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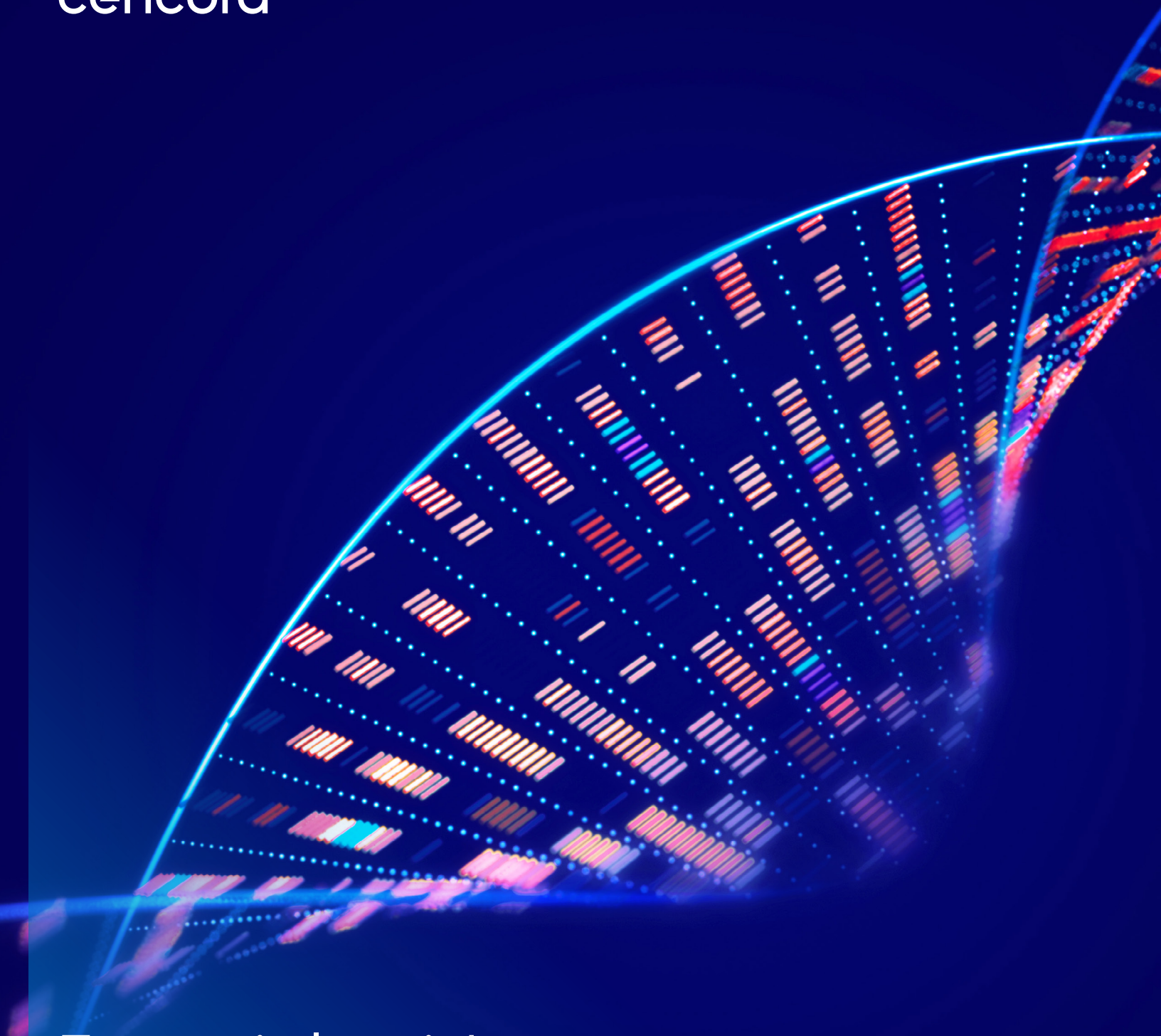

Essential guide to cell and gene therapy commercialization

Six considerations when bringing your new product to market

Having devoted your time, expertise, and financial resources to the development of a transformative cell or gene therapy that improves patients' lives, ensuring that patients can truly reap the benefits of your innovation is essential. Whether you are an established player or an emerging innovator, there are crucial commercialization considerations to take into account. Unlock the full potential of your product and make the most of your investments by following this step-by-step guide, which will provide valuable insights to help you navigate the market and maximize the impact of your therapy.

Cell and gene therapy: a dynamic and innovative space

Over the past few decades, there has been incredible progress in healthcare and personalized medicine, leading to the establishment of cell and gene therapy (CGT), an offshoot of precision medicine. These advanced therapies have not only revolutionized treatment options but also opened new avenues for targeted and individualized healthcare. While investors pulled back in 2022, a series of initial public offerings (IPOs) in the first six weeks of 2024 has put the sector on its strongest pace since the 2021 peak[1]. They continue to be keen on these one time therapies with curative intent, and the annual market growth rate is expected to be about 18.3% from 2023 to 2032[2]. Close to 3,000 CGTs are in development, ranging from preclinical through pre-registration. In Q4 2023, the number of gene therapies in Phase III clinical trials grew by 10%[3].

Key terms

Allogeneic therapies — Cells are manufactured in batches and originate from a donor who is not the patient

Autologous therapies — The patient's own cells are used as the therapeutic agent and are manufactured as a single lot

Cell therapy — Transplantation of live cells into a patient to repair damaged tissue or destroy diseased or infected cells

Chain of custody (COC) — Documentation and tracking of all points of transfer and control for a product or sample throughout its journey

Chain of identity (COI) — Maintaining documentation of the identity and traceability of a CGT throughout manufacturing, handling, storage, and distribution

Gene therapy — Adding, editing, or removing a gene in cells to treat or prevent disease

Good manufacturing practices (GMP) — A system to ensure products are consistently produced, documented, and controlled

With the advent of novel CGTs came a rapidly evolving field with unique hurdles to successful commercialization. Notable challenges in the space include patient access, alignment on regulatory requirements, manufacturing complexities, and market access. CGT development and administration involves complex patient and product journeys with unique safety and regulatory considerations. Therefore, drug developers will strongly benefit from a dedicated commercialization partner who can guide them through the entire process. This requires careful planning and timely orchestration of a growing number of stakeholders and decision makers. In this guide, we will outline six key considerations for commercializing your CGT asset(s). These resources will underscore the value of a dedicated full-service commercialization partner and give drug manufacturers tools to develop successful go-to-market strategies for these novel and life-changing therapeutics.

1. BIOPHARMADIVE. Biotech IPOs heated up to start 2024. Will the surge last? 5 Mar 2024. Accessed 19 Mar 2024. Available at: https://www.biopharmadive.com/news/biotech-ipo-venture-funding-outlook-2024/709084/
2. Precedence Research. Cell and Gene Therapy Clinical Trials Market Report by 2032. May 2023. Accessed 19 Mar 2024. Available at: https://www.precedenceresearch.com/cell-and-gene-therapy-clinical-trials-market
3. ASGCT. Gene,Cell, + RNA Therapy Landscape Report. Q4 2023 Quarterly Data Report. 12 Jan 2024. Accessed 19 Mar 2024. Available at: https://asgct.org/global/documents/asgct-citeline-q4-2023-report.aspx

01
Patient access and support: The driving force behind product success

Unique considerations for cell and gene

- **Patient health status.** CGT products are frequently utilized as treatments for terminal diseases, often serving as a last resort therapy; therefore, expedited manufacturing and delivery are of the utmost importance.
- **Targeted therapies for specific populations.** CGT drugs often treat rare diseases with limited patient populations. Qualifying for treatment is determined by a number of criteria, including genetic or other biological factors. Identifying eligible patients may be a challenge.
- **Health system capacity.** As the market sees an influx of new therapies, health systems must be adequately equipped to handle the growing patient volume. To accommodate the increasing scale, it will be necessary to streamline various processes, including benefit verification, patient education, treatment ordering and administration, as well as long-term follow-up.
- **Data collection.** Patients may transition between sites of care, providers, and insurance carriers, making it essential to implement a robust long-term data collection strategy.
- **Reimbursement.** Reimbursement processes can be complex, and payers may have specific requirements for reimbursement, such as prior authorization, appeals, and letters of medical necessity. It is therefore important to engage payers early and often when developing CGTs.
- **Limited sites of care.** Not all sites of care are equipped to store, handle, and manage CGTs, thereby significantly limiting available treatment options for patients. This creates a patient access barrier that can be alleviated with travel assistance and other patient service programs.

Navigating these obstacles can place a significant burden on patients, healthcare providers, and caregivers. Certain complexities arise from the nature of rare diseases, while others originate from the novelty of the modality. All stakeholders are simultaneously navigating unchartered territory.

When to start planning a patient services strategy? The earlier, the better.

While designing your pivotal trial, it is important to concurrently develop your patient services strategy. Initiating discussions early is crucial because it requires engaging multiple stakeholders, which can be time-consuming. Other factors to consider include reimbursement for site administration, establishing collaborations with patient foundations, and devising a plan for product delivery to patients. See Figure 1 below for an overview of the patient operations, support, and coordination cycle for cell therapy.

The process involves identifying and screening patients followed by referrals for enrollment and obtaining coverage. For complex autologous cell therapy, subsequent steps include coordinating apheresis, transportation from and back to the site of care, preconditioning, treatment administration, and long-term follow-up.

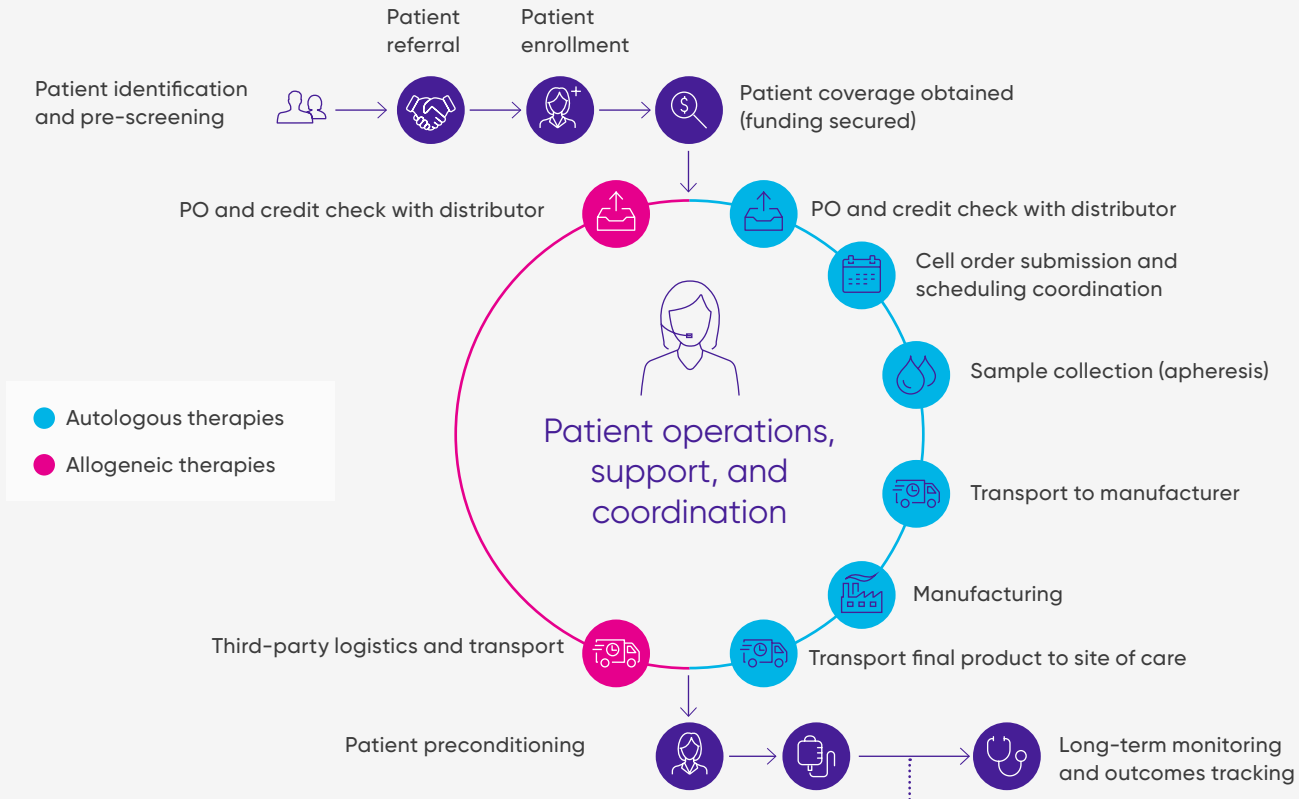

Figure 1: Overview of cell therapy patient operations, support, and coordination cycle

How a patient services partner can help

Patient services play an essential role in boosting providers' confidence regarding the reimbursement they may receive. They can provide various forms of support such as assisting with appeals, preparing prior authorization letters and letters of medical necessity, and offering travel-related assistance to patients.

A patient services partner will assist you in developing patient education materials that aid in preparing patients for treatment management, pre- and post-administration. Additionally, there should be a focus on care coordination and the capacity to monitor patients as they transition back to their homes.

Obtaining regulatory approval for CGTs necessitates having a comprehensive strategy for long-term data collection spanning up to 15 years[4]. To fulfill this requirement, a collaborative partner can employ various digital and remote strategies to maintain communication. By providing a customized yet adaptable service, a partner can effectively meet the complex coordination requirements of patients undergoing treatment. This ensures that these patients receive the necessary comfort and care they deserve after going through the demanding CGT treatment program.

4. Long Term Follow-Up After Administration of Human Gene Therapy Products. Guidance for Industry. The U.S. Food & Drug Administration. Jan 2020 Accessed 10 Apr 2023. Available at: https://www.fda.gov/media/113768/download

Further reading

Streamlining patient access to CGTs.
Gain a deeper understanding of the vital role patient services play in successful CGT launches.
Explore this topic

02
Regulatory considerations: Develop a plan sooner than you think

What is the importance of a regulatory strategy?

Drug development and regulatory considerations are closely intertwined. It is fundamental to formulate a robust strategy to address the concerns of regulators in order to bring a product to market safely and efficiently. A well-defined regulatory strategy offers several benefits:

- Leverages agency initiatives that facilitate a faster development process
- Mitigates the risks of regulatory delays
- Optimizes the regulatory pathway to reach the market efficiently
- Establishes a commercially viable product in the market

Why does regulatory oversight matter?

Biopharma companies must prioritize regulatory considerations from the early stages of clinical development. Having a well-defined plan to meet regulatory obligations in your primary target market and future markets is crucial to achieving commercial success. Here are some key considerations to keep in mind:

01 Comparative analysis: A regulatory plan should include a mechanism to easily compare phase III investigational drug with the drug used in phase I and phase II. This is particularly important when preparing for a Biologics License Application (BLA) submission in the United States.

02 Chemistry, Manufacturing, and Controls (CMC) framework: The CMC framework requires comprehensive information about the manufacturing process, validation, data control, and analytical methods. Thorough documentation and adherence to guidelines and precedents are essential.

03 Master protocols: Recently, the Center for Biologics Evaluation and Research (CBER) in the United States released draft guidance for the utilization of master protocols[5]. These guidelines describe the use of basket and umbrella trials as innovative approaches to increase the likelihood of success for your drug candidate[5]. Understanding trial design, statistical models, and regulatory restrictions is critical in this regard.

A commercialization partner can facilitate effective communication by acting as a liaison between you and regulatory agencies, formulating and executing an informed strategy. By integrating regulatory considerations into your development process, you can navigate the regulatory landscape more effectively.

5. U.S. Food and Drug Administration. Master Protocols for Drug and Biological Product Development. Dec 2023. Accessed 19 Mar 2024. Available at: https://www.fda.gov/media/174976/download

Optimize your regulatory strategy with a partner who can:

- Provide comprehensive technical guidance during product development, ensuring adherence to the quality standards and testing requirements necessary to meet regulatory expectations
- Conduct thorough assessments of programs to identify any weaknesses that could cause regulatory delays
- Facilitate productive interactions with regulatory authorities by aiding in the preparation and execution of meetings
- Assist in the preparation and submission of regulatory documents, optimizing the chances of acceptance for various applications and regulatory filings
- Leverage a deep understanding of the complexities and unique regulatory needs globally to ensure compliance with diverse regulatory frameworks
- Assist in strategy for designing and executing necessary long-term follow-up studies

03
Logistics and supply chain: Shared systems enable success

Considerations for personalized logistics and temperature control

CGTs require customized logistical solutions to ensure secure and timely transportation between multiple stakeholders. Logistical considerations for CGTs are complex, often bespoke to each new drug, and require seamless connectivity (see Figure 2).

Autologous cell therapies require the most complex logistical framework because the therapy must move to and from a manufacturing site while maintaining chain of custody (COC), chain of identity (COI), and good manufacturing practices (GMP) controls. On the other hand, allogeneic and gene therapies are manufactured in batches and may be stored in depots before being delivered to the site of care. Additionally, CGTs have strict temperature and storage requirements that necessitate special logistical considerations.

The cryopreservation of cell-based therapies using liquid nitrogen (LN_2) extends the crucial timelines needed for the commercial delivery of both allogeneic and autologous therapies. However, certain therapies necessitate fresh transfer to guarantee cell viability or product integrity, which puts pressure on transportation timelines. In cases where samples or therapies need to travel great distances, cryogenic logistics including cryostorage facilities and cryoshipping is the ideal solution to ensure cell viability and product stability.

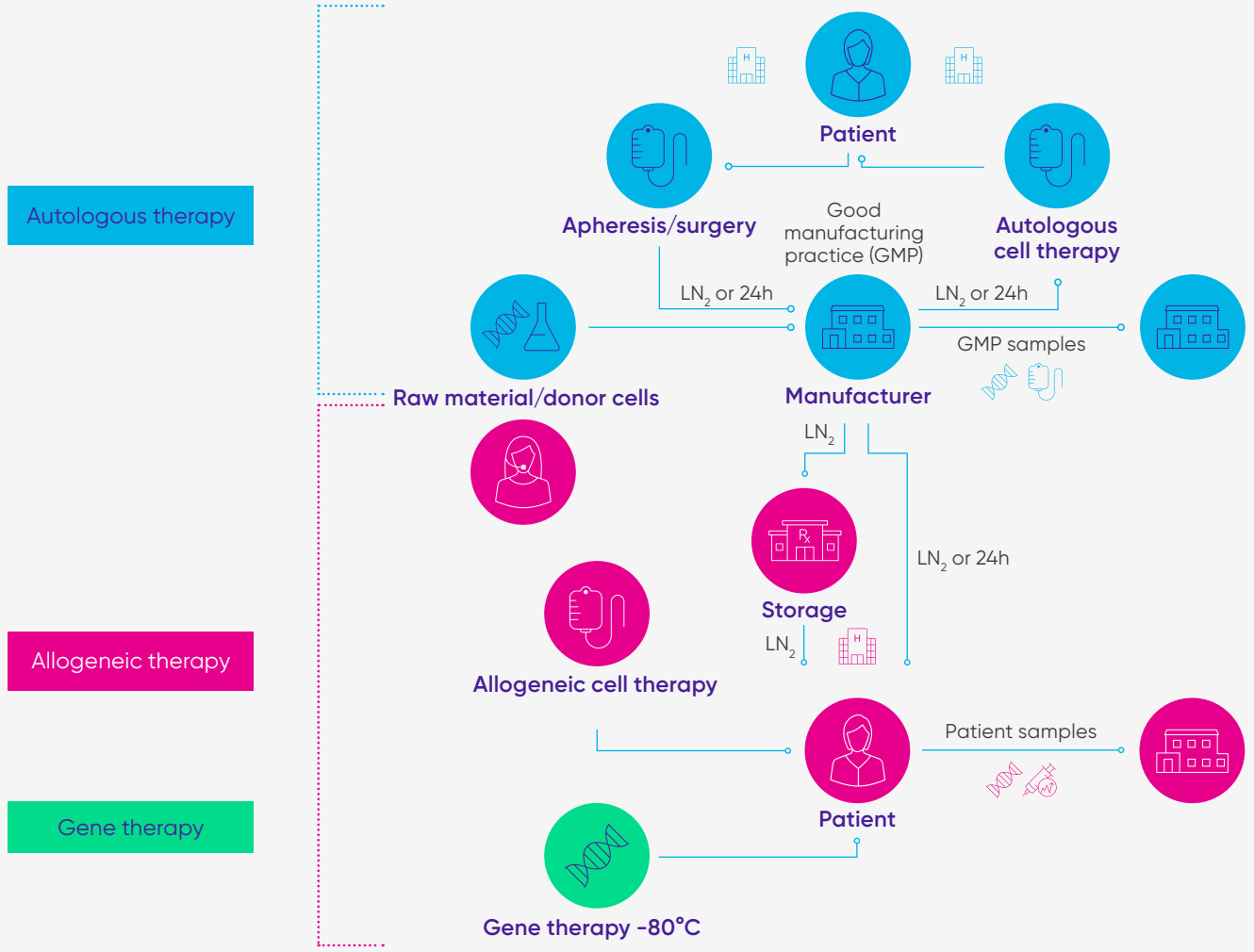

Figure 2: Time criticality of CGT supply chains — Fresh transfer versus cryopreservation (LN_2)

A reliable logistics partner with global capabilities can contribute to your success by optimizing your supply chain. By closely assessing your product's requirements, including temperature control, ordering processes, and regulatory compliance, they can overcome obstacles and ensure uninterrupted flow in the supply chain, expediting end-to-end delivery. Additionally, a partner with a global network offering storage facilities in all required temperature ranges including cryostorage, an integrated IT system, a standardized quality process, and a globally trained workforce is well positioned to support the expansion of your supply chain into new regions.

Maintaining COC and COI is critical for ensuring safe and viable therapies. Mishandling, contamination, or errors in processing can compromise the safety, efficacy, and quality of the product, potentially endangering the patient. Therefore, the integration of a logistics partner with a robust orchestration platform is essential for operating at scale. Having a global good manufacturing practice (GMP) depot network for storage and importation is particularly imperative for allogeneic and gene therapies, but it can also accelerate the timeline from manufacturing to patient for autologous therapies. With lengthy manufacturing release timelines, the ability to transport a therapy from the manufacturing site to a nearby GMP depot where it will undergo quarantine until all quality tests are completed can expedite delivery upon quality release.

Unique challenges in the CGT space	Potential solutions from a full-scale partner
Short shelf lives of fresh cells	Accelerate transportation of time-sensitive cell products, leveraging real-time temperature and location tracking while operating under compressed timelines
Lack of cryostorage infrastructure	Offer cryoshipper charging and cryostorage facilities positioned strategically in global markets
Long manufacturing release timelines	Ship out autologous products before quality release and store in a GMP depot close to the treatment center for immediate delivery upon release

Five ways a logistics partner can help you manage your supply chain

01 Establish and maintain import/export processes and licenses

02 Manage clinical logistics throughout the entire drug development process

03 Ensure sufficient transportation and depot capabilities, including contingency plans and an adequate supply of shippers

04 Enable global cryogenic storage capabilities

05 Maintain COI and COC utilization and adherence

Further reading

World Courier to expand storage capacity and cold chain capabilities with three new transport stations in the United States.
Explore this topic

04
Stakeholder management: Demonstrating value to payers, providers, and patients

Given the relatively high cost of CGTs, payers require sufficient time and evidence to assess their long-term value. It is crucial to meet the necessary evidence standards to effectively communicate value to payers, ensuring patient access. Initiate discussions with payers early on to foster open dialogue, understand their expectations, and tailor the evidence package accordingly. Continually engage with payers after launch, providing updated data and addressing any concerns they may have.

How to demonstrate value to payers?

To demonstrate value to payers, a comprehensive approach is necessary, encompassing clinical, economic, and patient perspectives. The evidence package should be tailored to showcase the therapy's potential benefits and justify its cost while also addressing the concerns and priorities of key stakeholders.

01 Clinical evidence: Present robust clinical trial data showcasing the therapy's durability, safety and efficacy.

02 Cost-effectiveness analysis: Compare the therapy's cost to that of standard of care and incorporate quality adjusted life year estimates.

03 Patient perspective: Highlight the therapy's impact on improving patient quality of life and reducing disease burden.

Payment models and contracting

Biopharma companies should prioritize understanding payer expectations for innovative contracts. According to a recent survey, payers view outcomes-based contracts as the most effective approach[6]. Payers will seek clarity on how to manage the cost of these therapies without exceeding their coverage budgets. Clinical study outcomes significantly impact innovative contracts; therefore, generating compelling evidence, including mechanism of action, clinical benefit, and durability data, is crucial to securing access and coverage. To take a comprehensive approach, biopharma companies should analyze the market landscape and actively seek input from payers, providers, and patients to address potential challenges associated with these therapies.

Payer engagement strategy

Engaging payers early is crucial to successfully navigate the complexities of CGT. Establishing strong stakeholder relationships should include preapproval engagement, transparent information sharing, and effective communication about the therapy's value and evidence generation.

Provider engagement strategy

Providers must understand which patients can derive benefits from specific therapies, how to direct them to suitable care facilities, and how to provide ongoing support throughout their follow-up treatment. Look for a resource that offers solutions and valuable insights to enhance the patient experience, enabling providers to prioritize delivering optimal patient care.

Patient engagement strategy

Patient advocacy groups can offer valuable insights into the patient journey and should be thoughtfully engaged. Biopharma companies should also demonstrate their commitment to addressing patient needs by providing support for financial concerns, transportation, insurance claims, and other critical matters. A hub service can offer a comprehensive approach to provide these necessary patient services.

Further viewing

Cencora's FormularyDecisions launches payer resource for CGT products.
Healthcare decision-makers will have centralized access to information on CGTs across the product lifecycle to help inform coverage decisions.
Explore this topic

6. Dodda, S. et al. U.S. payer perceptions of innovative contracts with cell and gene therapies. [Poster]. Presented at AMCP 2023 Annual Meeting. March 21-24,2023. San Antonio, Texas. Available at: https://www.amerisourcebergen.com/-/media/assets/xcenda/english/content-assets/conference-and-poster-presentations/2023/innovative-cgt-contracts_poster_amcp-2023.pdf

Three ways an outsourced reimbursement team brings value

01 Leverage long-standing relationships within the industry.

02 Understand the nuances of the reimbursement process to ensure claims are well planned.

03 Access a breadth of expertise across the sector.

05
Commercial distribution: Anticipate hurdles to ensure a smooth transition from clinical to commercial

Five questions to answer before creating a distribution strategy

Engaging a consultative partner can provide valuable guidance on identifying optimal distribution channels and devising an effective strategy. Making the right choice in channel strategy is vital to achieve commercial success and, most importantly, to bring patients access to the therapies they require.

01 Where are patients treated today? The geographical location plays a significant role in determining necessary infrastructure and capabilities to ensure patient access. It also impacts reimbursement and payment processes because coverage can vary depending on the patient's location, treatment facility, and healthcare system.

While many patients who could benefit from advanced therapies are treated in the community setting, the administration of these therapies often takes place at centers of excellence (COEs). Therefore, an essential aspect of your distribution strategy should focus on educating providers about patient identification and referral.

02 What clinical and logistical considerations must you include in your COE selection criteria? To ensure that COEs are willing and able to provide the therapy, it is important to consider various factors that could potentially limit their participation. These factors include complex dosing or surgical procedures, ultra-low or cryo storage requirements, adverse event profiles, or very high price points. Taking these considerations into account helps in understanding which sites are capable of and willing to offer the therapy effectively.

03 What is the ideal distribution network? It is important to have an understanding of the size of the patient population and the likely treatment locations to determine the number of partners required. Factors such as storage and cold chain requirements as well as existing relationships between distributors and potential treatment sites play a significant role in determining the appropriate distribution channels. By considering these factors, you can establish effective distribution strategies for your product.

04 What is the launch area? The selection of target countries will have a direct influence on the partnerships you establish. It is essential for your distributors to be responsive and able to promptly address any manufacturing, shipping, or other unforeseen delays that may arise. Collaborating with entities possessing a global reach and comprehensive understanding of local markets is prudent.

05 How might your strategy change over time? Your partner should possess agility and adaptability, demonstrating the capacity to grow alongside your product. For instance, if your product receives approval for additional indications, it may require expanding to other sites of care. It is important to ensure that you can adjust your channel strategy to meet such evolving needs.

Ideal criteria for a CGT distributor

- Retains strong business continuity and implements robust business resilience processes to effectively address potential issues, particularly when distributing products internationally
- Has a network that can evolve over time and establish strong long-term strategic partnerships to accommodate future product launches and potential changes in the channel strategy
- Is collaborative and can work seamlessly with many stakeholders

06
360-degree orchestration and realization: Putting it all together

In the ever-changing field of CGT, it is essential to search for experienced strategists who possess established processes and the flexibility to scale and adapt alongside your evolving approach.

Choose an integrated partner who can:

- Utilize expertise in navigating country-to-country regulations for seamless operations
- Implement end-to-end orchestration capabilities to ensure an active and patient-focused supply chain
- Enable real-time process updates to biopharma, providers, and patients, optimizing the treatment experience throughout the entire continuum
- Integrate workflows to eliminate silos and enhance transparency along both the product and patient journeys
- Provide awareness and visibility into near real-time data sets, empowering providers and biopharma companies to make informed decisions

Understand the value of a single collaborator

Engage with a comprehensive commercialization partner equipped with specialized teams of experts to ensure a thorough and all-encompassing process, leaving no aspect overlooked. Collaborating with a single end-to end commercialization partner rather than multiple vendors provides the necessary strength and support to build and seamlessly implement a successful commercialization strategy. A successful CGT launch entails considering cross-functional perspectives during strategy development, initiating crucial conversations as early as possible, and comprehending the interdependencies between research and development and commercialization. Your therapy holds immense potential, and fostering the right relationships will unlock it.

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At Cencora, our focus is on the patient at every stage of the cell and gene therapy commercialization and treatment journey. By working together, we can redefine the critical touchpoints that impact patients, clinicians, and our key stakeholders, ultimately delivering solutions that can save lives. Connect with our CGT team to see how our consultative approach drives innovative solutions. Reach out today