaking scientific innovations have turned experimental therapeutic agents into commercially available products. According to the latest report of the American Society of Gene & Cell Therapy (ASGCT),

the number of globally approved NGTs for clinical use has increased by 25 percent over the past two years, from 84 in Q1 2021 up to 105 in Q4 2022.⁶ To further sharpen the perspective, NGTs are usually divided into three main types. These three types are cell therapy, gene therapy, and nucleic acid therapy.



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Fig. 1. Types of next-generation therapies, their modalities, and enabling technologies⁵

Source: uniQure

* The combination of technologies and modalities form a company's proprietary platform (e.g., uniQure combines AAV technology with gene silencing and replacement modality for its GoQURE platform for Parkinson/Alzheimer candidates) | ** Including small-interfering RNA (siRNA) and micro-RNA (miRNA)

CELL THERAPIES

Cell therapies are a type of treatment that utilizes living cells to replace or repair damaged tissues or cells within the patient's body or that modifies cells to take over a specific task. These therapies can be categorized as either autologous or allogeneic, depending on whether the cells used are sourced from the patient or from a donor, respectively. One of the key advantages of cell therapies is their ability to target specific patient cells or tissues, stay in the body for a while, and—in the case of stable CAR-T proliferation—lead to long-lasting responses that are not possible with traditional small molecule or biological therapies.

Cell therapies can be customized to match the individual disease characteristics of each patient, potentially resulting in improved efficacy and safety compared to other treatment options. Despite these promising prospects, there are significant challenges associated with the production and administration of cell therapies, currently limiting their speed of adoption.

There are several different modalities of cell therapies that have been developed, including chimeric antigen receptor (CAR) T-cell therapy, T-cell receptor (TCR) therapy, and natural killer (NK) cell therapy.

Each of these modalities has its own unique properties and is suited to different types of disease and conditions.

GENE THERAPIES

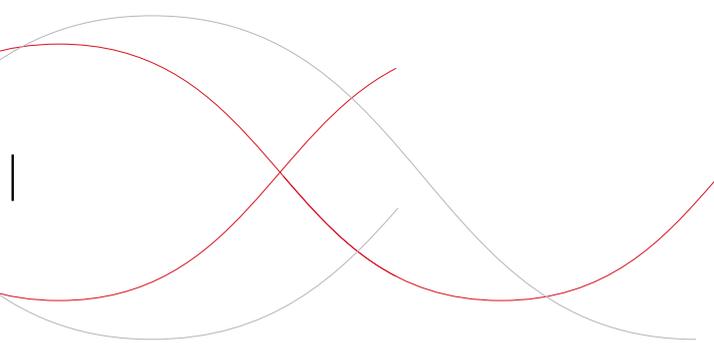
Gene therapies are a type of treatment that involves altering a patient's genetic material to change how a protein or group of proteins is produced by the patient's cells. This can be done by introducing new genes into the patient's cells, repairing or replacing faulty genes, or deactivating genes that are causing disease. Treatment with gene therapy is significantly more effective than traditional options because the patient's genomic profile is taken into consideration.⁷

What makes gene therapy unique is its potential to target the underlying cause of a disease, rather than just treating the symptoms. Like cell therapy, gene therapy can provide long-lasting or even permanent effects without ongoing administration. The manufacturing and delivery of gene therapies remain key challenges as the process complexity is very high and associated with significant costs.

Gene therapies can be broadly categorized into three different modalities, including gene replacement, gene editing, and gene silencing. Even though these modalities elicit responses through different functionality, they share significant similarities when it comes to manufacturing, process technology, and administration. Further, the modalities of gene therapy can be applied to ex-vivo cells, which are subsequently used in cell therapy. The result is a genetically engineered/modified cell therapy like CAR T-cell therapy.

NUCLEIC ACID THERAPIES

Nucleic acid therapies are a type of treatment that leverages small pieces of DNA or RNA to block the production of abnormal proteins related to a specific disease or to induce the production of a specific therapeutic protein. Customized to the respective disease profile, nucleic acid therapies provide a treatment option with potentially greater efficacy than traditional therapies.



Nucleic acid therapies are characterized by their ability to target specific genes or proteins involved in disease pathways, providing a highly targeted approach to treatment. Compared to traditional treatments like small molecules or biologics, they have the potential to achieve improved outcomes and reduced side effects. The main obstacle to the widespread adoption of nucleic acid therapies is their proneness to degradation, which is associated with severe logistic and administration challenges.

The most common modalities of nucleic acid therapies include messenger (m)RNA, interfering RNA(i), and antisense oligonucleotides (ASOs). With the successful development of COVID-19 vaccines, the proof of concept for mRNA has been achieved giving the modality an edge over the others.

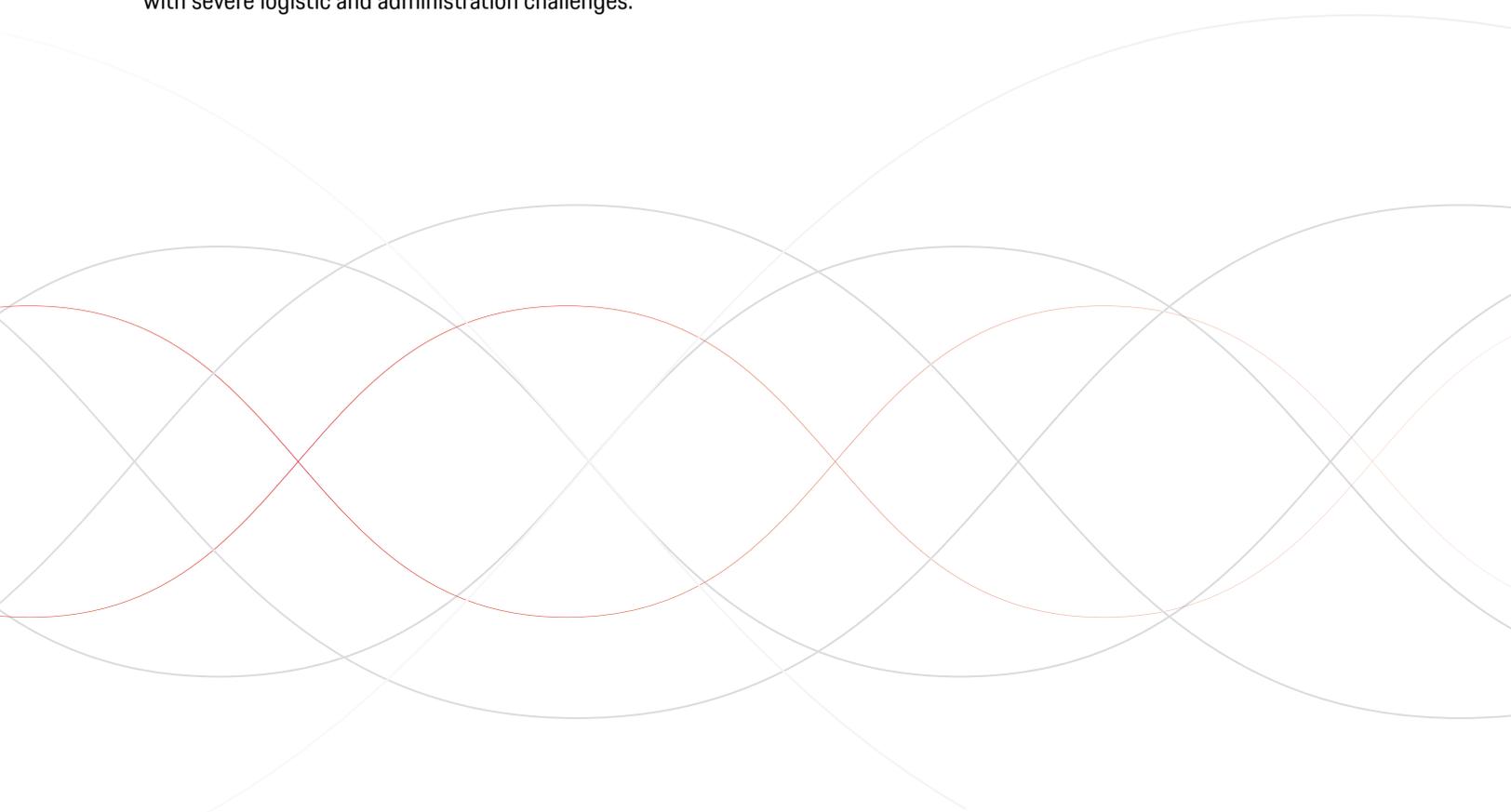
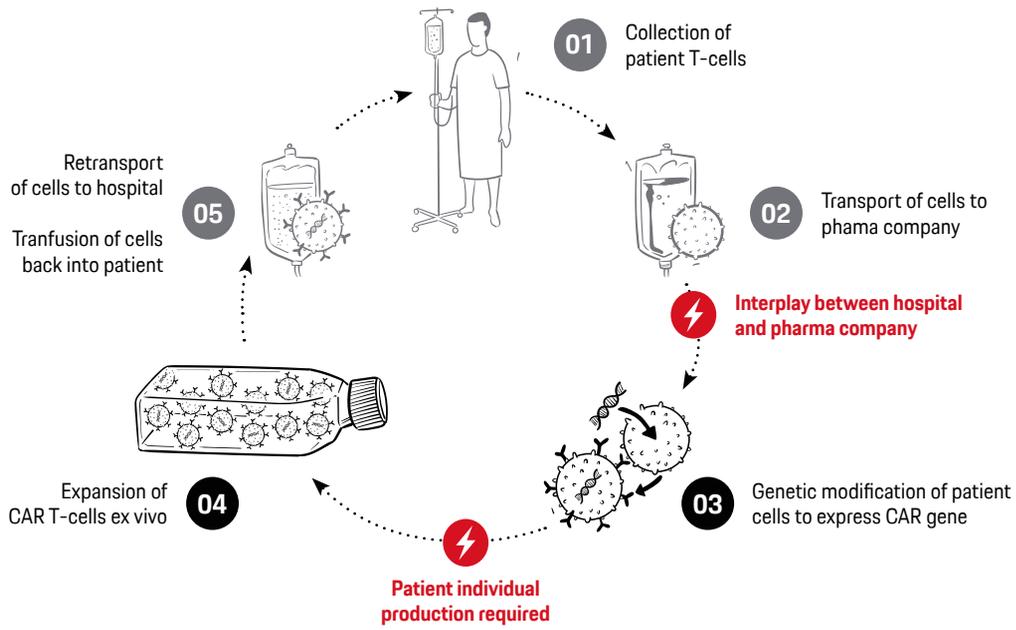


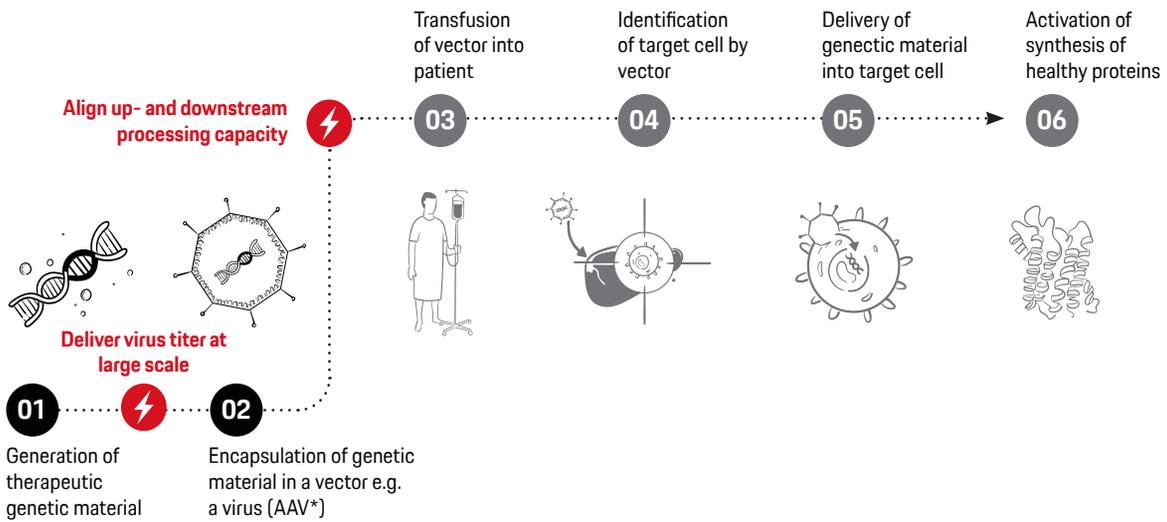
Figure 2 shows an example for each type of NGT as well as the processes that are involved in carrying it out. What becomes obvious is that NGTs require a more intense and complex interaction between hospitals and pharma companies in comparison to traditional drug types such as small molecules or biologics.



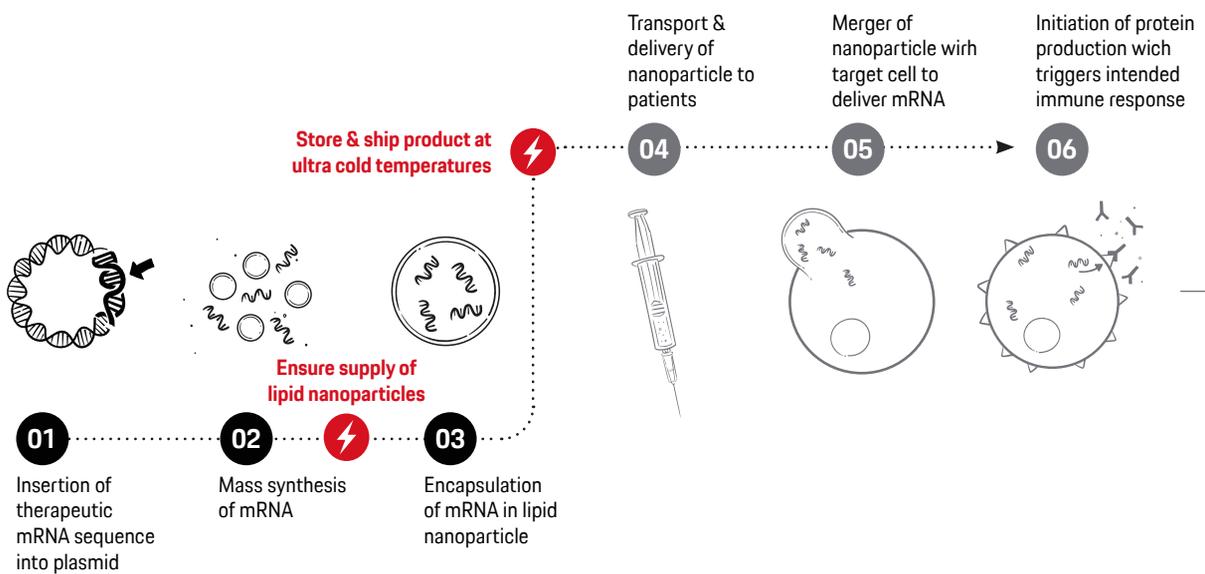
(CAR T-) CELL THERAPY



GENE THERAPY



mRNA THERATPEUTICS & VACCINES



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Fig. 2. Schematic depiction of NGT exemplary working modes. The process from pharmaceutical company to hospital and patient is depicted.⁸

* AAV = Adeno-associated virus

ENABLER TECHNOLOGIES

While NGTs can be sorted into the three different types with respective modalities, they may share the same kind of underlying enabler technologies. These can be applied individually or in combination with each other depending on the desired functionality. The most common enabler technologies include, but are not limited to, adeno-associated viral vectors (AAVs), lipid nanoparticles (LNPs), and the CRISPR/Cas9 technology.

Both AAVs and LNPs serve as effective delivery systems for therapeutic genetic material into living tissues. AAVs are small viruses that are commonly used as vectors to deliver therapeutic genes into cells. They are relatively well tolerated and can provide good gene delivery into target cells. AAVs have been in use for quite some time and are already used in a range of therapies. LNPs are nanoparticles composed of lipids that are used to deliver RNA-based therapeutics. LNPs can encapsulate RNA molecules, protecting them from degradation and enabling them to enter cells and exert their therapeutic effects.

Apart from the presented delivery systems, the technology CRISPR/Cas9 is used as a genetic scissor for splicing and editing DNA strands, enabling precise modifications to DNA sequences in living cells. The technology uses a small RNA molecule to direct Cas9 enzyme to the genome, where it makes a cut in the DNA. This cut can be used to introduce a desired gene change in the sequence. In the medical context, CRISPR/Cas9 is being explored as enabler technology for genetic disease. The technology has just recently experienced a breakthrough with the award of the Nobel Prize in chemistry in 2020 . In a groundbreaking advancement, in December 2023, the FDA approved the first CRISPR/Cas9-based gene therapy, Casgevy, developed by Vertex and CRISPR Therapeutics, marking a major milestone in gene therapy innovation. This groundbreaking treatment was specifically designed for patients over the age of 12 who suffer from sickle cell disease. The therapy utilizes CRISPR/Cas9 technology to modify hematopoietic (blood) stem cells, effectively altering the genetic code and preventing the sickling of red blood cells.⁹

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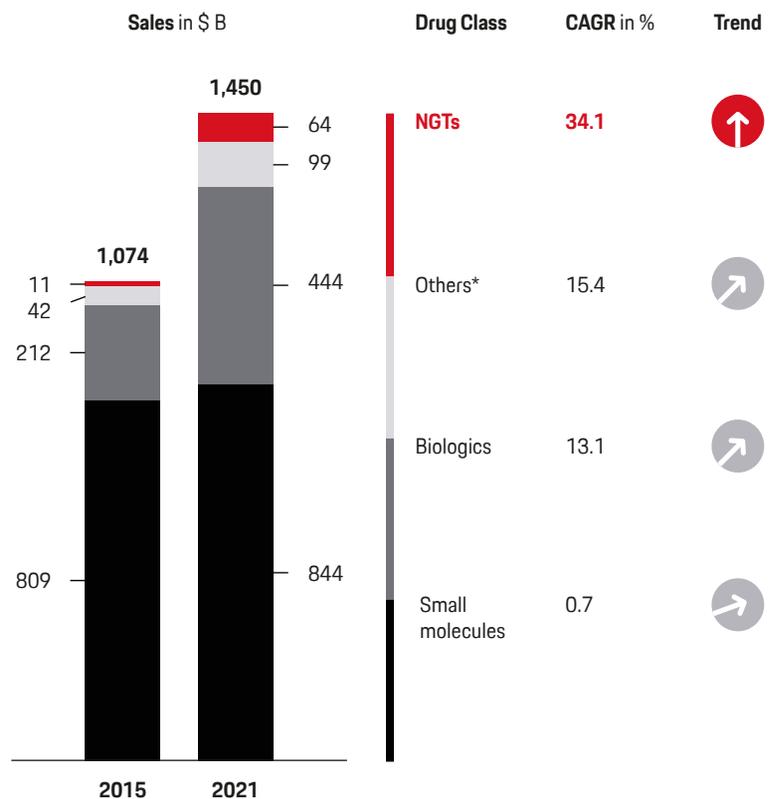
MARKET, COMMERCIAL, AND SCIENTIFIC DYNAMICS

Market dynamics for small molecules, biologics, and NGTs

Traditional small molecule drugs have been the dominant modality in drug research for the past century and still represent the largest class of pharmaceuticals around the world, accounting for 58 percent of the market volume and thus roughly \$ 840B in 2021.^{10,11} One of the oldest and most popular examples of small molecule drugs is Aspirin®, which was first registered by the German pharmaceutical company Bayer in 1899 and hailed as a wonder drug long ago. Small molecules represent major medical breakthroughs and have been established as the treatment class of choice in our medical system, largely due to their convenient mode of administration and advantageous cost-benefit profile. While they remain the most widely used drug class, small molecules only grew at a low rate of 0.7 percent CAGR in the period from 2015–2021, suggesting limited growth and innovation capacity in the space.

This is due to the relevance of biological drugs, which came onto the scene at the turn of the millennium. At this time, pharma companies marked the first wave of pharmaceutical innovation, moving their attention from small molecules to biologics, as evidenced by large scale M&A. Proving favorable safety and efficacy profiles and covering multiple indications with high unmet need, biologics have become the dominant drug class across the development portfolios of pharma companies. While trailing behind small molecules, with a market volume of roughly \$ 440 B in 2021,^{9,10} biologics grew at a solid rate of 13.1 percent CAGR in the period from 2015–2021, indicating plenty of innovation capacity in the space.

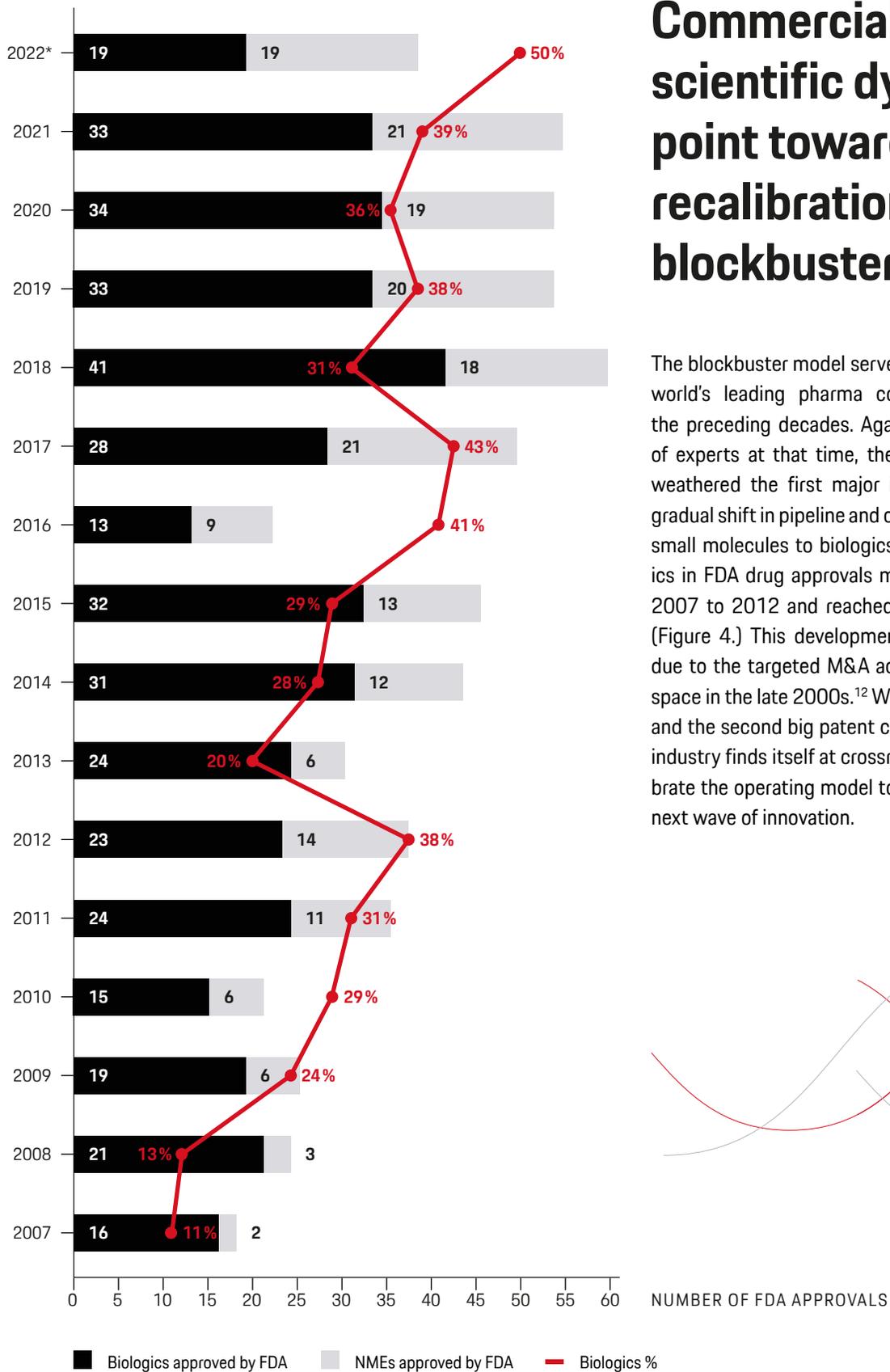
Parallel to the maturing field of biologics, the second major innovation wave has been heralded with the successful development and commercialization of NGTs. Reaching a market volume of merely \$ 64 B in 2021, NGTs currently represent a negligible fraction of the total pharmaceutical market.^{9,10} However, their tremendous potential in curing diseases and achieving unparalleled patient outcomes is underscored by a stellar growth rate of 34.1 percent CAGR in the period from 2015–2021. The ample innovation capacity in the NGT space constitutes a unique opportunity for pharma companies that do not shy away from challenging their legacy business model, which currently represents a barrier to widespread NGT adoption.



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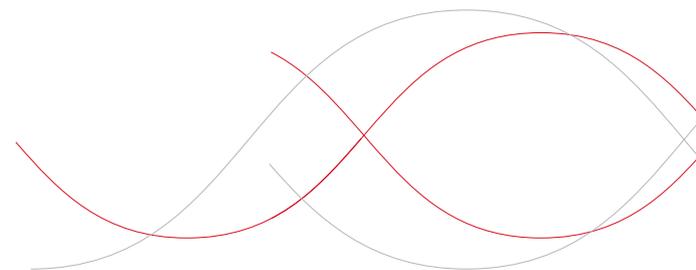
Fig. 3. Market volume and CAGR for different therapeutic classes: NGTs represent the fastest growing drug class.^{9,10}

* Others: Vaccines, blood products, naturals, radiopharmaceuticals



Commercial and scientific dynamics point towards a recalibration of the blockbuster model

The blockbuster model served as paradigm for the world's leading pharma companies throughout the preceding decades. Against the expectations of experts at that time, the business model has weathered the first major innovation wave—the gradual shift in pipeline and commercial focus from small molecules to biologics: the share of biologics in FDA drug approvals more than tripled from 2007 to 2012 and reached 50 percent in 2022 (Figure 4.) This development is in no small part due to the targeted M&A activity in the biologics space in the late 2000s.¹² With the advent of NGTs and the second big patent cliff on the horizon, the industry finds itself at crossroads and must recalibrate the operating model to successfully ride the next wave of innovation.



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Fig. 4. FDA approvals from 2007–2022, divided into NMEs (new molecular entities) and biologics¹²

* December 1–14

Following a one-size-fits-all approach, in which little consideration is given to patient-specific disease characteristics, pharma companies designed blockbuster drugs to serve large patient populations and address therapy areas with a high unmet need. As a result, multibillion-dollar drugs have become the cornerstone of every major pharma company's portfolio, creating a dependency risk that materializes with the loss of exclusivity. For

example, AbbVie's Humira, which accounted for 37 percent of the company's total net revenue in 2022, is anticipated to lose roughly one-third in sales to biosimilar competition due to patent expiration.^{13,14} Against the background of current commercial and scientific dynamics, pharma companies are more than ever under pressure to safeguard top lines by shifting their attention towards highly innovative modalities and alternative therapy areas (Figure 5).

Commercial and scientific trends are pointing towards a greater focus on NGTs

COMMERCIAL TRENDS

Competition

Increasingly crowded indications lowering launch and profit potential for new treatments

Anticipated biosimilar launches amplifying competitive pressure in established indications

Standard of Care

High standard of care incentivizing breakthrough innovation because of greater profit potential

Orphan diseases becoming more lucrative due to limited competition and high unmet need

Financial Austerity of HC Systems

Policymakers and insurers aiming towards a reduction of healthcare spending with altered coverage rationales

Streamlined regulatory pathways introducing common standards for novel therapeutics

SCIENTIFIC TRENDS

Technology Innovation

New technologies, such as mRNA and CRISPR/Cas9, opening new possibilities for enhanced treatment options

Rapidly evolving value chain embracing the shift towards new medicinal products

Precision Medicine

Shift in treatment paradigm, establishing a personalized care path supplemented by patient-individual data

Advanced diagnostics enabling therapeutics to become more tailored to specific disease characteristics

Shift in Innovation Capacity

Innovation potential in small molecules achieving a threshold at which only incremental innovation is possible

Biologics and NGTs becoming the focus of pipeline innovation due to ample innovation potential

Innovative therapeutics in indications with little competition and/or high unmet need represent the next big opportunity for leading pharma companies

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Fig. 5. Commercial and scientific trends in the pharmaceutical industry

From a commercial perspective, the shift towards NGTs is necessitated by two major dynamics. First, the competitive landscape in target indications with the highest revenue potential has become overcrowded, and biosimilar competition is poised to grab the vast majority of the market. Second, the high standard of care in target indications coupled with the financial strain of healthcare systems cast doubt on the return potential of incremental innovation. The need for a shift in strategic direction is further amplified by considering the interplay of scientific advancements.

Regarding the scientific perspective, three major trends stick out. First and foremost, major scientific breakthroughs have been achieved in enabling technologies, making the theoretical

impacts achievable and transferable to real-world drug development. Second, the trend towards a patient-individual and disease-specific treatment paradigm, which includes biomarker- and genome-based therapeutics, goes hand in hand with smaller target patient populations. Third, the innovation capacity within traditional drug classes has been exhausted to the extent that breakthrough innovation is not possible anymore.

Powered by these trends, the new class of pharmaceuticals has rapidly gained a foothold in the pipeline portfolios of all major drug manufacturers—leading pharma companies record double-digit number of NGT trials in their pipelines with the share of NGT trials reaching up to 17 percent (Figure 6).

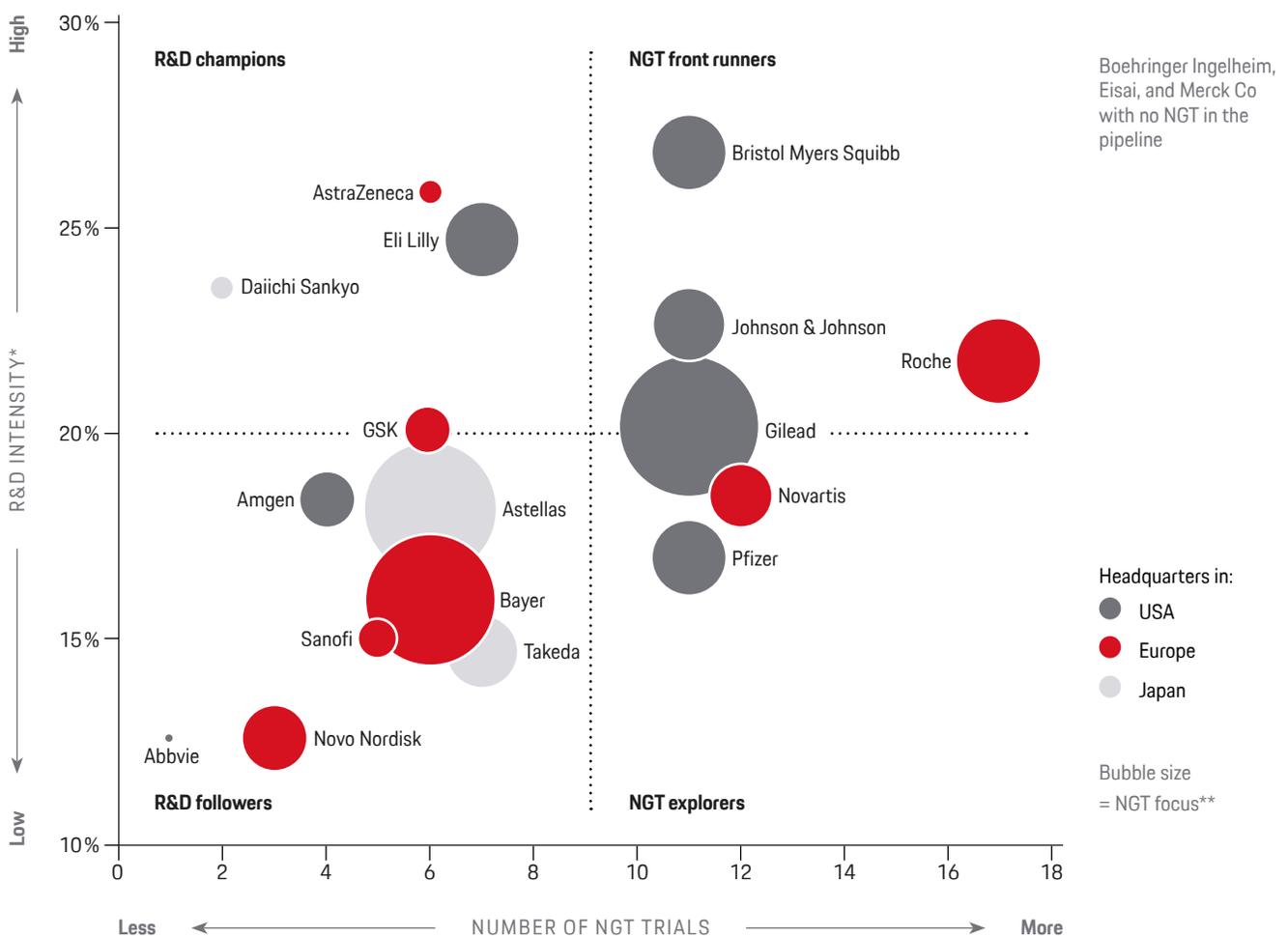
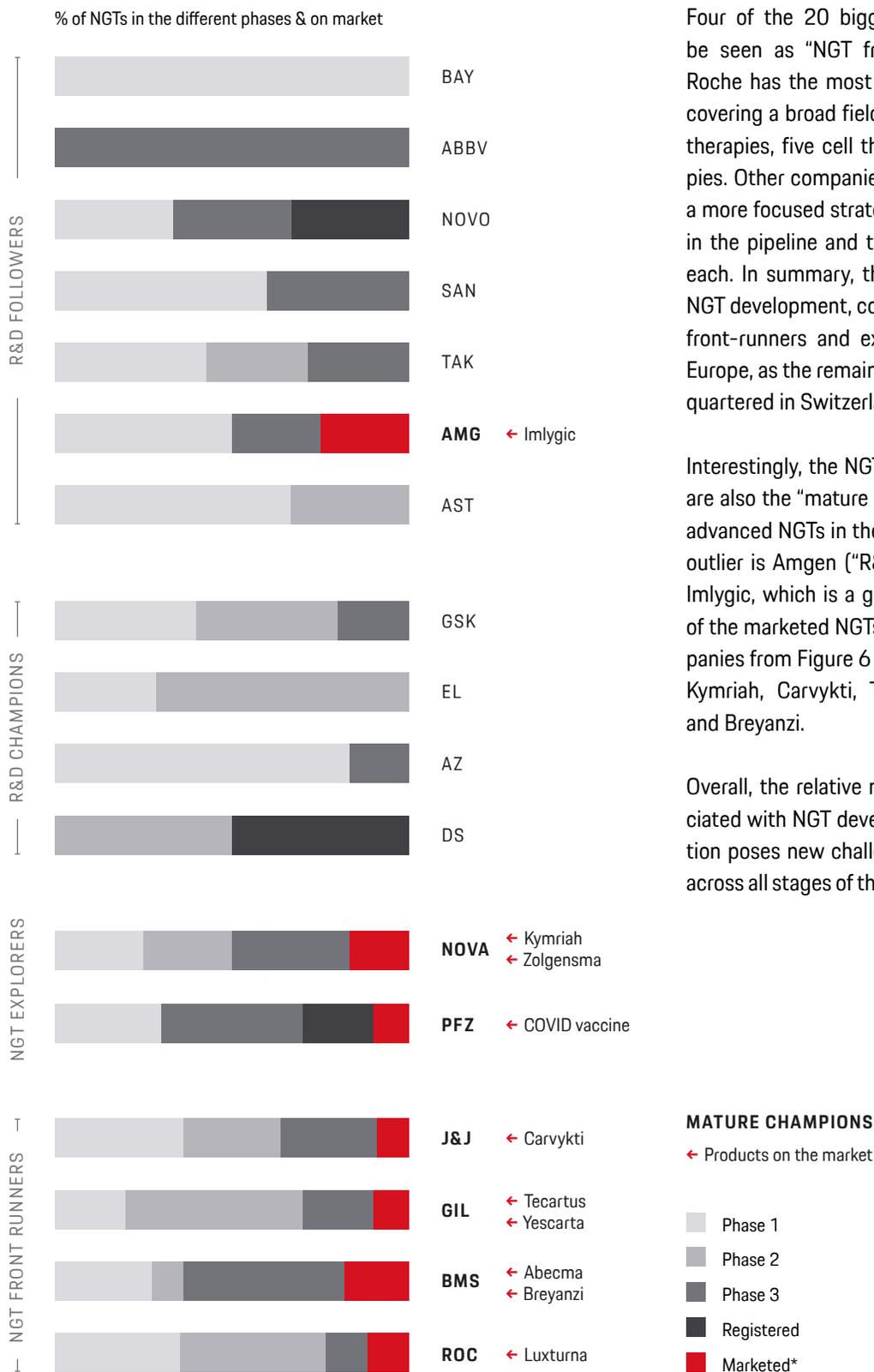


Fig. 6. Pipeline analysis of the global top 20 pharma companies by revenue

Source: American Society of Gene + Cell Therapy (ASGCT)

* R&D intensity = R&D expenditure as share of the total revenue 2 022 | ** NGT focus = all nucleic acid, cell, and gene-based therapies in relation to all entities in the pipeline



Four of the 20 biggest pharma companies can be seen as “NGT front-runners.” Among these, Roche has the most NGT entities in the pipeline, covering a broad field with six nucleic-acid-based therapies, five cell therapies, and six gene therapies. Other companies like Gilead and BMS follow a more focused strategy, having just cell therapies in the pipeline and two marketed gene therapies each. In summary, the US companies are driving NGT development, contributing four of the six NGT front-runners and explorers. This is followed by Europe, as the remaining two companies are headquartered in Switzerland.¹⁵

Interestingly, the NGT front-runners and explorers are also the “mature champions”, having the most advanced NGTs in the pipeline (Figure 7). The only outlier is Amgen (“R&D followers” segment) with Imlygic, which is a gene therapy for cancer. Most of the marketed NGTs by the top 20 pharma companies from Figure 6 are CAR T-cell therapies with Kymriah, Carvykti, Tecartus, Yescarta, Abecma, and Breyanzi.

Overall, the relative novelty and complexity associated with NGT development and commercialization poses new challenges for pharma companies across all stages of the pharmaceutical value chain.

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Fig. 7. Percentage distribution of the pipeline assets of the global top 20 pharma players in the different stages of development¹⁶
Source: FDA; EMA; Porsche Consulting analysis

* For the marketed entities, only US and EU registrations are considered.

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NEW CHALLENGES THAT CONTEST THE EXISTING OPERATING MODEL OF PHARMA COMPANIES

Even though NGTs have now been on the market for several years, pharma companies are still struggling to adapt their operating model according to the unique properties of the new drug class. From research and development through commercialization, NGTs place new demands on the industry (Figure 8). In the following, the challenges along the value chain will be described in more detail.

01

RESEARCH & DEVELOPMENT

Low odds of translation due to animal model limitations; need partners for high-quality research

02

SUPPLY CHAIN

Consistency, availability, & quality of raw materials; short shelf stability and logistical challenges

03

MANUFACTURING & SCALE-UP

Variability of cells; low production capacity; complexity & manual nature of processes

04

REGULATORY PROCESSES

Small patient populations limit design & robust data; uncertainty about process (timelines/evidence level)

05

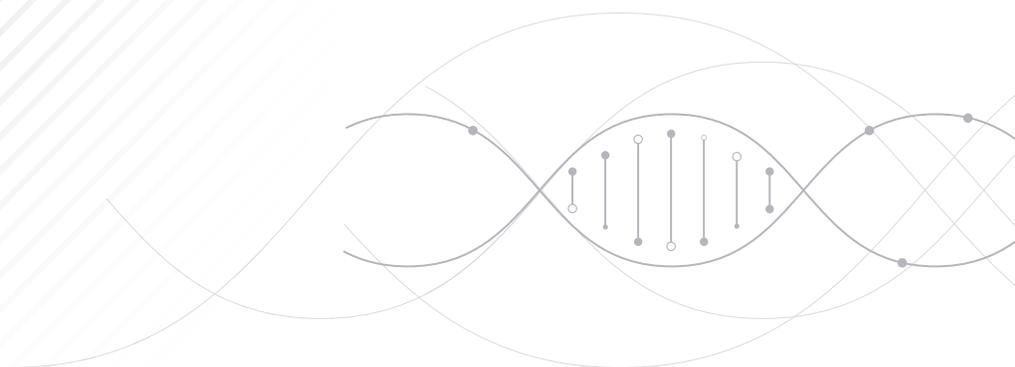
PRICING & REIMBURSEMENT

Systems not set up to assess value of curative therapies; fragmentation; line of treatment limits

06

GO-TO-MARKET & ROLLOUT

Low capacity to adapt due to lack of infrastructure, staff, or skills; care path not adapted; ethics/bias



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Fig. 8. Exemplary challenges of NGTs along the value chain

Source: Fierce Pharma

01

Research and development

When it comes to the basic research and development of NGTs, the groundwork was laid over the preceding decades, with academia and specialized biotechnology companies leading the way. Some modalities and enabler technologies had already been discovered in the 1980s, but it is only now that they have achieved a state of maturity fit for commercial application, with several challenges remaining. Two of the current challenges encountered in the research phase relate to immunogenicity and translatability.

With regard to immunogenicity, it is not yet completely understood how the human immune system responds to genetically modified therapeutics. First, the creation of antibodies may lead to the clearance of the therapeutic effects of NGTs, exacerbating the patient's condition and lowering the treatment's efficacy upon reinfusion. Second, unintended immune response to foreign genetic material can cause serious toxicity, resulting in severe side effects or adverse events. Since NGTs are highly customized to patient and disease characteristics, the effectiveness and safety profile may vary starkly from one batch/patient to another, making it even more difficult to establish causal relationships in immunological pathways.

Two of the current challenges encountered in the research phase relate to immunogenicity and translatability.



As for translatability, the traditional animal models that are routinely used in basic research for small molecules and biologics are not suitable for NGTs, since the latter are customized to a patient's unique genetic constituencies.

First and foremost, it is the species-specific differences in the immune system that limit the validity of animal models, questioning the predictiveness of preclinical trials as well as the preliminary efficacy and safety profiles. Second, animal models are not sufficiently tailored to mimicking certain human diseases, particularly certain types of genetic disorders. Third, a lack of standardization across applied animal models puts into question comparability of results.

The development of NGTs in clinical trials and the subsequent filing and approval processes present their own hurdles. Starting with the characterization of donors for cell products up to the selection of adequate endpoints, pharma companies must take a comprehensive set of variables into consideration when setting up clinical trials for success. Three main challenges regarding NGT development include small patient populations, vague guidelines for trial design, and an altered health technology assessment landscape.

Since many NGTs are catered to the needs of patients with very specific characteristics, like the defect of a particular gene, the available patient pool for specific NGTs is naturally very small. Under this circumstance, pharma companies face the challenges encountered by rare disease specialists, including patient identification, diagnosis, and recruitment. Finding and recruiting eligible patients is not only difficult because there are only a few of them, but also because there might be an existing standard therapy in the respective target indication, dissuading potential candidates from joining an experimental pathway. Once sufficient patients are recruited, the robustness and validity of data becomes a challenge. This is because the data gathered in a trial with a limited number of patients frequently provide insufficient statistical power to demonstrate a solid medical profile, reducing acceptance by payers and providers.

Even though numerous therapies have successfully moved through clinical development and received regulatory approval, clinical trial guidelines for NGTs are still vague, which complicates setup and planning. With limited guidance on how to set up robust trials for NGTs, pharma companies struggle to meet the demands of regulators and bear the risk of freezing or terminating trials with limited chances of success because of insufficient evidence. Finally, the eligible patient population for exploratory clinical trials is very heterogeneous with respect to pretreatments, such as chemotherapy, radiation, and antibiotics, casting a shadow on the reliability of collected data.

Clinical trial guidelines for NGTs are still vague, which complicates setup and planning.

The safety and efficacy profile of both small molecules and biologics is assessed using standard protocols put forth by health technology assessment bodies. Due to the complex nature of NGTs, however, it is questionable whether using the same endpoints as with other modalities makes sense. To be more specific, NGTs might prove highly effective in a particular subpopulation for which no separate endpoints are outlined. Furthermore, the lack of standardized endpoints among health technology assessment bodies poses a challenge, since EMA and FDA have different thresholds for clinically meaningful benefits. As a result, pharma companies face uncertainty regarding the acceptance of clinical trial data once assets reach late-stage development, creating a substantial risk to clinical success.

How these challenges affect company results can be seen in the example of Gilead. The CAR T-cell therapy KITE-585 showed slow progress in the development process and was finally stopped. This resulted in an \$ 820 million impairment charge.¹⁷

02

Supply chain

Global supply chains for NGTs are not yet mature. This could be seen in 2021, when demand for Bristol Myers Squibb's Abecma outstripped its supply due to the global viral vector shortage. Following this, BMS put ensuring a stable vector supply as a top priority on their strategy agenda.¹⁸ However, viral vector production is inefficient and requires complex, specialized facilities.

Current viral vector demand requires two to three billion liters of bioreactor capacity per year, expected to increase to five to six million liters of capacity per year in the future. Change is needed for both upstream and downstream development, and a streamlined process would be desirable. Major CDMOs like Catalent, Lonza, and Thermo Fisher Scientific have committed to increase their viral vector capacities. This can also be seen by M&A activities, as TFS acquired the specialists Brammer Bio and Henogen, while Charles River acquired Cognate BioServices and Vigene Biosciences. On the other hand, some pharma companies like Gilead, Merck, and Sanofi are investing in in-house viral vector manufacturing capabilities. This reduces the potential risk of long lead times resulting from working with CDMOs.¹⁹



Change is needed for both upstream and downstream development, and a streamlined process would be desirable.

The high demand is driven by the fact that viral vectors are the preferred tool for delivering genetic material into cells, both for ex-vivo engineering of cell therapies and for the delivery of gene therapies. All different types of viral vectors, like lentiviruses and adeno-associated viruses, have limitations, which is driving investment in viral and non-viral delivery methods, which are free from the restricted gene packaging capacities of the current options.

Another challenge in the supply chain results from the patient-individualized nature of many NGTs. CAR T-cell therapy is just one example of a personalized treatment. Complex logistics are necessary here, because patient cells are required, which are then genetically modified and transferred back to the patient (Figure 2).

NGT material is also often very temperature-sensitive, resulting in additional logistical challenges (cold chain) and increasing transport prices significantly.

03

Manufacturing and scale-up

Perhaps the most evident bottleneck in NGT commercialization relates to production and scale-up. This is because the entire value chain is being built from scratch, as NGTs demand new manufacturing and distribution standards. Accordingly, the most pressing challenges for NGT production and scale-up relate to manufacturing capabilities, such as technology, processes, and talent, as well as material management, including supply, distribution, and quality.

NGTs are manufactured using elaborate and highly regulated processes that require specialized expertise, equipment, and facilities. Due to the relative novelty and complexity of NGTs there is a lack of qualified talent and adequate infrastructure, as clinical candidates originate from dedicated research centers affiliated with universities, hospitals, and non-profit research organizations. Consequently, high-risk investments into process development, talent management, and manufacturing infrastructure are needed to build production expertise and enable scalability. Nevertheless, establishing production capabilities does not ensure immediate success, as the very high-quality requirements for this new type of medication often result in the rejection of entire production batches.²⁰

Since NGTs are made using living cells, which can vary in quality and potency depending on the source and preparation method, they are highly fragile and require closed systems for the transfer from one device/location to another. The variability in quality and fragility during transport can affect the safety and efficacy of the final product to the extent that it cannot be delivered to patients or may cause detrimental effects to patients in case of delivery. As a result, rigorous quality control and testing is required across all stages of the manufacturing process to ensure safety and efficacy. This includes testing for purity, potency, identity,

Establishing production capabilities does not ensure immediate success.

and safety of the final product, as well as testing of starting materials and intermediates. Just like manufacturing, quality assurance, and control require specialized equipment and expertise as well as suitable processes and protocols to guarantee the safety and effectiveness of NGTs.

The importance of quality can be seen in the example of Novartis' CAR T-cell therapy Kymriah. This therapy had "out of spec" issues due to the number of inactive cells impacting 10 percent of the batches for more than a year.²¹ Consequently, the focus was set on improving the manufacturing process to increase efficiency and reduce variability. Therefore, the automation of the process was pursued, initially targeting the parts of the process that required the most manual labor and had the highest potential for variability. The overall objective included creating a custom-built system that would consolidate a range of blood processing equipment into one automated unit.²²



04

Regulatory processes

A 2022 survey from the NGT-focused company Synthego revealed unclear regulatory guidelines as the main challenges when starting clinical trials of gene therapies. Indeed, the complexity of the regulatory process can be seen in a 2021 study, which showed that cell and gene therapy development programs had significantly more disruptions than monoclonal antibody development programs.²³ While 43 percent of the cell and gene therapy development programs had disruptions, this was only 28 percent with monoclonal antibodies. Strikingly, significantly more chemistry, manufacturing, and control issues were recorded for cell and gene therapies. Within this category, comparability and analytical issues were predominant. Another study from 2019 revealed clinical pharmacology, clinical efficacy, and clinical safety as major objections in the assessment of gene therapeutic medicinal products.²⁴ In order to address the unclear regulatory guidelines, the FDA released two new guidance



Harmonization of requirements and improved inter-country communication is the key to success.



documents in March 2022 to help sponsors who are developing NGT products. These documents contain recommendations on study design, safety, manufacturing, and analytical comparability.

Another challenge results from the fact that many clinical trials are performed in multiple countries. Here, the sponsors face different regulatory requirements. Harmonization of requirements and improved inter-country communication is the key to success.

Moreover, there is a lack of agreement on surrogate endpoints in clinical trials of NGTs. These endpoints are markers that can predict clinical benefit but are not actual measurements of clinical benefit as would be expected from standard trials. Surrogate endpoints are especially important when developing gene therapies for rare disease populations.

05

Pricing and reimbursement

Having advanced to this stage with significant investments made, it is time to execute on a solid launch and sale agenda guaranteeing adequate future returns. Key challenges that industry players are experiencing with commercialization relate to pricing and reimbursement as well as stakeholder education and awareness. According to GlobalData, pricing and reimbursement constraints present the second most pressing regulatory and macro-economic trend for pharma companies in 2023.²⁵

It is an underappreciated fact that even when NGTs obtain marketing authorization, they are still often hampered by substantial delays between their date of approval and the time they launch. The reason for this lies in a combination of multiple factors—manufacturing and patient preparation being one, not having a payment or reimbursement system in place being the other.



Manufacturing and patient preparation being one obstacle, not having a payment or reimbursement system in place being the other.

BioMarin's Roctavian is an example of such a delay. The gene therapy won approval from the European Medicines Agency (EMA) as a single-dose treatment for hemophilia A in August 2022. As European authorities were reluctant to pay the expected price of around € 1.5 M (with about 9,000 patients eligible in the European Union), the first treatment of a patient in Europe occurred only in August 2023 in Germany, with final price negotiations still ongoing.²⁶

Another example is Bluebird Bio's Zynteglo. This gene therapy for the treatment of beta thalassemia was approved by the EMA. However, Bluebird Bio withdrew the treatment from the German market following unsuccessful price negotiations between Bluebird Bio and the union of health insurance companies, at which a price was defined that was less than half the price originally sought by Bluebird Bio.²⁷

From a cost-based pricing perspective, payers will have to dig deep into their pockets to secure a supply of NGTs, as the initial investment from the industry into the nascent niche is associated with extremely high expenditures and risks. As outlined further above, the development of NGT-related capabilities is so costly because talent is scarce, infrastructure is built from scratch, and complexity consumes a vast number of resources. Against the background of financially scathed healthcare systems, payers are hesitant to cover the high cost of NGTs. This leaves the industry wondering whether entering certain markets is worthwhile at all.

For NGTs to gain more traction within the pharmaceutical landscape, both patients and healthcare providers must be educated as to where the state of the science stands and how powerful scientific tools are applied. Patients and healthcare providers may not be familiar with or have misconceptions about new treatments. Equally, policymakers

and other non-governmental organizations that oversee and steer the regulatory landscape in the healthcare space must be aware of the benefits and potentials of NGTs. Only then will it be possible for all involved stakeholders to make well-founded decisions, whether it is the prescribers selecting the right treatment for their patients or the politicians guiding the regulatory policy in a certain direction.

The high setup cost for NGT capability development must be recouped to justify the investment; at the same time, prices must not be too high to get payers on board and accelerate patient access. Regarding stakeholder education and awareness, pharma companies may face difficulties in sufficiently communicating the value proposition of NGTs because of the scientific complexity of their work. This becomes even more difficult against the background of an increasingly complex stakeholder landscape covering a wide range of demands.

The development of NGT-related capabilities is so costly because talent is scarce, infrastructure is built from scratch, and complexity consumes a vast number of resources.



06

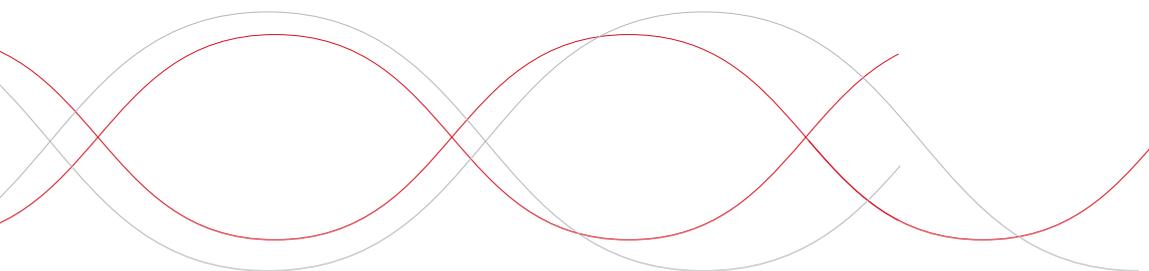
Go-to-market and rollout

Navigating the challenges of launching products in the field of NGTs is imperative for pharma companies, especially given the substantial R&D costs associated with this drug class. While traditional drug launch strategies involve prescriber-based methods across diverse contexts, the complexity of NGTs demands a more effective approach: centralized specialized centers capable of both recommending treatments to suitable patients and efficiently delivering NGTs on a larger scale. This strategic shift, as highlighted in previous stages of the supply chain and manufacturing processes, recognizes the intricate nature of NGTs and the necessity for targeted care environments to optimize patient outcomes.

Furthermore, a significant focus should be placed on the products themselves. Upon NGT launch, the seamless functionality of closed-loop manufacturing processes becomes paramount to ensure precise administration of patient-specific drug dosages at the right time and place. Finally, the whole organization must be ready to hit the market. One aspect that might sound trivial but holds an immense risk for NGTs is the ability to meet the demand. Launching an NGT product follows the same market rules as those for other products such as small molecules or biologics—patent protection is not infinite. After 10 to 11 years in the EU and 12 years in the US, the market will be open to generic products, significantly reducing the shares of the originator. This underlines the need for sufficient capacities as long as patent protection stands.

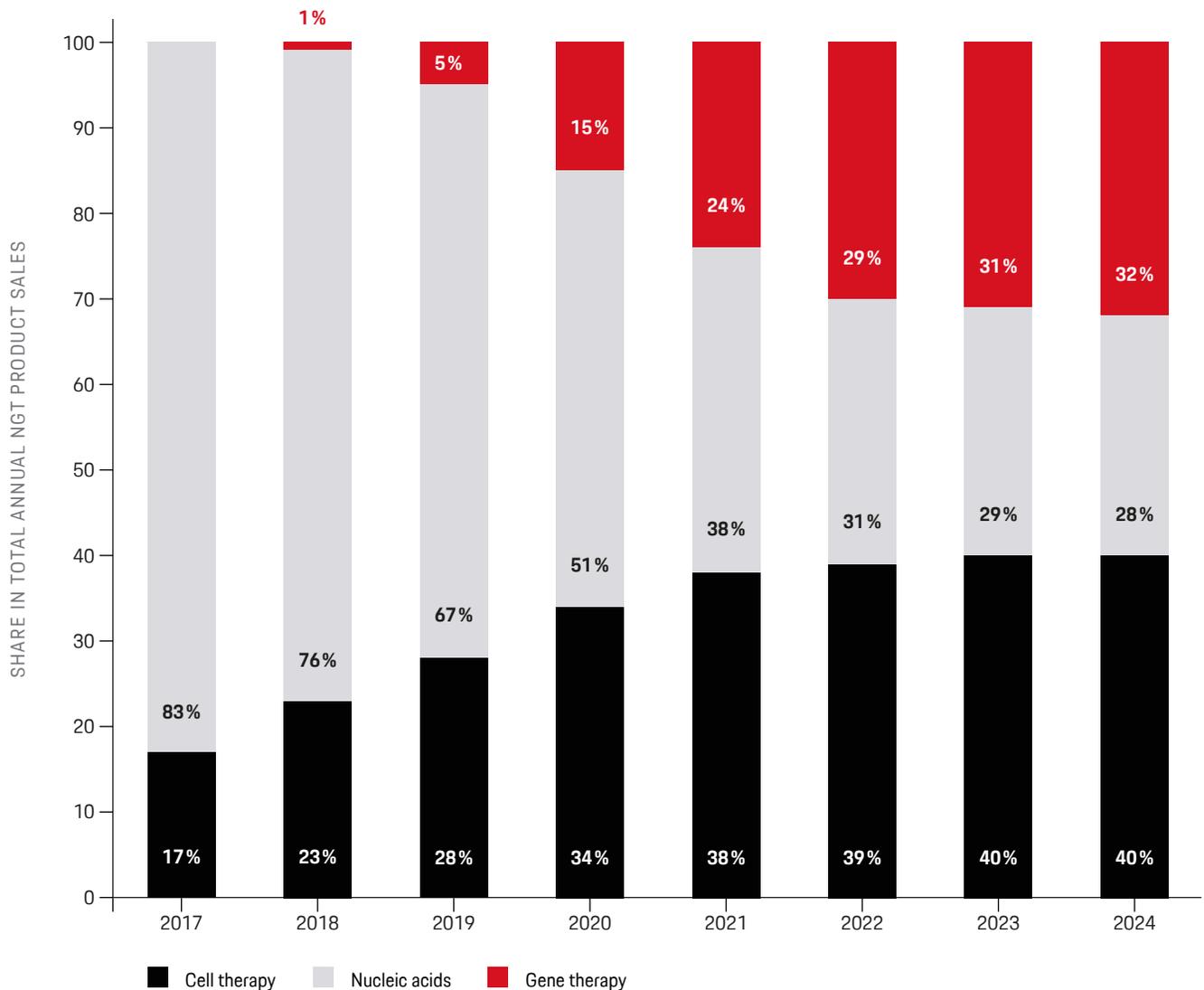
The example of Bluebird's Zynteglo illustrates the issue described. In this case, production problems led to a delay in commercial availability: despite receiving approvals from the European regulatory organization EMA in June 2019, the product only became commercially available at the beginning of 2021. The company stated that the main reason for the delay was the need to first tighten up Zynteglo's production. The launch in the US market was comparatively more successful. After receiving FDA approval in August 2022, the first patients were treated as early as the following month.²⁸

Launching an NGT product follows the same market rules as those for other products such as small molecules or biologics.



However, the impact of production difficulties on launch and rollout activities is not solely experienced by Bluebird. The continuously increasing number of NGT approvals appears to be pushing production capacities in the sector to their limits.²⁹ Overall, this affects the adherence to established launch schedules and limits rapid scalability. The involvement of contract development and manufacturing organizations (CDMOs) can only initiate a long-term alleviation of the situation, as the complex production of NGTs can lead to significant waiting times.

It is also worth taking a closer look at sales distribution inside NGTs. While nucleic-acid-based therapies were leading the market with more than 50 percent share between 2017 and 2020, the two remaining segments have gained momentum ever since.³⁰ This is especially true for gene-therapies, which are expected to account for about one-third of NGT-related sales in 2024. This progression underscores a significant revelation: the triumph within the NGT landscape is not singularly attributed to any one segment, but rather, it is the collective strength across all segments that propels the attainment of success.



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Fig. 9. Total annual NGT product sales from 2017–2024 (exp.) divided into cell, gene, and nucleic acid therapies³¹

Source: Evaluate Pharma

Interim conclusion

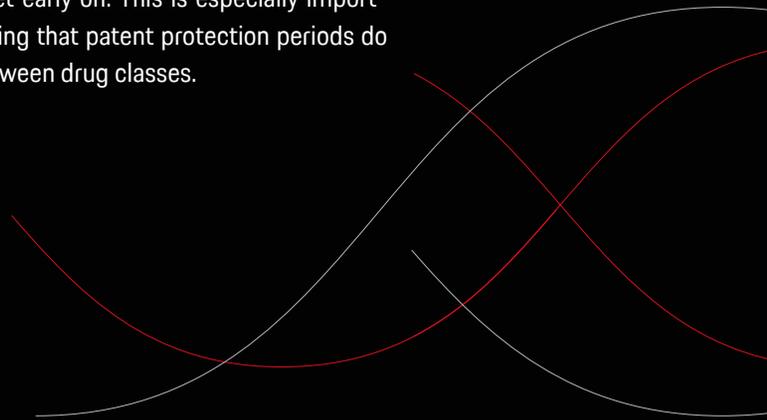
To summarize the challenges faced in the initial stages of research and discovery, predicting the medical profile of NGTs is a complex task. This complexity poses a significant risk to the success rate of clinical development. It is essential to understand that NGTs are innovative therapeutic treatments that require extensive research and development to determine their efficacy and safety profiles. Accurately predicting their medical profile is crucial to ensure their success in clinical trials and eventual approval for widespread use in humans. Therefore, addressing the challenges of immunogenicity and animal models is key to advancing the likelihood of success for NGTs from an early stage.

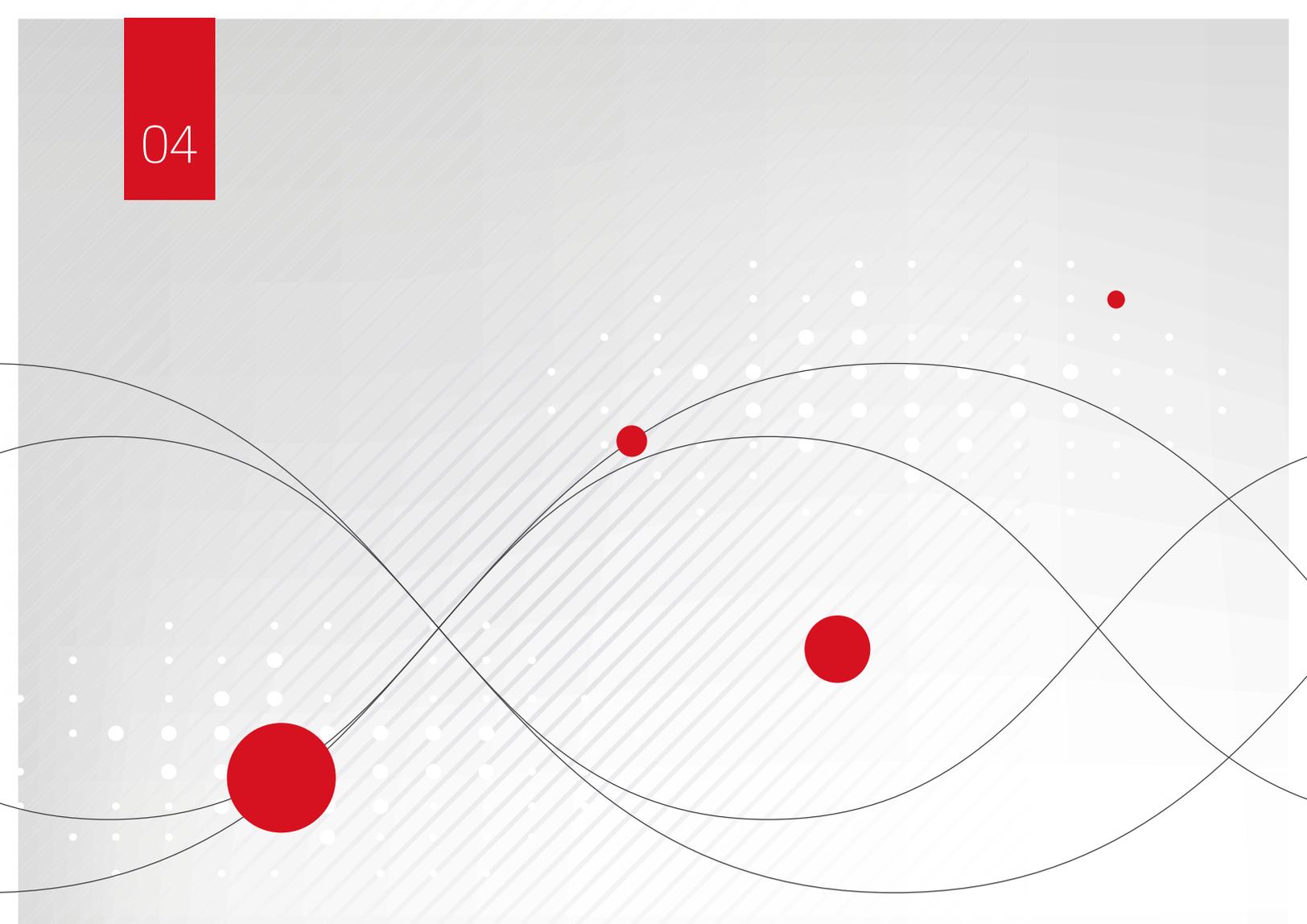
Additionally, there is a multitude of challenges faced by pharma companies in NGT development, relating to a variety of factors. Firstly, the limited patient pool makes it difficult to identify, diagnose, and recruit eligible patients. Additionally, the existence of standard-of-care therapies in the target indication can discourage patients from joining NGT trials. Furthermore, the data gathered from trials with a small number of patients often lack statistical power, questioning their validity and acceptance by payers and providers. Unclear clinical trial guidelines for NGTs complicate trial setup and planning, increasing the risk of trial termination. The heterogeneity of the patient population's pretreatments raises concerns about data reliability. Lastly, the use of standardized endpoints for assessing NGT efficacy is questionable, as these therapies may be highly effective in specific subpopulations without predefined endpoints, and the lack of standardized endpoints among regulatory bodies adds uncertainty to the acceptance of clinical trial data in late-stage development.

Also, the production and scale-up of NGTs post-regulatory approval present significant challenges. Establishing the entire value chain, including new manufacturing and distribution standards, is crucial. Manufacturing capabilities, material

management, and quality control require attention. However, the novelty and complexity of NGTs contribute to talent and infrastructure shortages, necessitating high-risk investments from pharma companies. Nonetheless, manufacturing failures can still occur, leading to supply shortages. Additionally, the delicate nature of NGTs demands closed systems for safe transport. Rigorous quality control and testing are essential to ensure purity, potency, identity, and safety. Specialized equipment, expertise, and protocols are vital for successful NGT production.

In the advanced stage of NGT development, industry players may also face challenges in pricing and reimbursement. BioMarin's Roctavian and Bluebird Bio's Zynteglo are two exemplary cases, that experienced delays in Europe due to pricing disputes. The high development costs for NGTs pose a risk for manufacturers, as payers are reluctant to cover substantial expenses while education on beneficial results in the long term is complex. Successful market entry thus does not only require educating payers, but also patients, healthcare providers, and policymakers. Figuring out a viable balance between setup costs and accessible prices is crucial to build the foundation for a successful commercialization. When it comes to the actual launch of NGTs, the seamless functionality of closed-loop manufacturing is crucial for precise drug administration. A special emphasis should be placed on a fast scaling of capacities, as market demands should be met early on. This is especially important, considering that patent protection periods do not differ between drug classes.



An abstract graphic featuring several overlapping circles of varying sizes and colors (red and white) on a light gray background with a subtle grid pattern. The circles are arranged in a way that suggests a network or a path. The red circles are prominent, while the white ones are smaller and more numerous.

IMPERATIVES FOR CREATING A FUTURE READY NGT ORGANIZATION

While the challenges in the NGT space are pronounced and will certainly keep pharma companies busy over the short and medium term, there are several strategic levers with which the industry

can make a leap forward. Some companies are already paving the way and best practices can be found along the complete value chain (Figure 10).

RESEARCH & DEVELOPMENT



EXAMPLE



Building innovative facilities for gene therapy R&D in Philadelphia (\$ 550 M) & Boston (\$ 700 M) respectively

SUPPLY CHAIN



EXAMPLE



Built its own 67,000 sq. ft. plant for producing viral vectors, approved by FDA in late 2022

MANUFACTURING & SCALE-UP



EXAMPLE



Automated approaches are being developed to simplify production & increase success

REGULATORY PROCESSES



EXAMPLE



Used results from 2 real-world evidence studies on Kymriah to back safety profile

PRICING & REIMBURSEMENT



EXAMPLE



Deployed outcomes-based agreements* for Zolgensma & Kymriah in the United States

GO-TO-MARKET & ROLLOUT



EXAMPLE



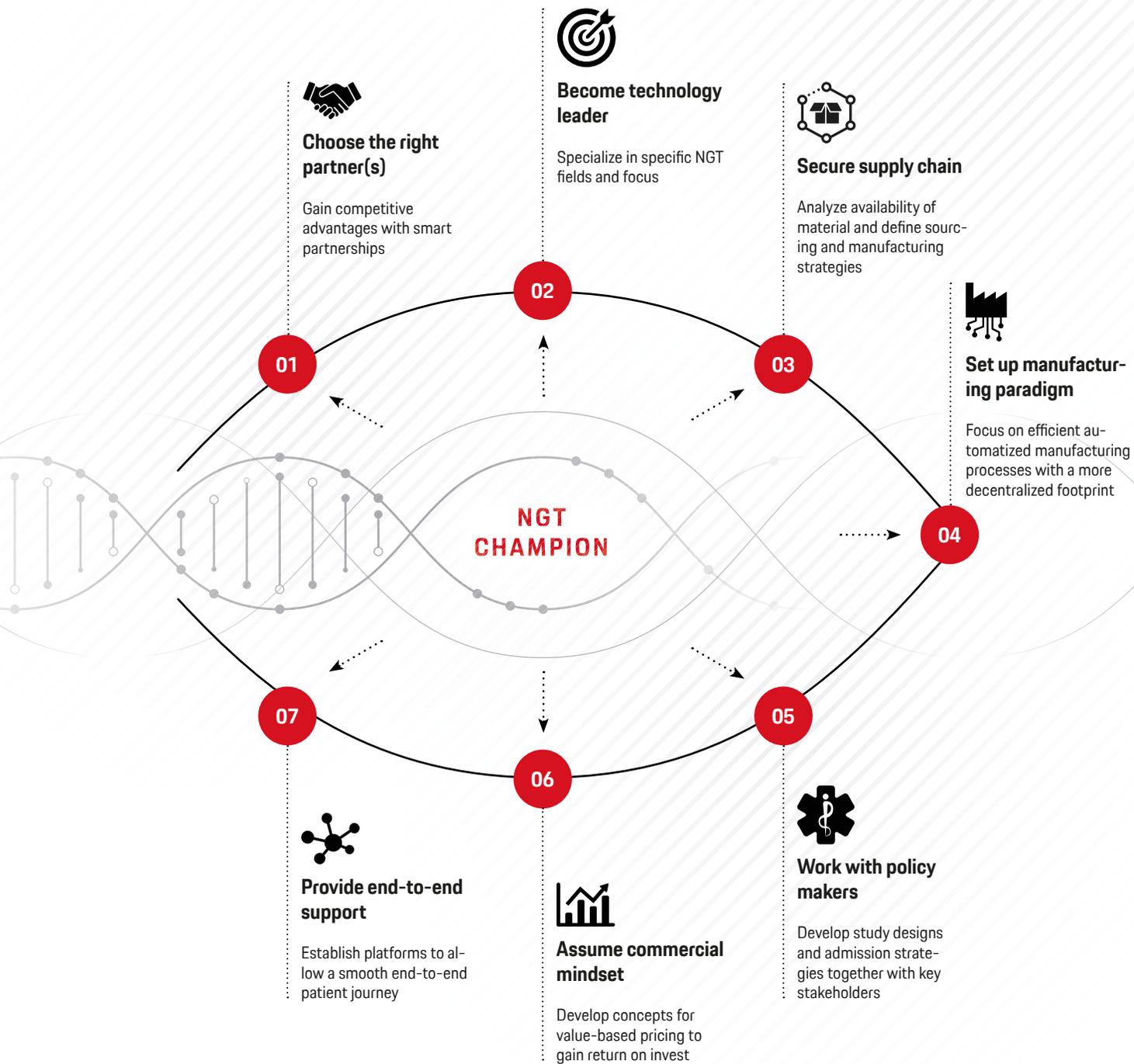
Providing end-to-end support across CAR-T journey with digital tool (CellTherapy360)

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Fig. 10. Best practices by forerunners based on a Porsche Consulting Analysis on publicly available information show promising avenues towards future success of NGTs³² Source: Fierce Pharma; IPG Health

* Of 25 FDA-approved CGTs, only four products (incl. two from Novartis) have publicly identifiable OBAs in place

Following seven imperatives (Figure 11), pharma companies can adjust their operating model to better meet the demands of NGTs and set themselves up as future leaders in the space.



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Fig. 11. Imperatives for a winning NGT organization

01

Scout for the right partner and choose the right alliance model

To secure the best future profit and revenue pools within the NGT space, pharma companies must first envision their prospective role in the value chain based on their strategic direction and inherent capabilities. In the process, they decide which technological platform to acquire or build up and how wide the scope of activity should be. Once the vision is set, it comes down to choosing the right partners, as it is the specialized research networks and biotechnology companies that have developed cutting-edge NGT know-how throughout the last decade. Besides selecting the right partners and acquiring rights to proprietary platforms, the right mode of collaboration/alliance model must be elaborated upon.

Leading players in the field of NGTs have successfully established partnerships using a variety of approaches ranging from targeted licensing to full-scale acquisitions.³³ Partnerships have been built with three types of external parties—early-stage, pre-IPO companies, publicly listed

advanced therapy asset and technology companies, and academic institutions that can receive direct funding. While leading pharma companies in the NGT space have largely relied on acquiring biotechnology companies with advanced technology platforms—BMS's \$ 74 B acquisition of Celgene, Novartis' \$ 8.7 B acquisition of AveXis, Roche's \$ 4.8 B acquisition of Spark Therapeutics—the general trend suggests a shift towards a more collaborative partnering approach with licenses accounting for a major share of transactions. It becomes obvious that aside from building internal capabilities either in the form of an autonomous NGT subsidiary or integrated NGT business units, external partnerships, in the form of traditional license agreements or collaborations with academic centers, are vital to excel in the competitive NGT space. With decreasing transaction activity over the preceding two years (Figure 12), however, the success of existing partnerships and alliances becomes more important than ever as the NGT space reaches a state of maturity.⁵

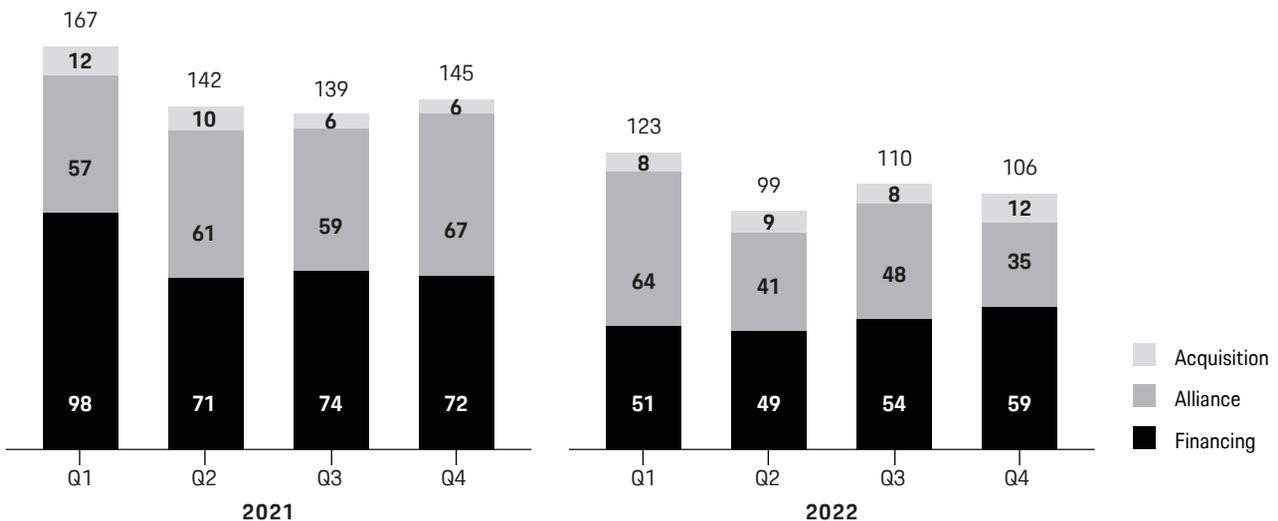


Fig. 12. Development of transactions in the NGT space between 2021 and 2022⁵

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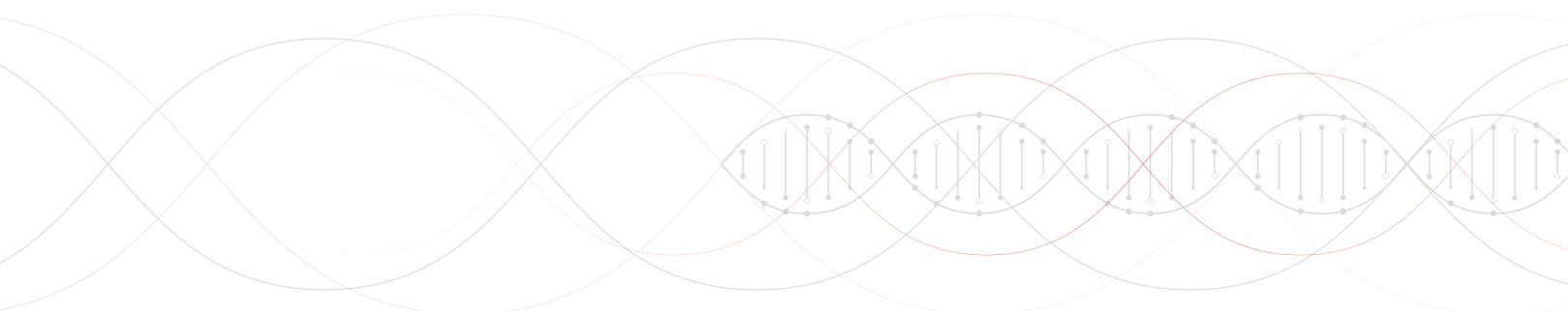
Source: ASGCT

02

Specialize and become a technology leader

As already mentioned, finding the right position in the value stream to identify gaps and eventually close gaps with partnerships is one important topic. However, NGTs are a wide field and most companies do not have the capacities to win in all three therapy types: cell therapies, gene therapies, and nucleic acid-based therapies. So, defining the right focus is key to success. Here it is important to evaluate one's own capabilities, possible synergies, and future growth options. Once the focus has been defined, strategic investments are important to secure technology leadership. In this context, Roche and Eli Lilly are good examples. Roche invested \$ 550 million via its daughter company Spark Therapeutics in a new state-of-the-art gene therapy innovation center. It is located on Drexel

University's University City campus in the heart of Philadelphia, ensuring strong collaboration with academia and direct contact with new talents.³⁴ Eli Lilly built the Lilly Institute for Genetic Medicine to focus on RNA- and DNA- based medicines for \$700 million in Boston's Seaport neighborhood. The site will also include a shared space—modelled after Lilly Gateway Labs in San Francisco—to support biotech start-ups in the Boston area. This space will provide dedicated and configurable lab and office space, access to Lilly scientists, and opportunities for collaboration.³⁵ Overall, to fully realize technology leadership, it is also important to leverage the potential of innovative R&D solutions like AI and data analytics.³⁶



03

Secure the supply chain

For NGTs the global supply chain is not as mature as for small molecules and biologics. Here, it is critical to have transparency on the supply chains and the availability of material at any time. Key questions are: What is critical raw material? What are the global capacities? What are reliable suppliers? What are potential future risks?

Having the right supplier for critical material is crucial. As mentioned earlier, many CDMOs are now specializing in NGTs. However, some are still

struggling with capacity and quality issues. So, for certain materials it makes sense for companies to leverage backward integration as a means to building operational resilience and acquiring proprietary process and technology know-how. Gilead is an example of a company assuming greater control over the supply chain by building its own 67,000 sq. ft. plant for producing viral vectors. It was approved by the FDA in late 2022. Gilead cites its three global manufacturing centers as "a real competitive strength."³⁷

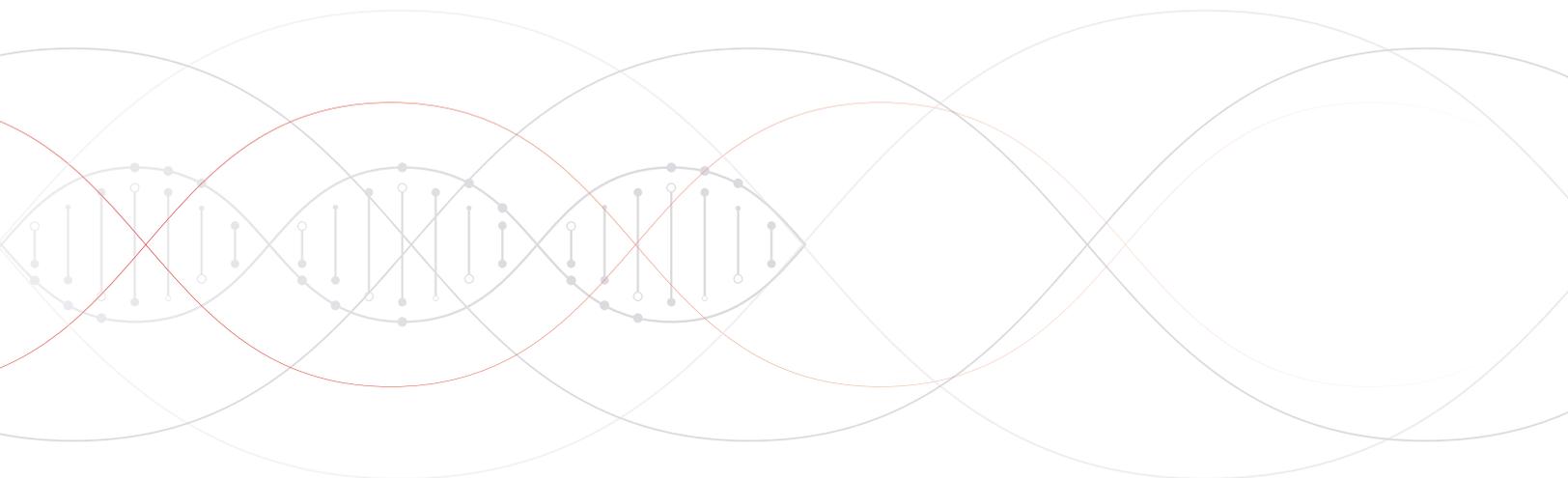
04

Set up a new manufacturing paradigm

When it comes to manufacturing, pharma companies must adapt a completely new mindset, as the requirements for manufacturing capabilities and material management are changing considerably. NGTs require specialized handling and a closed-loop manufacturing infrastructure for the transfer of genetic and cellular material. Depending on the type of NGT, the entire manufacturing footprint may need to be redesigned (Figure 13). Especially for cell therapies, a more decentralized footprint is required.

Best manufacturing practices and setups are identified in the clinical trial phases and subsequently transferred during scale-up. In this vein, technology transfer and process development play a decisive role in building up commercial-scale NGT production from small-scale laboratory environments. Engaging with regulators early in the process and enforcing phase-appropriate quality policies and their implementation is another critical pillar to reach a commercial grade manufacturing infrastructure.

Manufacturing at scale is still one of the key bottlenecks in the industry. It is not without reason that the White House Office of Science and Technology Policy lists “biomanufacturing of cell-based therapies” and “advanced techniques in gene editing” as two themes in one of their latest executive orders. More important, however, is the quantified goal outlined: manufacturing cost of cell-based therapies should be decreased tenfold and production capacity of gene-editing systems should reach at least five million doses over the next two decades.³⁸ Currently, both large pharma companies and small biotechnology companies are struggling with the manufacturing process; so far, the solution has been to involve specialized contract development organizations or direct competitors. In April 2023, Johnson & Johnson and Legend Biotech signed a three-year manufacturing contract with Novartis to tackle supply issues tied to the cell therapy product Carvykti.¹⁹ In 2022, Novartis in turn experienced huge batch variability problems with its Kymriah drug, leading to a decline of sales compared to 2021 (Figure 15).





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Fig. 13. Typical challenges in the NGT manufacturing process

In order to tackle the many challenges of NGT manufacturing and to become more efficient, processes are being automatized more and more. Companies like Ori Biotech and Cellares offer end-to-end manufacturing process automation for cell and gene therapies in a closed platform. The Multiply Labs company specializes in robots for cell

therapies. Companies like these promise a reduction of around 70 percent in costs and a threefold reduction in process failure rates.³⁹ Nonetheless, the increasing automation also enables a much more decentralized manufacturing footprint while retaining globally standardized processes and quality standards.

05

Work hand in hand with patients and policymakers

During clinical development and regulatory approval, it comes down to patients, HCPs, and regulators. Since NGTs focus often on diseases with small patient populations, pharma companies must better understand patient journeys by engaging with families, treatment centers, and biotech-healthcare providers. Additionally, engagement with patient advocacy groups can offer valuable insights, as they can be regarded especially close to patients' and caregivers' reality of life. Only a deep understanding of what patients are going through, from early diagnosis to post-treatment monitoring,

will make pharma companies trusted partners with the capability to adequately accompany patients through their clinical trial experience. In addition to winning patients' trust, demands of regulators must be identified and addressed early on to set up clinical trials for success. Pharma companies should proactively engage with regulators to identify innovative ways of accounting for the specificities of NGTs and define a clear path forward for the evaluation of candidates. Specifically, building a mutual understanding of NGT endpoint selection and value assessment is key.

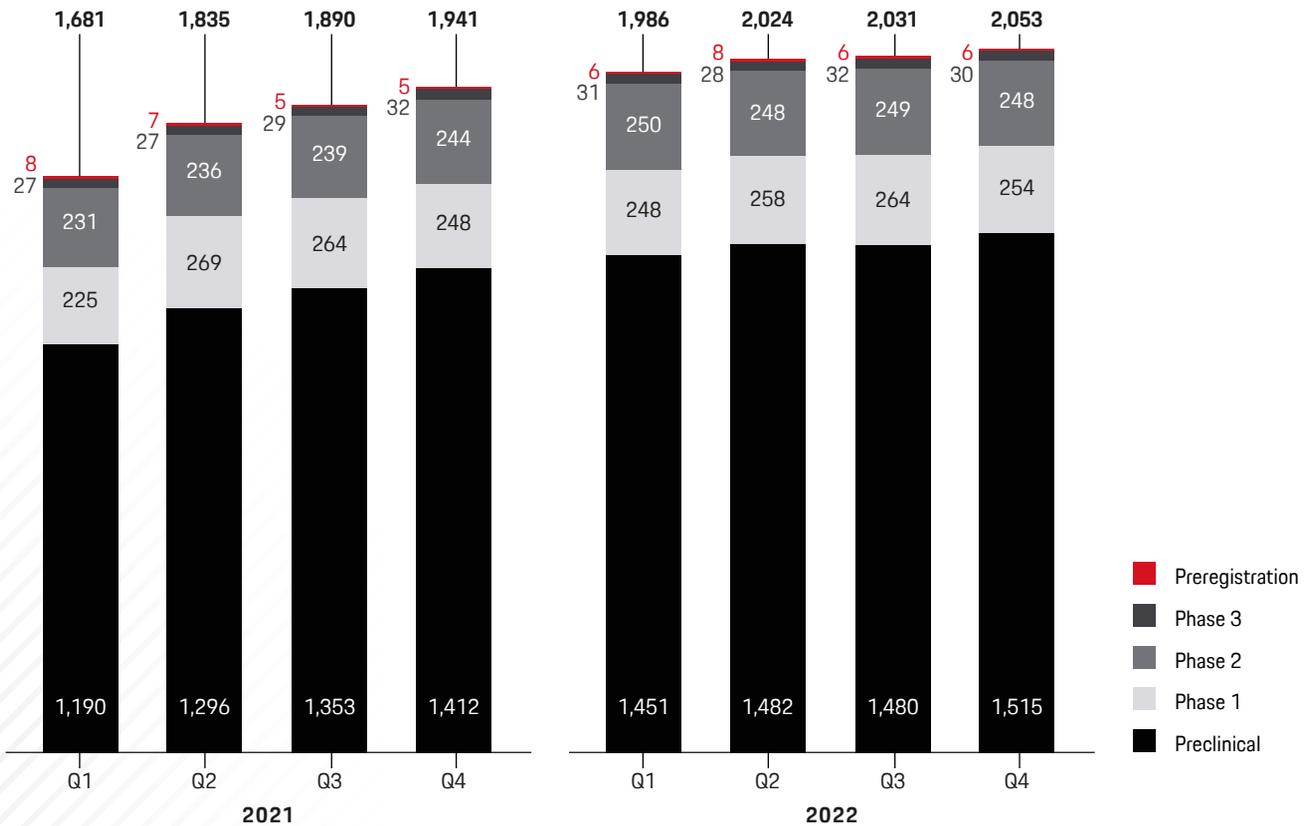


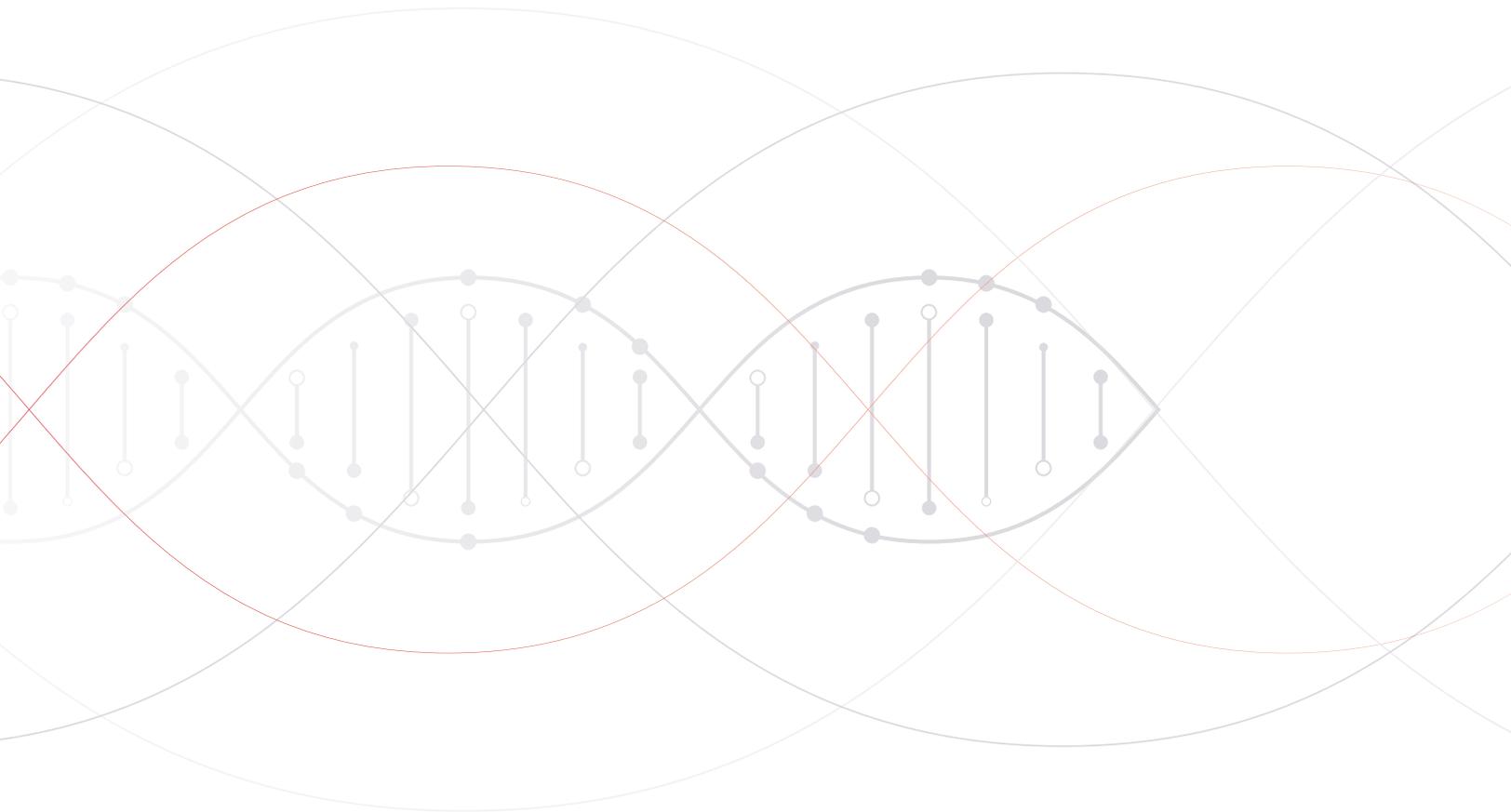
Fig. 14. Number of gene-based therapies in development pipelines in 2021 and 2022 per quarter⁴⁰

© Porsche Consulting.

Source: ASGCT

Pharma companies have come forward with clear strategies to make their case for NGTs, addressing both patients and policymakers. To improve recruitment, enrollment, and retention, the minimization of patient burden and optimization of patient experience is key.⁴¹ In this vein, financial and non-financial deterrents are addressed by pharma companies, with special patient access programs allowing patients to overcome the hurdles and pain points associated with clinical trial participation. Building visibility and garnering support through special initiatives already in early stages of development lays the foundation for future acceptance and support by patients and advocacy groups. Equally the support of policymakers must be won with compelling argumentation. ASGCT, for instance, has impacted the FDA in the creation

of the first guidance on gene therapies for neurodegenerative diseases and a policy for using multiple versions of NGTs in early-phase clinical trials. While the interest group is influencing regulatory decisions, it acknowledges the importance of early and frequent communication between the FDA and sponsors in the pursuit of NGT trials. As the primary source of failure has been and remains an inability to demonstrate efficacy—57 percent of failed phase 3 trials are linked to inadequate efficacy—pharma companies must engage with regulators to make sure that they choose a sound trial design as well as appropriate statistical endpoints.⁴⁰ With a growing number of gene-based clinical trials,⁵ defining strategic approaches that address patients and regulators is critical to maximize prospects of success (Figure 14).



06

Assume a stakeholder-driven commercial mindset

As NGT sales rise (Figure 15), it is important to address the challenges of NGT pricing and reimbursement (P&R). Pharma companies must drive the transition from a volume-based towards a value-based pricing approach with novel contracting solutions. With traditional approaches to P&R mainly focusing on the size of target populations and comparative assessment of clinical benefits, payers, providers, and HTA (health technology assessment) bodies are facing unprecedented challenges. High upfront costs as well as limited evidence are hindering them to boost NGT access. Consequently, pharma companies must change their P&R strategies to appeal to stakeholder concerns and provide appropriate solutions. By shifting the focus to value and leveraging innovative contracting solutions, P&R strategies can reflect the true benefits and outcomes provided

by NGTs, ensuring that their costs align with the value they bring to patients and the healthcare system. Innovative contracting solutions may include outcome-based agreements, installments, coverage with evidence generation, subscription models, and payer reinsurance.⁴² Bluebird Bio, for example, whose price negotiations in the European market were unsuccessful (as mentioned previously) chose a different strategy in the US, opting to address payers' needs by devising an innovative outcome-based contract that includes a single upfront payment and up to 80 percent risk sharing.⁴³

Furthermore, pharma companies must identify other relevant counterparts along the different stages of the commercialization process and engage with them using convincing messaging of clinical and non-clinical benefits as well as flagging potential risks and contingencies. In the end, the widespread adoption of NGTs hinges upon the acceptance and benevolence of stakeholders whose concerns must be addressed with innovative approaches and genuine engagement.

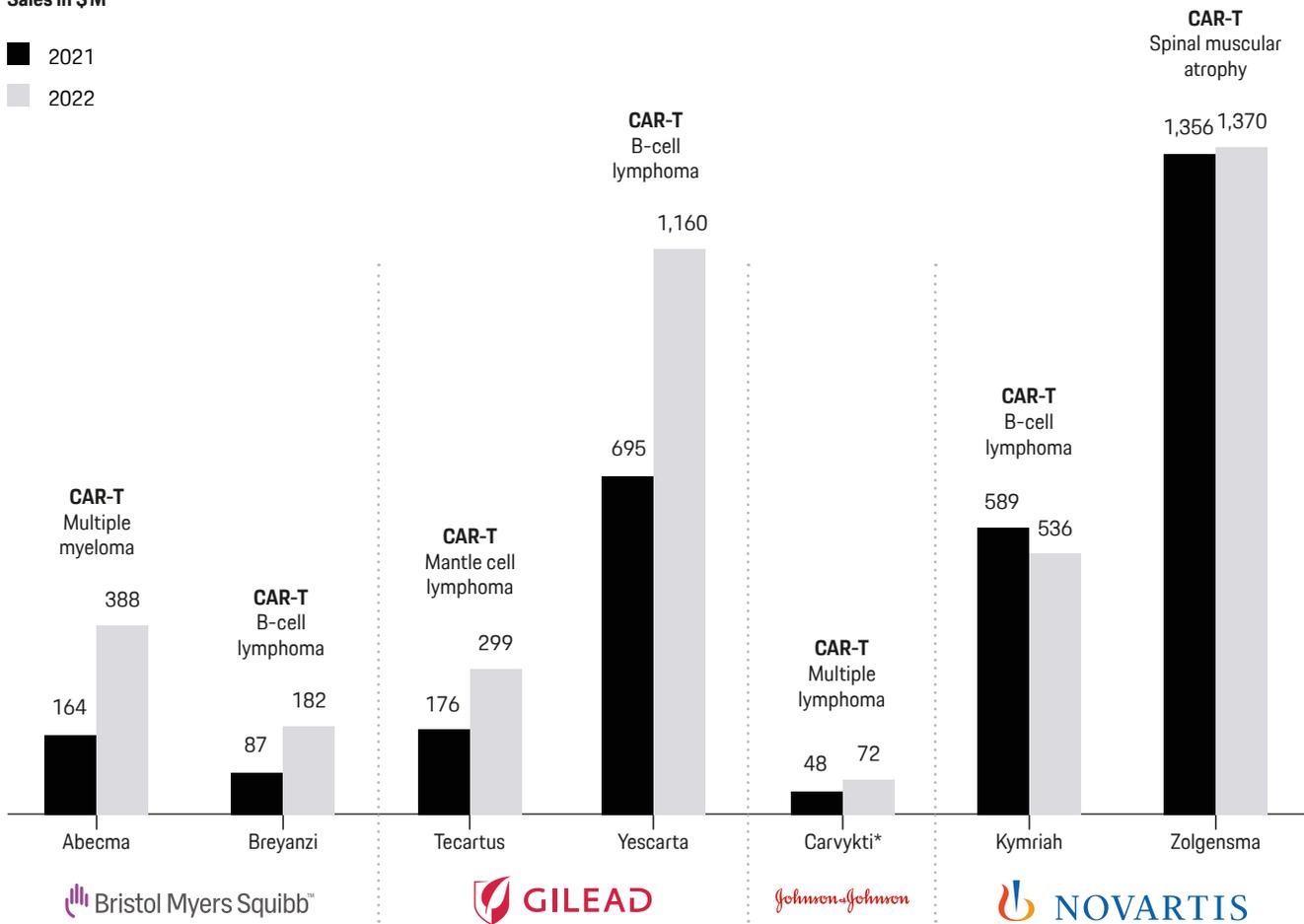


Pharma companies must drive the transition from a volume-based towards a value-based pricing approach with novel contracting solutions.

Johnson & Johnson's pharmaceuticals division Janssen and Gilead Sciences have joined the UK Advanced Therapy Treatment Centers (ATTC) network program to address the unique and complex challenges of bringing advanced therapy medicinal products to patients. The three-year program, which is operated within the NHS and funded by the Industrial Challenge Strategy Fund, brings together multiple players from the industry and the public sector to develop the necessary processes, skilled staff, and infrastructure required to accelerate the uptake of NGTs. In their common pursuit, the parties will conduct a gap analysis of the CAR-T patient referral pathways involving numerous stakeholders, including treatment centers, patient advocacy groups, and key opinion leaders.^{44,45}

Sales in \$M

■ 2021
■ 2022



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Fig. 15. Sales volume of leading NGT products in 2021 and 2022

Source: ASGCT

07

Provide end-to-end support for specific indications

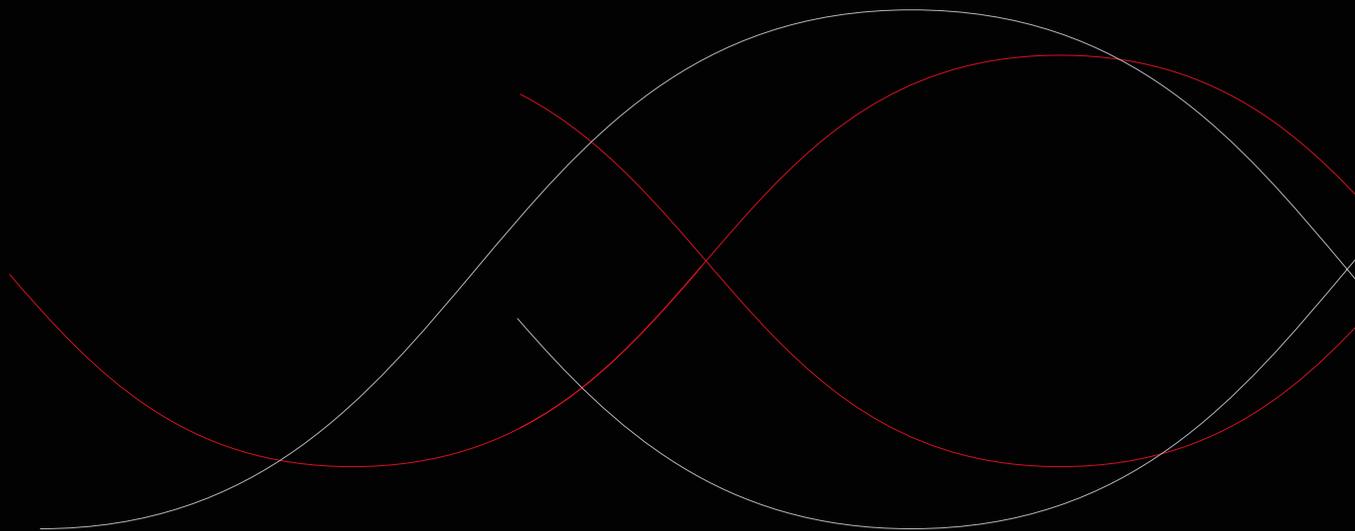
NGTs can include complex therapies. A clear process support for caregivers and patients is key. A good example of an elaborated end-to-end solution is CellTherapy360 from Bristol Myers Squibb. This online tool guides treating providers, referring

providers, patients, and caregivers through the complete process of cell therapies. This way a patient-centric customer journey can be established, and outcomes improved.

*Approval in 2022—therefore: 2022 vs. 2023

Conclusion

NGTs are a new field for Pharma companies. Top players are positioning themselves to leverage the huge opportunities. Building up expertise and gaining competitive advantage in selected fields is key. With this positioning the top players are unveiling new pathways of curing diseases and opening new revenue pools. However, entering the NGT field entails certain risks. Significant investments need to be done, which also need to result in significant return on investments. Nonetheless, the huge opportunities and the risk of missing this innovative trend imply the worth of entering this field. The complexity requires an extremely strategic and elaborated approach. If companies follow the seven depicted imperatives, they will have the chance to become real NGT champions.



IN BRIEF

- 01** Innovation in cell and gene therapy has been ongoing since 1970, but in recent years, approvals of next-generation therapeutics have increased sharply, resulting in a fundamental change in the pharmaceutical landscape.
- 02** Within the broader pharmaceutical market landscape, NGTs already demonstrate a tremendous pace of growth. To make use of this potential, most major pharma companies are already conducting trials or have even successfully launched NGTs on the market.
- 03** Entering the NGT field is far from easy, as challenges present themselves along the whole value chain. This paper creates awareness of the most complex challenges and focuses on the specific characteristics to be considered.
- 04** To tackle the challenges presented here, pharmaceutical players should follow seven imperatives to successfully play the NGT field. This paper examines best practices of companies that follow these imperatives.
- 05** NGTs present tremendous commercial and therapeutic opportunities for companies that are prepared to embark on this challenging journey. Having a deep understanding about this new class of drugs will present a strategic necessity for the leading pharma companies in the future.

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As a leading consultancy for putting strategies into practice, we have a clear mission: we generate competitive advantage on the basis of measurable results. We think strategically and act pragmatically. We always focus on people—out of principle. This is because success comes from working together with our clients and their employees. We can only reach our aim if we trigger enthusiasm for necessary changes in everyone involved.

Appendix

References

- (1) U.S. Food & Drug Administration (2017): FDA approval brings first gene therapy to the United States; <https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states>
- (2) European Federation of Pharmaceutical Industries and Associations (2022): The Pharmaceutical Industry in Figures; <https://efpia.eu/media/637143/the-pharmaceutical-industry-in-figures-2022.pdf>
- (3) BioNTech SE (2023): Press Release—BioNTech Announces Fourth Quarter and Full Year 2022 Financial Results and Corporate Update; <https://investors.biontech.de/news-releases/news-release-details/biontech-announces-fourth-quarter-and-full-year-2022-financial>
- (4) Handelsblatt (2023): Bayer meldet Erfolg bei erster Zelltherapie gegen Parkinson; <https://www.handelsblatt.com/unternehmen/industrie/pharmakonzern-bayer-meldet-erfolg-bei-erster-zelltherapie-gegen-parkinson/29229260.html>
- (6) American Society of Gene + Cell Therapy (2023): Gene, Cell, & RNA Therapy Landscape – Q4 2022 Quarterly Data Report; https://asgct.org/global/documents/asgct_citeline-q4-2022-report_final.aspx
- (5) Porsche Consulting
- (7) American Society of Gene + Cell Therapy (2022): Gene Therapy Basics; <https://patienteducation.asgct.org/gene-therapy-101/gene-therapy-basics>
- (8) Porsche Consulting
- (9) U.S. Food & Drug Administration (2023): FDA Approves First Gene Therapies to Treat Patients with Sickle Cell Disease. In FDA News Release. Retrieved December 13, 2023; <https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease>
- (10) Torrey Partners (2021): The Pharma 1000 - Value share of the pharmaceutical market worldwide in 2015 and 2021. In Statista. Retrieved June 19, 2023; <https://www.statista.com/statistics/1245284/pharmaceutical-value-share-worldwide-by-subsector/>
- (11) IQVIA (2023): Revenue of the worldwide pharmaceutical market from 2001 to 2022. In Statista. Retrieved June 19, 2023; <https://www.statista.com/statistics/263102/pharmaceutical-market-worldwide-revenue-since-2001/>
- (12) Senior, Melanie (2023): Fresh from the biotech pipeline: fewer approvals, but biologics gain share. In Nat Biotechnol, Volume 41, 174-182; <https://doi.org/10.1038/s41587-022-01630-6>

-
- (13) AbbVie Inc. (2023): 2023 Notice of Annual Meeting & Proxy Statement;
<https://investors.abbvie.com/static-files/e3047152-75b3-44b3-95a8-18e4fa991768>
- (14) Reuters (2023): AbbVie sees 37% drop in Humira sales this year as biosimilars hit U.S. market;
<https://www.reuters.com/business/healthcare-pharmaceuticals/abbvies-2023-profit-forecast-misses-humira-faces-heat-rivals-2023-02-09>
- (15) Porsche Consulting Analysis based on annual reports of involved companies
- (16) Porsche Consulting Analysis based on annual reports of involved companies and websites of EMA and FDA
- (17) Taylor, Phil (2019): Gilead drops anti-BCMA CAR-T from Kite, takes \$ 820 M charge:
<https://www.fiercebitech.com/biotech/gilead-drops-anti-bcma-car-t-from-kite-takes-820m-charge>
- (18) Liu, Angus (2021): Bristol Myers hits CAR-T manufacturing bottleneck as Abecma demand outstrips supply:
<https://www.fiercepharma.com/manufacturing/bristol-myers-hits-car-t-manufacturing-bottleneck-as-abecma-demand-outstrips-supply>
- (19) Taylor, Nick P. (2022): Demand for viral vectors seen outpacing capacity growth despite investment surge. In: The Science Advisory Board:
<https://www.scienceboard.net/index.aspx?sec=ser&sub=def&pag=dis&ItemID=4733>
- (20) Lehmicke, Michael (2019): Manufacturing Cures: Infrastructure Challenges Facing Cell And Gene Therapy Developers. In: In Vivo Pharma Intelligence,
<https://in vivo.citeline.com/IV124277/Manufacturing-Cures-Infrastructure-Challenges-Facing-Cell-And-Gene-Therapy-Developers>
- (21) Pagliarulo, Ned (2019): Novartis still hasn't solved its CAR-T manufacturing issues:
<https://www.biopharmadive.com/news/novartis-kymriah-car-t-manufacturing-difficulties-cell-viability/568830/>
- (22) Palmer, Eric (2018): Novartis, still struggling with Kymriah manufacturing, is providing some out-of-spec doses to patients who ask:
<https://www.fiercepharma.com/manufacturing/novartis-still-struggling-kymriah-manufacturing-providing-some-out-spec-doses-to>
- (23) Yang, Guang; Liu, Ling; Suhendra, Michelle; Agarwal, Stuti; Smith, Jeffrey F. (2022): Disruptions in the development of cell and gene therapies. In: Nature Reviews Drug Discovery, Volume 21, Issue 3, 171;
<https://doi.org/10.1038/d41573-022-00004-6>
- (24) Carvalho, Marta; Martins, Ana P.; Sepodes, Bruno (2019): Hurdles in gene therapy regulatory approval: a retrospective analysis of European Marketing Authorization Applications. In: Drug Discovery Today, Volume 24, Issue 3, 823-828;
<https://doi.org/10.1016/j.drudis.2018.12.007>
- (25) Pharmaceutical Technology (2022): Inflation, drug pricing and reimbursement constraints will challenge pharma sector:
<https://www.pharmaceutical-technology.com/comment/inflation-pharmaceutical-sector/>

-
- (26) *The Pharma Letter* (2023): BioMarin treats first patient in Europe with its gene therapy Roctavian:
<https://www.thepharmaletter.com/article/biomarin-treats-first-patient-in-europe-with-its-gene-therapy-roctavian>
- (27) Pagliarulo, Ned (2021): Bluebird to withdraw gene therapy from Germany after dispute over price. In: *BiopharmaDive*:
<https://www.biopharmadive.com/news/bluebird-withdraw-zynteglo-germany-price/598689/>
- (28) Manalac, Tristan (2023): Bluebird Pins Hopes on Zynteglo Uptake, FDA Verdict Amid Cash Constraints. In: *BioSpace*:
<https://www.biospace.com/article/bluebird-pins-hopes-on-zynteglo-uptake-looming-fda-verdict-amid-cash-constraints/>
- (29) Cohen, Joshua (2023): Cell And Gene Therapies Face Persistent Manufacturing Capacity Constraints. In: *Forbes*: <https://www.forbes.com/sites/joshuacohen/2023/07/06/cell-and-gene-therapies-face-persistent-manufacturing-capacity-constraints/>
- (30) Verdin, Paul; Urquhart, Lisa (2019): Next-generation therapeutics: cell and gene therapy gathers pace. In: *Biopharma Dealmakers*, B15-B17; doi: <https://doi.org/10.1038/d43747-020-00715-y>
- (31) Evaluate Pharma
- (32) Porsche Consulting analysis based on publicly available information
- (33) Smith, Devyn M.; Culme-Seymour, Emily J.; Mason, Chris (2018): Evolving Industry Partnerships and Investments in Cell and Gene Therapies. In: *Cell Stem Cell*, Volume 22, Issue 5, 623-626; <https://doi.org/10.1016/j.stem.2018.03.004>
- (34) Spark Therapeutics (2021): Spark Therapeutics to Invest \$ 575 M in New 500k Square Foot State-of-the-Art Gene Therapy Innovation Center on Drexel's University City Campus:
https://sparktx.com/press_releases/spark-therapeutics-to-invest-575m-in-new-500k-square-foot-state-of-the-art-gene-therapy-innovation-center-on-drexels-university-city-campus/
- (35) Eli Lilly and Company (2022): Lilly Institute for Genetic Medicine, Boston, Massachusetts, USA:
<https://www.pharmaceutical-technology.com/projects/lilly-institute-genetic-medicine-boston/>
- (36) Eli Lilly and Company (2022): You Have Questions About Genetic Medicine -- Lilly Has Answers:
<https://www.lilly.com/news/stories/genetic-medicine>
- (37) Becker, Zoey (2023): Gilead, looking to grow in oncology, posts big gains for its cell therapies and Trodelvy:
<https://www.fiercepharma.com/pharma/gilead-confident-cancer-sales-car-t-manufacturing-capabilities>
- (38) The White House Office of Science and Technology Policy (2023): Bold goals for U.S. biotechnology and biomanufacturing – Harnessing Research and Development to further societal goals:
<https://www.whitehouse.gov/wp-content/uploads/2023/03/Bold-Goals-for-U.S.-Biotechnology-and-Biomanufacturing-Harnessing-Research-and-Development-To-Further-Societal-Goals-FINAL.pdf>
- (39) Porsche Consulting analysis based on publicly available company information

(40) Porsche Consulting analysis, ASGCT

(41) Fogel, David B. (2018): Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review. In: *Contemporary clinical trials communications*, Volume 11, 156-164; <https://doi.org/10.1016/j.conctc.2018.08.001>

(42) Sabatini, Marco T.; Xia, Tia; Chalmers, Mark (2022): Pricing and Market Access Challenges in the Era of One-Time Administration Cell and Gene Therapies. In: *Pharmaceutical Medicine*, Volume 36, Issue 5, 265-274; <https://doi.org/10.1007/s40290-022-00443-x>

(43) Reuters (2022): Bluebird falls on worries over \$ 2.8 m In gene therapy's commercial success: <https://www.reuters.com/business/healthcare-pharmaceuticals/bluebird-bio-falls-worries-over-gene-therapys-commercial-success-2022-08-18/>

(44) Advanced Therapy Treatment Centres:
<https://www.theattcnetwork.co.uk/about>

(45) Janssen Pharmaceutica N.V. (2023): Janssen UK: Collaboration Agreements:
https://www.janssen.com/uk/sites/www_janssen_com_uk/files/janssen_uk_website_collaboration_agreements_updated_jan_2023.docx

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