COMMERCIALIZING CELL AND GENE THERAPIES

Clinically promising, commercially challenging. Discover the go-to-market strategies to succeed when the patient is in the supply chain.

AmerisourceBergen®

A message from AmerisourceBergen

Cell and gene therapies promise to transform patient outcomes by unlocking cures for diseases with high-unmet need. Yet, their complex nature presents therapy owners with unprecedented challenges across logistics, commercialization, market access, and reimbursement that threaten to derail a product's success.

As we have the privilege of speaking to and working with many cell and gene therapy innovators, we recognize a pattern in the challenges presented. We know that there is no distinct handoff between clinical and commercial settings, so therapy owners must design forward-looking, patient-centric plans to navigate the journey from preclinical development to commercial manufacturing and commercialization success.

AmerisourceBergen, leveraging its best-in-class solutions and proven track record, provides the experience cell and gene therapy innovators require to design and optimize the execution of an end-to-end clinical to commercial solution. Through our industry-leading business units, AmerisourceBergen brings expertise in each area required for successful commercialization:

- **Global Specialty Logistics:** World Courier and ICS
- **Patient Support Services:** Lash Group
- **Strategic Consulting:** Pharmacy Health Solutions and Xcenda
- **Product Sourcing and Supply Chain Management:** Strategic Global Sourcing

In collaboration with our external partners Invetech and TrakCel, this white paper is representative of our broad and deep combined experience and the result of our collaborative approach to propose action-oriented solutions to cell and gene therapy commercialization.

We have enjoyed creating this guide. We hope you find it useful and insightful as we partner to create healthier futures.

Sam Herbert – *President, World Courier*

Pete Belden – *President, ICS*

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Navigating *Commercializing Cell and Gene Therapies*

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Key:


Definition icon


Additional information on the topic area


Key chapter takeaways


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Contributors & cell and gene therapy working group


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It takes a commitment to innovation, seamless coordination, and the support of an experienced partner to overcome every barrier on the journey from clinical to commercial success.

Introduction

Manufacturing and cGMP

Integrating Supply Chain and Logistics Strategy

Securing Regulatory Approval

Critical Success Factors for Market Access: Coding, Coverage, and Reimbursement

Creating a Differentiated Patient and Provider Experience

Managing Payment and Distribution

Conclusion

Overarching data management architecture delivers needle-to-needle insights

As a committed partner for your cell and gene therapy, AmerisourceBergen will design a customized strategy that integrates proven solutions to deliver a superior customer experience for patients and providers.

Start a conversation:
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INTRODUCTION

Cell and gene therapy: Is it truly the future?

Medical advances allow for the creation of targeted, personalized, and potentially curative treatments for patients. But with these innovations come new considerations for therapy owners as they bring cell and gene therapies to market.

Cell and gene therapies create the opportunity to significantly transform how diseases are treated and cured. With billions of dollars of investment and a projected market size of more than $50 billion by 2025,[1] cell and gene therapy advances bring much hope for enhanced patient outcomes and for the future of medicine.

The stakes are high for therapy owners too; the nature of these treatments and their use of living cells or genetic material create new intricacies and dependencies that disrupt the traditional commercialization process. For the first time, the patient is now part of the supply chain.

Cell and gene therapy: An overview[2]

Cell and gene therapy are fields of medicine that involve replacing, manipulating, or engineering cells, and/or genetic material to fight disease.

- Cell therapies are treatments that involve inserting manipulated human cells into the patient to treat the disease

Autologous therapies use modified cells from a patient's own cellular population	Allogeneic therapies use a donor's modified cells to treat several patients

- Gene therapies are treatments that introduce genetic material into the patient's DNA to replace faulty or missing genes to modify or correct the defects that are the cause of the disease
- Some therapies combine cell and gene therapy approaches by manipulating DNA in harvested cells and then reintroducing them into the patient

Traditional commercialization model

The prevailing model of supply chains and patient programs for small molecules and biologics evolves linearly from clinical to commercial. Each individual component may be complex but there are only marginal dependencies between them.

VS

Cell and gene therapy commercialization model

This is interconnected and personalized, requiring a higher degree of integration between specialized logistics, **patient programs**, and the health outcomes evidence required to drive physician adoption and payer coverage. A patient's treatment has entirely different dependencies, a different sequence of events, and as a result, the decisions a manufacturer will make in clinical trials have implications for the commercial supply chain to an extent not present in traditional products.

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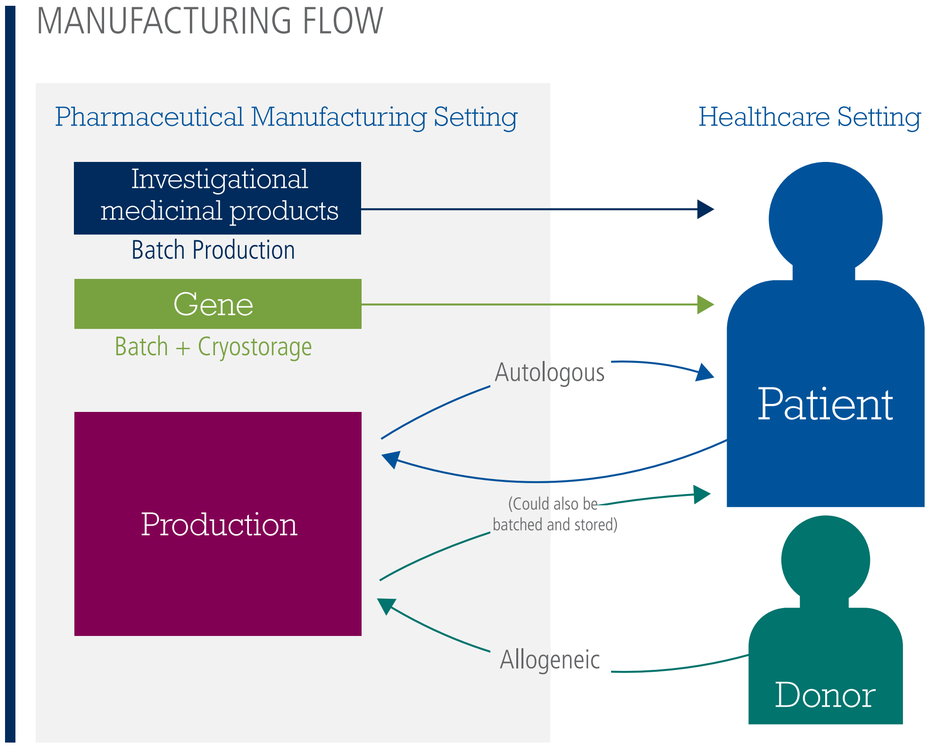
Patient programs overcome access and affordability challenges and can provide resources to support patient education and improve the treatment experience.

Enabling increased patient access to these novel therapies is contingent on successfully navigating the journey from clinical development to commercialization. The challenges across manufacturing, logistics, reimbursement, as well as education and access for physicians, are well-documented. The aim of this paper is to examine these challenges, to propose a way forward, and to guide therapy owners in the creation and execution of customized programs that enable cell and gene therapies to fulfill their full potential as the medicine of the future.

The supply chain redefined

People are part of the cell and gene therapy supply chain. For autologous therapies, the patient is at the start and end of a circular pathway. Along this non-traditional therapeutic journey, harvested patient cells and tissues exit and re-enter traditional supply chain boundaries in a biologically altered state. Meanwhile, a few healthy donors can provide the starting material for hundreds of allogeneic therapy doses. For gene therapy, new genetic material is introduced into the patient's DNA. In all cases, this means the supply chain needs to be Current Good Manufacturing Practice (cGMP)-compliant with chain of custody tracking and overall orchestration.

Cell and gene therapy manufacturing requires seamless coordination with logistics to adequately support patients and to safeguard the return on investment in the therapy. Administration is reliant on physicians and sites of care; given the complexity of the products, it's important that therapy owners treat providers as customers. Enabling easy administration, creating an efficient process, minimizing business impact, and acknowledging competing therapies all support the provider in putting the patient first.



To meet patient and provider expectations, the therapy owner must ensure that collection, manufacturing, and administration are coordinated, and that therapy-appropriate handling techniques, environmental controls, worker protection, and unbroken data traceability extends needle to needle. The focus on the human material supply chain is vital, of course—but the scheduling, access, and logistics dependencies are equally important and add complexity.

Regardless of the reason, a breakdown in the supply chain—whether it's the manufacturing cycle, logistics coordination, or shipping process—has an extremely high cost. At best, it's expensive and

disruptive for the manufacturer. At worst it may be catastrophic, with the potential to impair individual patient outcomes. Regulatory compliance at each step along the therapeutic path with seamless coordination of FDA cGMP considerations are top of mind. Ultimately, a breakdown has implications for data used by therapy owners to justify market access, coverage, reimbursement, as well as with physicians to justify use—all of which can impact the uptake of the therapy in a marketplace that is likely to become more crowded with competing products.

As the manufacturer is one stakeholder—whether in-house or outsourced—within the broader supply chain, the therapy owner must design a system that coordinates internal scheduling, manufacturing execution, and electronic batch record creation, while seamlessly integrating these within the overarching data management architecture that supports the product's transition from clinical to commercial availability.

To design and build such a complex system, the manufacturer may need to partner with a solution provider who brings expertise in data aggregation and integration, as well as the execution of solutions such as cGMP manufacturing equipment, sterile single-use disposables, specialized logistics, patient access programs, and the analysis of health outcomes evidence. These solutions, and the related data their activities generate, will need to integrate with the therapy owner's overarching infrastructure.

Commercialization considerations

There will be no distinct hand-off from the clinical to commercial supply chain. Manufacturing and logistics must scale up and scale out to serve an increasing number of patients while additional stakeholders join the supply chain. The commercial supply chain is the clinical supply chain—only further reaching with added complexity. This complexity is caused by the barriers patients will face relative to access and affordability, as well as the high degree of interdependencies between the specific steps required.

To successfully transition from a clinical to commercial state, therapy owners should ask:

1. Is *manufacturing* set up to coordinate perfectly with logistics to optimize throughput and turnaround—and have the potential to be automated and maintain sufficient capacity to handle expected peak demand?
2. Is manufacturing prepared to coordinate, validate, and document all required patient tissue collection, handling, environmental control and active drug product re-introduction and therapy administration steps with health system stakeholders?
3. Can the *supply chain* scale up, scale out, or scale up and out to serve an increasing number of patients?
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Manufacturing

There is no established handover from clinical to commercial manufacturing of cell and gene therapies; this means decisions made during clinical development will influence the product's future viability to an unprecedented degree.

Read the "Manufacturing and cGMP" chapter to find out more.

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Supply chain

Given the interdependencies between each stage in cell and gene therapy, bespoke and integrated supply chain elements are essential. Personalized medicine requires a personalized supply chain, complicated from the outset and only growing in complexity as studies move rapidly through the clinical phases to market.

Read the "Integrating Supply Chain and Logistics Strategy" chapter to find out more.

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Interdependencies

The dependencies between each touchpoint in cell and gene therapy are far greater than in traditional specialty pharmaceutical production—and the coordination needed to manage them effectively demands true connectivity.

Read the "Integrating Supply Chain and Logistics Strategy" chapter to find out more.

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Reimbursement

The characteristics of cell and gene therapies magnify some of the limitations of a service fee model and will require a thoughtful strategy from the therapy owner based on proactive discussions with both providers and payers.

Read the "Reimbursement/Payment" section to find out more.

6. Can compelling evidence be provided to demonstrate product value and secure/retain *coverage* —both at product launch and over time?
7. Can a *patient-services* hub be designed that will provide a consistent experience for both prescribers and patients and ensure that barriers to access and affordability are overcome?
8. Will balanced *channel and product access strategies*, taking into account both established centers of excellence and other potential prescribers, be considered?
9. Will health systems be educated on how to order and obtain payment for the services related to cell and gene therapy and made aware of therapy owner-sponsored patient support programs?
10. Have the patient population characteristics and product requirements been considered to create a truly *optimized distribution strategy* ?
11. Has a valid process model been built considering impacts to health system stakeholders, including equipment and infrastructure investments, state and federal regulatory compliance, cGMP support, staff training and competency verification, and health system risk mitigation?
12. Is the framework in place to enable the development of an overarching data management architecture that provides a single view of the patient/product journey? Will this fulfill coordination and scheduling, chain of custody management, and product tracking and monitoring requirements, including manufacturing batch records?

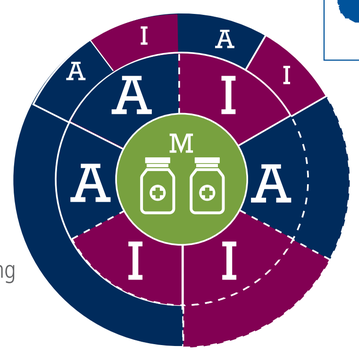
LOGISTICS AND MANUFACTURING SCALING UP AS THE STUDY MOVES THROUGH THE PHASES

Phase 1
Co-located manufacturing

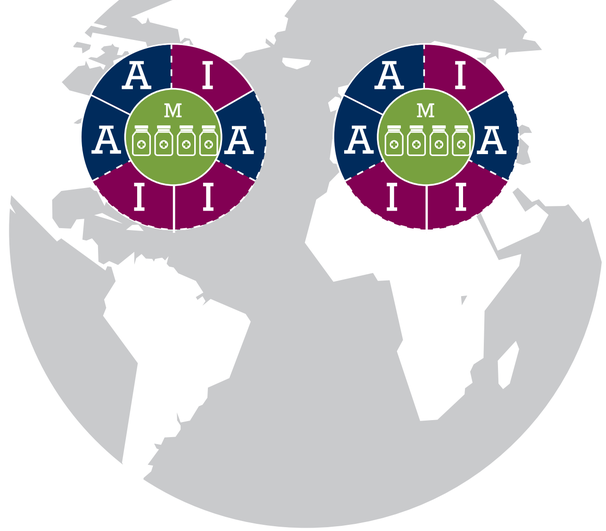
# of patients

A = Apheresis Site
M = Manufacturing
I = Infusion Site

Phase 2
Some community apheresis and regional manufacturing



Phase 3 and commercial
Community apheresis common with multiple regional manufacturing locations



The number of supply chain participants increases exponentially as cell and gene products move into commercialization

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Coverage

It is essential to engage in discussions with payers early in the cell and gene therapy development process to glean invaluable insights into the possible evaluation pathways, associated steps, and evidence packages required.

Read the "Coverage" section to find out more.

LOGISTICS AND MANUFACTURING SCALE AS A STUDY MOVES THROUGH THE PHASES

Phase 1
Co-located apheresis and regional manufacturing

Phase 2
Some community apheresis and regional manufacturing

Phase 3
Community apheresis common with multiple regional manufacturing

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Patient-services hub

The end goal is to position the patient-services program as a single point of contact for the provider and patient, and aid in the coordination of product and treatment insurance coverage, and logistics and/or distribution services.

Read the "Creating a Differentiated Patient and Provider Experience" chapter to find out more.

LOGISTICS AND MANUFACTURING SCALING UP AS THE STUDY MOVES THROUGH THE PHASES

Phase 2
Early continuity
apheresis and
regional manufacturing

A = Apheresis Site
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I = Infusion Site

Phase 3 and commercial

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Channel and product access strategies

Access to cell and gene therapies is contingent on developing an appropriate channel strategy when bringing a product to market. It requires strategic thinking and has a significant impact on product uptake and commercial success.

Read the "Creating a Differentiated Patient and Provider Experience" chapter to find out more.

LOGISTICS AND MANUFACTURING SCALING UP AS THE STUDY MOVES THROUGH THE PHASES

Phase 1
Co-located apheresis and regional manufacturing

Phase 2
Some continuity apheresis and regional manufacturing

Phase 3 and commercial
Regional apheresis and regional manufacturing

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Optimized distribution strategy

Because cell and gene therapy products evolve differently than traditional specialty pharmaceutical products, therapy owners will need to overcome several significant obstacles to create a truly optimized distribution strategy.

Read the "Managing Payment and Distribution" chapter to find out more.

LOGISTICS AND MA… THROUGH THE PHASES

Phase 1
Co-located…

Phase 2
Some community apheresis and regional manufacturing

Commercial
Community apheresis common with multiple regional

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The number of supply chain participants increases exponentially as cell and gene products move into commercialization

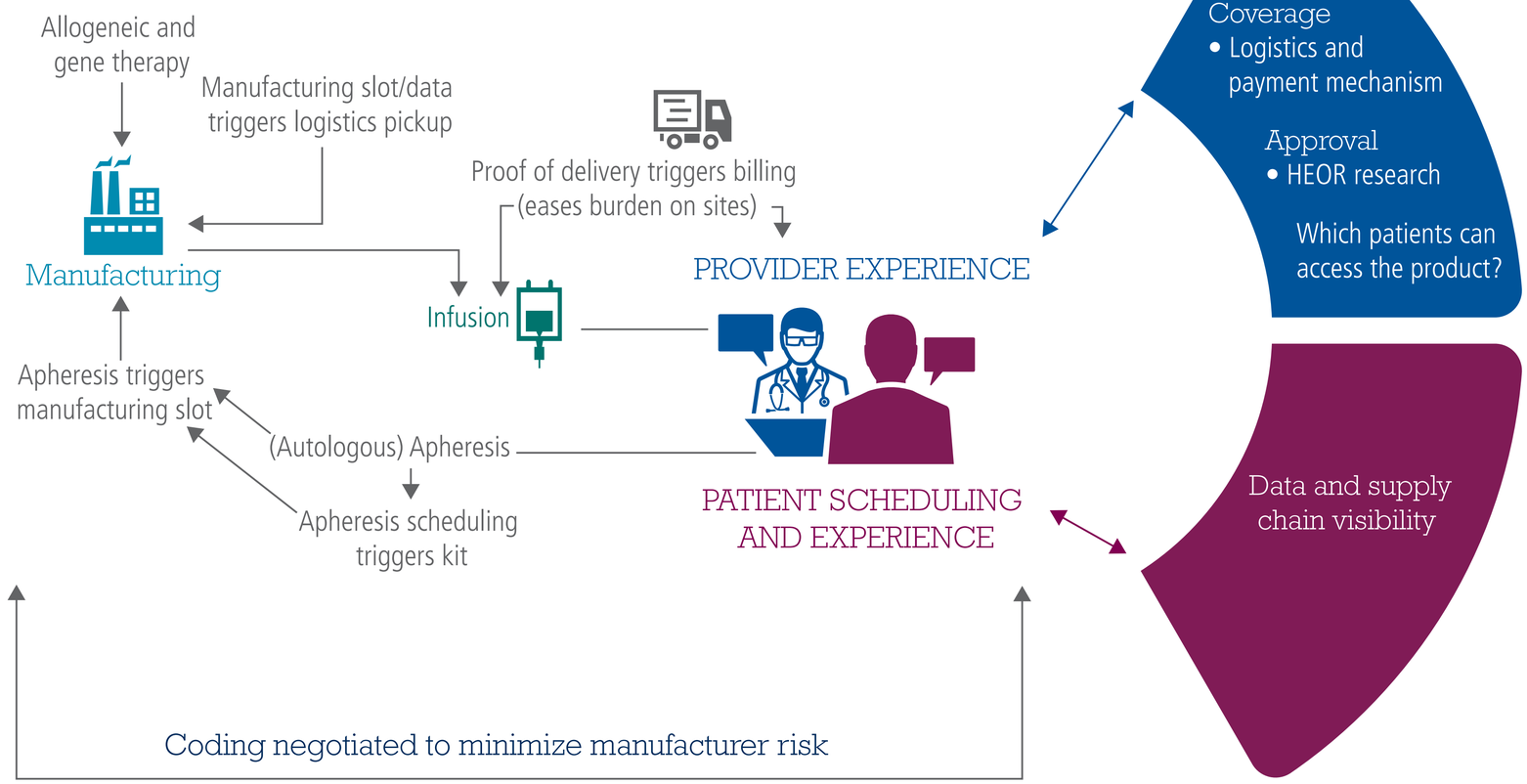
A path forward

As outlined, the challenges related to the commercialization of cell and gene therapies are well recognized. It's important to accept that these challenges must be handled via a coordinated, linked approach, not on an isolated case-by-case basis.

The starting point is recognition that each of these challenges is interrelated to a degree not present in other therapies. Therefore, an attempt to solve for one process step in isolation does not optimize the whole and is likely counter-productive. Decisions made optimally build on one another, so it is vital to have the end state in mind with consideration of multiple process interdependencies to inform early decision making.

Only partially addressing the interdependencies will result in lower efficiency, dampening return on investment and the potential impact on patients. Engaging an integrated partner with a proven track record of delivery and continuity of leadership is vital to implement a forward-looking solution that addresses each stage in the commercialization journey. Taking an integrated approach to these challenges from an early stage lays the best foundation for maximizing patient benefit and return on investment while scaling up and out.

INTERDEPENDENCIES BETWEEN COMPONENTS *(note—a non-exhaustive example)*



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MANUFACTURING AND cGMP

Roadmapping manufacturing

There is no established handover from clinical to commercial manufacturing of cell and gene therapies; this means decisions made during clinical development will influence the product's future viability to an unprecedented degree.

But there is a path that can be successfully plotted through complex commercialization challenges. Therapy owners who actively plan from an early stage can anticipate their technology transfer needs more efficiently to avoid costly adjustments further down the line. This approach also provides an optimized framework for selecting a partner who can support a therapy owner's product along the path to commercialization.

> *"Into phase 1 and definitely by phase 2, cell therapy companies need to make definitive choices related to manufacturing. To be able to do so, they also need a clear view about their indication, the size of their target patient population, and the way the product will be used in the hospital environment."*
>
> – VP Operations, biopharma company specializing in cell therapy

But inevitably, therapy owners at any stage of clinical development will be asking the where, who, how, and what of manufacturing:

1. "Where should manufacturing be located?"

This is dependent on the target end-state; while minimizing manufacturing sites is favored, regional hubs or in-country manufacturing shouldn't be dismissed out of hand.

After all, location can allow for greater flexibility and responsiveness to patient needs. As manufacturing processes evolve, manufacturing co-located with provider sites becomes feasible—creating centers of excellence for the target disease.

Ultimately, it will be the concentration of demand that will likely inform potential manufacturing sites and centers of excellence—and understanding where these concentrations are located is vital. For autologous therapies, typically, the primary site will be hospital-based but this may move into the community as technology progresses. Any detailed logistics plan must consider the entire process from both perspectives—from receiving apheresis-starting materials to delivering the finished product to provider sites.

This initial mapping process will influence the choice of the potential manufacturing locations needed to maximize the catchment area, which in turn can be served efficiently and swiftly through a nearby logistics hub.

From internal to external

For allogeneic therapies, centralized, large-batch manufacturing combined with cryogenic logistics is the default standard. The ability to closely observe the manufacturing process and the end product's characterization is vital, given the variability of input materials and of the sector's typical manufacturing conditions.

Beyond the factory doors there is a further challenge—the delivered frozen product may require a final wash and formulation prior to

administration, and depending on the indication, specific methods for administration may also be required. In both cases, the therapy's success will be reliant on a skills-based operation that is arguably part of the manufacturing chain.

These steps need to be controlled with the same cGMP rigor expected within the manufacturing facility, likely through training and certification of clinicians in the final preparation and delivery of the therapy.

Choose wisely

Autologous therapies, by virtue of their "one batch per patient" nature and circular logistics, typically require greater consideration of the appropriate manufacturing model. Various degrees of manufacturing localization are possible:

- **A more centralized production approach** favors therapies with greater manufacturing complexity and frozen logistics
- **A more decentralized production approach** increases the feasibility of fresh logistics and favors therapies where the manufacturing capability is more easily duplicated
- **A hybrid production approach** where manufacturing is decentralized but complex analytical testing is centralized provides the feasibility of fresh logistics but centralized process control

Cryopreserved product could be considered an aspirational goal in either case, given the significant benefits of logistical and administrative flexibility. Cryopreservation can also reduce tight coupling of the manufacturing process, adding scheduling flexibility, both to the in-factory process, as well as patient collection and administration—critically ill patients cannot be expected to attend an apheresis center to accommodate a manufacturing cycle.

Yet the cryopreservation cycle almost always impacts cell yield and viability, and hence therapeutic potency.

The key advantage of a "fresh" therapy is the ability to deliver an equivalent or greater potency with reduced process complexity (both manufacturing and administration) and in-process loss (which may allow less invasive collections, smaller expansion targets, and reduce product contamination with lysed/apoptotic cells).

The manufacturing and logistics cycle in the case of fresh logistics is "tight," impacting collection and administration scheduling, and requiring latency (excess capacity) in manufacturing capability to accommodate schedule variation. Ultimately, the "fresh vs frozen" question will be a trade-off between product potency and robustness, and manufacturing and supply chain cost. Critically, to avoid expensive and time-consuming comparability studies after the manufacturing process is locked down, these decisions need to be made early in the clinical trial program.

"Near-patient" manufacturing

This is a special case of autologous therapy, where the patient material collection, therapy manufacturing, and therapy administration occur within a center of excellence, hospital, or clinic. This approach has the potential to shrink the logistics cycle, with distinct advantages in delivery cost and responsiveness to patients.

There are associated risks, though—adopting this approach may cross the threshold to medical device status as they approach the patient, moving out of the standard cGMP realm, as hospitals typically don't have the qualified GMP manufacturing spaces or possess the infrastructure and required equipment to produce cell and gene therapies throughout the clinical trial process. This drives toward the development of "GMP in a box" solutions (cells in → product out), probably operated by non–GMP-trained hospital staff during the manufacturing process. Ultimately, this is an emerging space, and the thresholds and treatment by the regulatory authorities are yet to be defined but equipment of this type could become subject to regulatory approval as a medical device, which adds complexity and cost to the design and approval process for the manufacturing equipment.

2. "Who should manufacture the product: in-house vs outsourced?"

A critical commercial decision is whether to manufacture in-house or to outsource manufacturing through contract manufacturing organizations (CMOs) or licensed third parties.

There are three core reasons for considering outsourcing—capacity, capital preservation, and geographic reach—driven in each case by the business model the therapy owner is pursuing. For instance, many will choose to partner with CMOs who can provide capacity for early-stage clinical trials.

The initial investment required by the therapy owner will be offset by the process management expertise brought by the CMO. In turn, this frees up the best developmental internal resources to focus on refining the therapy production process for phase 3 and commercial manufacturing.

With intermittent manufacturing requirements, the advantages of such a capital preservation rationale become clear. For example, large-scale allogeneic therapy production may require only a handful of batches annually to serve the entire affected population. In such cases, in-house manufacturing would see equipment, personnel, and expertise languishing for much of the year, whereas a CMO can redeploy these resources far more effectively. Finally, regional licensing is often used to provide rapid global market access that would otherwise be hard to achieve.

Regardless of the driver, the robustness and cost-effectiveness of the therapy manufactured at a third party is only as good as the process being transferred. Additionally, the third party, irrespective of capability, is unlikely to share the therapy owner's cost-reduction incentive.

Ultimately, large-scale therapy owners will want their commercial manufacturing in-house as a core competency. Retaining that option, even while outsourcing manufacturing itself, means the in-house team must always maintain a detailed understanding of the nuances of their therapy manufacturing process.

Two targets, one goal

To successfully navigate manufacturing's complexities, therapy owners should focus on two objectives:

1. To deliver an advanced therapeutic benefit to patients
2. To capture a return on investment

Achieving both objectives requires manufacturing decisions are taken *throughout* the therapy development process; after all, therapeutic development is a game of resource allocation and risk management. How should therapy owners strike the right balance?

Balance occurs with the integration of manufacturing, data management, and logistics.

Coordination is king

As the therapy development progresses, these three tenets will offer therapy owners complete visibility of their overall commercial model, providing a critical top-down view of both the ecosystem's key elements—and critically, the interfaces between them.

This approach will enable therapy owners to understand each element sufficiently to define a "hierarchy of needs"—the critical aspects of their manufacturing, data management, and logistics plans that will drive and support commercial success.

With a hierarchy in place, objectives can then be defined for the teams managing each element. In turn, as the commercial vision evolves over time, so, too, will the refinement of the ecosystem itself, each informing one another.

3. "How should the product be manufactured: manual processes or via automation?"

During therapy development, and even into early-stage clinical trials, cell therapy manufacturing processes are typically manual, extremely labor intensive, and require a high degree of skill.

While acceptable at a small-scale, this creates a raft of issues for larger operations:

- Makes **recruitment and training** of operators difficult
- Creates a significant **quality control and validation challenge**
- Adds **significant cost**
- Ultimately is **not scalable**

Using manual processes, the rate at which production can be scaled up is also impeded by the requirement to build and validate clean rooms and recruit, train, and retain highly qualified staff; it's a model that rapidly becomes untenable.

Suitable automation processes will inevitably become critical to the therapy's ongoing commercial evolution.

If developed ahead of time, an understanding of the production cost-drivers at commercial scale will allow process changes to be introduced sufficiently early on in the development and clinical trials process to avoid the need for comparability studies. Ideally, therapy production for phase 3 clinical trials will utilize "production-prototype" equipment and processes.

This approach doesn't imply total automation—it will be the targeted application of automation to eliminate specific sources of process variability, typically skills-based steps, to ensure the processes deployed are suitable for closed automation without the need to redefine the "cell journey."

Establishing this embryonic form of the therapy manufacturing process by phase 3 will also demonstrate that the process is mature, automation-friendly, and scalable. Establishing manufacturing in parallel with Biologics License Application (BLA) submission then allows commercial-scale therapy production immediately following regulatory approval, a primary driver of return on investment.

> *"As therapies scale up to commercialization, there is an opportunity for more automated coordination processes. There will be various clinical and manufacturing sites across multiple geographies."*
>
> – Former VP of Commercialization, top 10 pharmaceutical company

4. Manufacturing and development: The wider view

When considering the transition from therapy development to commercial manufacturing, it's critical that the business model supports the needs of both states.

Commercial manufacturing must be lean, while development requires flexibility and responsiveness.

To support the management of a complex cell therapy supply chain, these three guidelines can help visualize the manufacturing facility:

1. Focus on global cost drivers

- Downgrade clean room requirements (grade and required area) by closing the process
- Reduce personnel costs (number and skill level) through targeted automation, including global facility coordination and data management

2. Target high resource utilization

- Reserve expensive automated equipment for high value-added processes; use standard solutions for simple process steps (eg, long-term incubations in simple incubators)

- Ensure that the critical path's process steps are robust; the incidence of failure at this point drives the throughput of the entire system

3. Reduce variability

- Eliminate the "art" in high-skill steps through automation; process steps requiring operator finesse typically have variable outputs and are failure prone
- Know and control the drivers of product quality—the "cell journey" should be as consistent as possible

Putting the patient first

Despite cell and gene therapies' extraordinary therapeutic and even curative potential, its administration likely comes at a difficult time for patients and their families.

The patient's expectation is for a set of well-managed interactions throughout their treatment journey. The experiences that an individual has as a customer, in all areas of life, influence the level of service they expect and should receive as part of their cell and gene therapy treatment plan. Meeting and exceeding patient expectations is a performance baseline that the industry should always strive to meet. For example:

- Collection and administration should be as convenient as possible, completed correctly every time and performed as scheduled
- No patient should be forced to return for a second collection to compensate for inadequate manufacturing or supply chain robustness

Ultimately, the industry must ensure that patients have trust in the system delivering their complex therapies. While the oversight of federal regulators offers legitimacy, it is ultimately the integrity of the therapy owners, and the coordinated ecosystem of their expert partners, that will maintain the industry's reputation and aid its growth. Patients (and their physicians) expect to be able to access and afford treatment. It's the role of the therapy owner to make this a reality, through the creation of comprehensive patient programs that encompass tactics such as the provision of travel vouchers if the treatment is only available in select locations.

Provider/physician expectations

Along with the impact on patients and their families, we also need to consider what will change for providers/physicians. Poor administration could potentially be a major blocker in the uptake of new therapies.

The administration of cell and gene therapies in many cases will require new skills and techniques from physicians and also require new processes to be implemented in their practices. Physicians will require training in new delivery techniques and the use of tools to perform these. Cell and gene therapy owners should aim to make the physician's life as easy as possible by:

- Making the acquisition of any new skills simple
- Minimizing the impact of new therapy delivery processes on a practice's normal working routine

Any new tools or techniques should ensure that the delivery process is repeatable and consistent and delivers improved patient outcomes.

The evolving cell and gene therapy manufacturing space will also have implications for hospital activities, with a drive to move the GMP production space closer to the patient for some simpler treatments. This aims to reduce the logistical complexity around delivery (eg, receiving a treatment of cryo-preserved cells and thawing and washing these prior to administration, or, in some cases, potentially housing a full "GMP in a box" manufacturing process within the hospital).

Regardless of treatment complexity, the potential implications for health system stakeholders, ranging from fiscal to required infrastructure investments, competency of qualified staff, regulatory compliance, agency accreditations, and risk management, must be successfully addressed before a product launch.

The reach of cGMP manufacturing decisions

It's essential to understand that cGMP manufacturing decisions will impact all other aspects of cell and gene therapy program creation:

- Supply chain (logistics, chain of custody)
- Cost of finished product
- Temperature profile of the finished product that can be altered in manufacturing to add flexibility—yet, in some cases, this is not always possible due to therapy characteristics
- Potential for patient-specific storage for multi-dose products
- Patient program delivery integration with the centers of excellence for therapy administration
- Need for manufacturing to scale and supply to a number of global sites. This is even more important to maximize patient and provider experience (eg, community apheresis); designing a burdensome manufacturing and supply chain process can impact product viability and adoption
- The viability of managed access programs to make cell and gene therapies available to patients in global markets, beyond the centers of excellence established in select developed countries

Manufacturing and cGMP

KEY TAKEAWAYS

To advocate a complete consideration of the manufacturing pathway for early-stage therapies is naïve. In reality, therapeutic development is a game of resource allocation and risk management. Balancing the combined risks of a non-linear therapy development pathway, funding limitations, clinical trial progress, and scarcity of skilled personnel means giving the "right" amount of attention to commercial manufacturing considerations. Too little attention, paid too late, risks embedding schedule or cost burdens. Conversely, expending too much effort, too early, could distract from the core therapy development—a pitfall that could conceivably kill the company. How, then, can therapy owners appropriately consider manufacturing establishment as they progress their development toward commercialization?

Transitioning from pre clinical development to commercial manufacturing is a challenge, one that must be proactively engaged. In summary, therapy owners should consider the following:

- ☑ Location of manufacturing dependent on target end-state—"fresh" vs cryopreservation
- ☑ Manufacture of the product—in-house or outsourced—to meet commercial objectives of advanced therapeutic benefit to patients and demonstrate a return on investment for the therapy owner
- ☑ Manufacture of the product—via manual processes or automation—to provide a sustainable setup that supports production scaling up through the commercial evolution of the therapy
- ☑ A business model that supports both clinical and commercial states through a focus on global cost drivers, high resource utilization, reduced variability, and optimal patient experience

Overarching data management architecture delivers needle-to-needle insights

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Contributors & cell and gene therapy working group

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INTEGRATING SUPPLY CHAIN AND LOGISTICS STRATEGY

Charting the new frontier

For therapy owners developing cell and gene therapy logistics programs, there is a natural flow from clinical trial logistics to commercial logistics.

Many small- and mid-sized—and even large—manufacturers need support to handle the logistics that cell and gene therapies require, whether that be sourcing material from patients, maintaining proper temperature controls, or distributing the products widely enough for patient impact.

Although the specifics of each treatment may vary, all have one thing in common. Each therapy is composed of living cells with an extremely limited lifespan. It is absolutely critical that the therapies are transported on time and in pristine condition both to and from the manufacturer and ultimately to the treatment site for patient administration.

Cell and gene therapies: Shipping requirements

Specificities vary per therapy but all are subject to cGMP compliance. Common transport and storage requirements include:

- **Gene therapies:** "Off-the-shelf" product batch manufactured—cryostorage and temperature-specific shipment
- **Allogeneic cell therapies:** "Off-the-shelf" product batch manufactured—temperature-specific delivery within 18–24 hours
- **Autologous cell therapies:** Temperature and time-specific transport of apheresis sample and personalized product. Patient receives specialty product manufactured using his/her own cells

AUTOLOGOUS SUPPLY CHAIN WITH TRANSPORT AND STORAGE REQUIREMENTS

"Cell and gene therapies are unlike small molecules, where a set of processes will work for over 80% or 90% of products. Each therapy requires a unique process."

– VP of Technology and Product Development, clinical stage cell therapy—biotechnology company

The supply chain challenge

The dependencies between each touchpoint in cell and gene therapy are far greater than in traditional specialty pharmaceutical production—and the coordination needed to manage them effectively demands true connectivity.

In the case of autologous therapies, the patient becomes part of the supply chain, which is a situation that presents new challenges. Add to this patient care and the highly specific logistics required, and it's safe to say there is no one-size-fits-all logistics solution available anywhere in the world that brings all the stages and processes together to deliver on the promise of cell and gene therapy—from supply, the blood draw, the manufacturer's process through the delivery to the patient infusion and, inevitably, the billing for the cell and gene therapy product. Detailed knowledge of the complete supply cycle is necessary to develop therapy-specific risk assessments, and these risk assessments should then be used to design the logistics strategy for these products; patient-specific therapies require therapy-specific supply chains.

It's a significant step to go from the clinical trial setting to a fully commercialized product, and sometimes that can present issues. It's why integrated partners are best suited to pull all these disparate elements together, rather than manufacturers struggling to achieve such complex goals by themselves. The right partner will be able to offer:

Global reach and local knowledge

Demand for cell and gene therapy products will be global and as a result the scaled-out supply chain will cross international boundaries, time zones, and climatic regions. The right logistics partner will help therapy owners navigate these challenges and minimize risk to the product, and, in turn, the patient's treatment.

Partners who can offer a global network, operating on a single IT system and quality processes, with employees trained to the same standards worldwide, are well placed for support as the supply chain extends into new countries. In addition, a global presence offers enhanced flexibility and response times—for example, collecting an apheresis sample with pre-conditioned packaging—wherever in the world the patient is located.

Local knowledge is equally critical in ensuring a successful outcome. Knowledge and experience of cross-border shipment regulations is vital for the smooth transfer of novel cell and gene therapies, particularly where the regulatory landscape is still evolving. When the patient is counting on their therapy, the best logistics partners work proactively with customs and other agencies to ensure the quickest possible clearance.

To bring it all together, product-specific and detailed route-by-route planning is required, covering all aspects of the shipment, including packaging, airline choice, and contingency options. Logistics partners who use data to complement their knowledge and experience give therapy owners additional confidence in the safety of their product. For example, logistics providers can bring greater certainty to packaging choice decisions through route-specific temperature data. Equally, a risk-based contingency plan can save valuable time in case the preferred routing is not available. For example, a pre-formulated plan to use ground option alternatives in case of an air traffic control strike in a European country could mean the difference for the patient receiving their treatment.

A trusted logistics partner gives therapy owners more flexibility in other aspects of their commercialization plans (for example, allowing a larger geographical area to be served from a single manufacturing site, thereby reducing the investment required to serve patients globally).

Tested innovations

As momentum builds around cell and gene therapies, it will drive innovations beyond the therapies themselves. For example, the specific combination of size and temperature requirements for cell and gene therapies can be expected to drive packaging innovations to more efficiently meet these needs. Logistics partners have a dual role to play in identifying these advances, and robustly testing them before introduction.

Lean alliances

Within this sector, less is actually more—in other words, choose fewer partners who can deliver more. This removes complexity in an already intricate process, plus it will purge any potential points of failure. With a reduced number of partners, the therapy owner will also enjoy more efficient logistics tracking and kit management, and be able to monitor the performance of the logistics provider more easily, all while optimizing spending and minimizing co-dependent data exchange activities.

Patient-centric solutions

These activities will capture the complete journey of the patient from the initial pre-treatment consultation, to enrollment in the patient support program, to appointment scheduling, shipment coordination, and more. It is essential that such an integrated commercial solution exists, offering fully coordinated patient-centric processes for each and every stage of the treatment journey. Critically, the right partner will set a high bar—because they'll know one missed delivery could mean a patient's life.

Scalable processes

Strategic decisions will need to be made to scale up and out. Planning for future success must be emphasized from the very beginning with any initial processes/providers able to grow into fully fledged commercial operations. Processes must also enable learning and optimization during the clinical trial stage and, critically, produce data to verify the effectiveness of the supply model for regulatory submissions.

Integrated data into action

The right partner will offer data integration capabilities that will allow for effective communications between all stakeholders involved in the process. Data should act as a communication driver. At minimum, it should enable the supply chain to be choreographed so that the arrival of starting material is coordinated with available manufacturing slots, and that pre-conditioned packaging is delivered as soon as the product is ready for delivery. Beyond this, it could enable "navigators" to serve as a single point of contact for providers and patients, coordinating all activity and streamlining communications. It could also enable teams to evaluate the patient journey holistically, identifying opportunities to continuously improve offerings that reduce barriers to access and increase speed to therapy.

For instance, data aggregated from various sources can provide transparency and visibility for patients' caregivers and providers, while informing what requirements are needed for the commercial supply chain. Critically, the analysis of the data can act as a "single source of truth" for audit purposes and serious adverse events, as well as chain of custody and tracking.

Full end-to-end temperature monitoring of cell and gene therapies is a requirement to demonstrate that the cold chain was maintained throughout transit. Therapy owners are also looking for real-time GPS tracking to supplement other shipment tracking data. Beyond peace of mind, a key question is how to make the most of this data; knowing that a shipment is almost out of range is not useful if the only available option is to return to the start of the supply

chain. The value of temperature and GPS data is amplified when combined with a logistics partner who can intervene in case of a temperature anomaly or delay in transit, wherever the shipment is located worldwide.

> *"Real-time temperature and location tracking is important because these products are very costly and very fragile. A temperature excursion reduces viability, and most products have a short shelf life, so delays can be costly."*
>
> – Head of Manufacturing, clinical stage cell therapy—biotechnology company

Invaluable volume

The right partner will have the ability to handle volume, enabling a true "economics of scale" and genuine leverage. They should be able to offer high-quality contingency planning, achieve a high return on investment on packaging and transport costs, and roll out an integrated systems strategy.

Tapped talent

Therapy owners will be able to move to a robust system earlier with a suitable partner in place, ensuring large lifts later in the product cycle are avoided while safeguarding the supply chain (eg, moving from paper/Excel-based tracking to a digital solution). Designing the supply chain model with the right partners will also enable the scaling out of the operation, becoming a vital training exercise.

Parallel programs

Working with the manufacturer, the supply chain and patient programs can be designed to work in tandem with one another to ensure the best possible outcomes for cell and gene therapy development and commercialization. To help deliver this strategy, robust patient programs are required with the "navigators" in the patient program playing a key role in directing the commercial supply chain.

Imagine the programs as **hub models** with case managers whose actions will trigger supply chain activities. For instance, patient enrollment triggers the apheresis scheduling; this triggers a kit distribution and the need to arrange logistics for the sample to be delivered to the manufacturing site, which, in turn, must have a slot reserved.

Logistics know-how

Accounting for commercial logistics infrastructure and process is a requirement for pre-market launch. Apheresis kit warehousing, customer service, returns, accounting, contract/chargeback administration, and, most importantly, the front-end ordering system should be tailored to customized product requirements.

Looking at financial services, an integrated third-party logistics partner can provide proven methodologies and processes, and offer comprehensive accounts receivable management, including account setup, invoicing, collection, and cash application efforts. Because the complexity of this therapeutic category is so immense, the financial services to support each product must be customizable based on business model, including credit procedures, payment terms, cash application, collection efforts, and monthly reporting.

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A **hub model** streamlines the delivery of valuable services to patients, providers, and payers.

Transformed supply chains

As the product moves into full commercialization, the existing visibility in the supply chain will transform into the need for visibility of the entire patient journey, including enrollment and access, as well as logistics events to trigger order-to-cash processes and payment collection.

"For example, phase 1 studies for a cell therapy may happen at a single location and move to multiple sites for phase 2 and 3 studies, with apheresis happening at one of those sites. As the product moves to commercialization, manufacturing and apheresis may each occur at many sites. Seamless logistics mean that apheresis scheduling in a patient hub program links to an available manufacturing slot, which triggers logistics preparations, such as the shipment with temperature-controlled packaging and a time-definite pickup, which should in turn initiate invoicing."[3]

The number of participants involved in the supply chain will grow and the right partners will ensure that this transitional period is fully mapped, rather than being rolled out on an ad hoc reactive basis.

The reach of supply chain decisions

It's essential to understand that supply chain decisions will impact all other aspects of cell and gene therapy program creation:

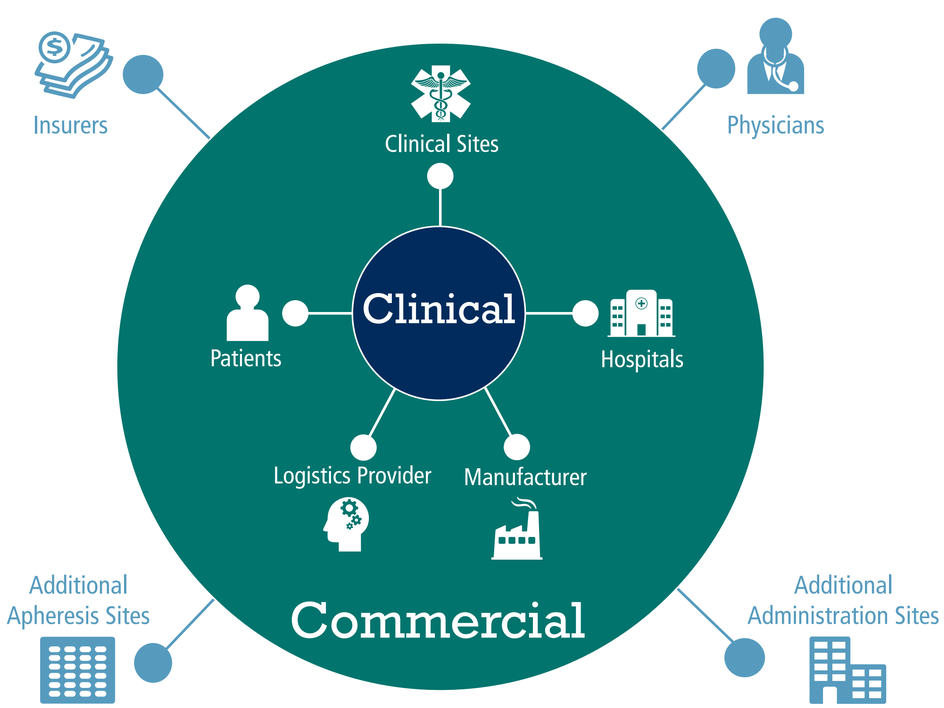
- cGMP manufacturing capacity to scale up and out
- Data integration and architecture design for needle-to-needle reporting and to provide information on patient outcomes over time
- Product coding strategy, a flexible manufacturing and supply chain approach to allow adjustments to meet payer requirements
- Patient programs designed to inform a hub model where actions trigger supply chain activities

Supply chain/logistics: KEY TAKEAWAYS

If you consider the moving parts and the "cost" of the product for the patient—simply put, there is no backup vial that can be overnighted because this is their own material—we must be extremely demanding and require the highest standard. There's no room for error in the supply chain.

Given the interdependencies between each stage in cell and gene therapy, bespoke and integrated supply chain elements are essential. Personalized medicine requires a personalized supply chain; complicated from the outset and only growing in complexity as studies move rapidly through the clinical phases to market.

GROWING NUMBER OF STAKEHOLDERS



There is no distinct hand-off from the clinical to commercial supply chain, it just increases in complexity. Aligning the growing number of stakeholders is a challenge, and one that must be proactively engaged. In summary, therapy owners should consider the following:

- ☑ Make clinical decisions early on that have the capacity to scale up and out as the product moves to market
- ☑ Focus on the logistics—from time and temperature-shipping requirements to the financial processes required to support the commercial launch
- ☑ Select a partner who can support the growing complexity—from increased production volumes to geographical reach and the creation of patient programs
- ☑ Create joined-up, integrated processes that prioritize the patient in the supply chain
- ☑ Integrate data to support multiple outcomes—needle-to-needle tracking, chain of custody evidence, proof points for regulatory approval—to inform patient care and experience improvement, ultimately enabling effective communication between all stakeholders

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SECURING REGULATORY APPROVAL

Navigating regulations: Mission impossible?

The regulation of cell and gene therapy development involves many competing interests that can cripple a program before its therapeutic benefits have even been realized.

To ensure a program complies with complex regulatory requirements, therapy owners must analyze and navigate the legal processes in their targeted territories to guarantee a successful outcome.

One country, multiple approvals

In the US, cell and gene therapies are subject to oversight by two federal agencies within the Department of Health and Human Services—the Food and Drug Administration (FDA) and the Office of Biotechnology Activities at the National Institutes of Health. Gene therapy protocols are, in turn, reviewed by the Recombinant DNA Advisory Committee (RAC).

The FDA and RAC have overlapping review roles—both consider pre-clinical and clinical issues—however, the latter serves as an open forum to publicly examine gene therapy concerns that extend beyond safety and efficacy and into the ethical, legal, and social realms. By contrast, the FDA's reviews and deliberations are confidential unless scientific issues are discussed publicly at an FDA Advisory Committee meeting.

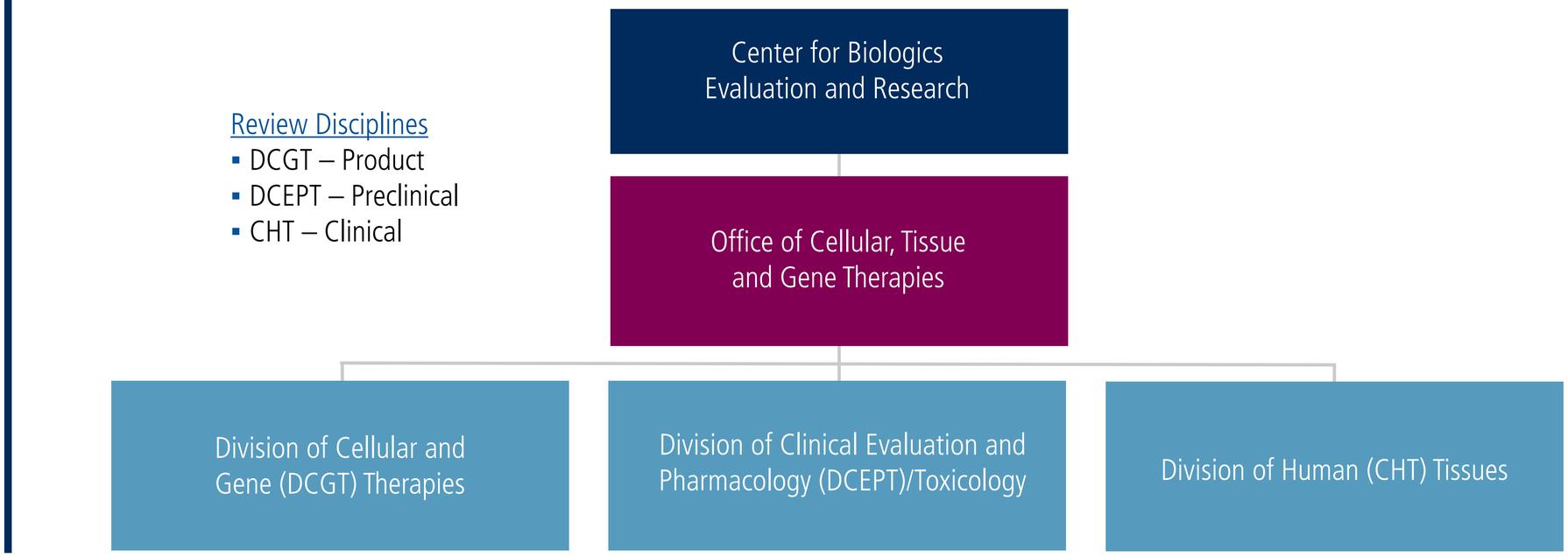
The RAC's recommendations are also non-binding in contrast to the FDA, which has the legal authority to regulate cell and gene therapy products under the Investigational New Drug application, the Biologics License Application (BLA), and the Investigational Device Exemption. Finally, any cell and gene therapy products are evaluated by the Office of Cellular, Tissue and Gene Therapies at the Center for Biologics Evaluation and Research.

To successfully conform to the FDA's procedures, manufacturers must:

- Provide complete information on all components and materials used during the development of a cell and gene therapy product
- Provide information on both the manufacturing process, facility, and supply chain; this information will be used to assess a host of criteria, including the quality, potency, and safety of the final cell and gene therapy product
- Provide information on methods, facilities, and manufacturing controls to ensure that the cell and gene therapy product meets appropriate standards of safety, identity, potency, and purity
- Consider how to best ensure the implementation of standards, practices, and procedures so the product conforms to cGMP

> *"The process is the product. Logistics for cell and gene therapies are very critical for approval. The FDA doesn't like change so composition of cell, methodology, and protocols need to be clear."*
>
> – VP of Technology and Product Development, clinical stage cell therapy—biotechnology company

APPROVAL PATHWAY FOR GENE THERAPIES[4]



The US & EU Relationship: A work in progress

Challenges persist over the differences between US and EU regulatory processes, with the latter's overseen by regional and centralized regulatory bodies.[5]

Typical obstacles include the cost and the time it can take for cell and gene therapies to proceed from concept to approval under the regulations of each territory. In recent years, there have been calls to tighten approval processes and to establish regulatory consistency between the FDA and the EU.[6]

Efforts include recent legislation in the US Congress to enable the release of drugs in the US that have already attained European approval. Proposed changes to regulations of the European Commission (EC) regarding cell and gene therapy approval are also under discussion,[7] but are vigorously opposed by industry and patient groups who insist that such regulatory moves will impede the availability of innovative therapies to the public.

Clinical considerations

Because cell and gene therapy is an emerging scientific breakthrough, there are questions around their long-term safety and efficacy.

Many of the collection and administration procedures are highly invasive and complex, which makes blinded trial designs difficult or potentially unethical. In addition, over 30% of these therapies target rare disease, which compounds the challenge of assessing outcomes due to the small patient sample sizes.

This creates several study design challenges for manufacturers and regulatory bodies to appropriately assess these therapies. For example:

- Use of single-arm or crossover trial designs to maximize the number of patients exposed to active treatment; therefore, head-to-head comparison is not feasible
- Complex blinding techniques
- Controlling for variation in skill of surgical procedures associated with collection and administration
- Use of surrogate markers to assess efficacy and safety, since sample size and trial length may prevent the ability to power trials appropriately to measure true clinical events and outcomes
- Limited trial length (3–5 years) to assess long-term safety and efficacy of therapies with an anticipated long horizon of benefit

Embracing efficacy

The western world's first approved gene therapy, Glybera, is particularly relevant in the discussion around confidence of long-term efficacy. The therapy is an ultra-orphan treatment for lipoprotein lipase deficiency (LPLD) and treatment involves a one-time series of injections of viral vector carrying an intact copy of the LPL gene. While preliminary results from clinical trials showed that Glybera affects lipid metabolism, the long-term effects were uncertain, thereby requiring four submissions before finally gaining approval under exceptional circumstances by the European Commission in November 2012.

Due to the uncertain long-term effects, coupled with its ~$1 million price tag and small patient population, the product has only been used in one patient on the commercial market. Due to the lack of utilization after commercial launch, the manufacturer announced in April 2017 that it will not renew its marketing authorization in Europe in October.

To help mitigate this concern and outcome, therapy owners should use a proactive, integrated approach with providers, payers, distributors, and patients to generate a data strategy that helps not only prove the clinical benefit in the short term, but also continues to document the benefit in the long term.

Defining value

The level of uncertainly of treatment in the real world, which is particularly high for cell and gene therapies, will strongly affect stakeholder confidence in their use. Payers will be reluctant to pay large sums for treatments based on the benefits and cost-savings from small, carefully selected patient groups in controlled clinical settings. They will look for evidence of long-term efficacy in order to justify product coverage over time. Because of this, data collection and processing should start before approval and continue after launch to improve the evidence package to document the long-term benefits of cell and gene therapies.

High-quality data based on real-world evidence (RWE) from programs such as the UK's Early Access to Medicines could also be used for

potential leveraging; the program allows for the distribution and treatment of promising phase 2 and 3 products free of charge to NHS patients with life-threatening or debilitating disease. The first therapy to pass the initial step of Early Access Designation was a dendritic cell therapy targeting malignant gliomas, DCVax-L.

Other cell and gene therapies are also likely to be suitable for similar expanded access programs in other countries due to their targeting of diseases with high unmet needs.

Therapy owners who are considering this path should be clear at the outset how expanded access fits into their overall product strategy and how real-world and pharmacoeconomic data will support their approval case. This will ensure a positive return on the costs of product supply, as most expanded access programs do not provide for reimbursement, and avoid unintentional impact on future demand for the product. Real-world data may be better suited to cell and gene therapies targeting chronic conditions and where the aim is to demonstrate long-term improvement, over those therapies that are one-off curative products.

The reach of approval decisions

It's essential to understand that approval decisions will impact all other aspects of cell and gene therapy program creation:

- Manufacturing and supply chain; needle-to-needle data integration to fulfill regulatory body requirement for full component and material information
- Patient programs; a dependency to collect data on patient outcomes over time
- Considering expanded access programs to collect real-world data; supply chain designed to serve patients outside the geography of the targeted clinical trial

Securing regulatory approval: KEY TAKEAWAYS

Satisfying safety, quality, and efficacy standards set by the relevant authorities takes significant time and investment and should be considered from the outset.

From the therapy owner perspective is it essential to work with the regulatory authorities to develop the best possible clinical package in the lead up to launch. By developing an RWE plan prior to approval, the therapy owner can continue to collect data after launch to document the longer-term benefits of the product.

> Regulatory cooperation and alignment are essential for progress in the development and commercialization of cell and gene therapy products and must be proactively managed. In summary, therapy owners should consider the following:

- ☑ Collection and processing of accurate and required data should start from the earliest clinical phases, through pre-approval and launch, and continue post-launch to:
  - Provide clear evidence of meeting the required standards in relation to safety, identity, potency, quality, and purity—as well as cGMP requirements for product and manufacturing operations
  - Provide clear evidence to ensure better therapeutic use of cell and gene therapy
  - Provide clear evidence and stronger positioning for payer and provider negotiations
- ☑ Design of RWE plan in the early stages of development and implement pre-launch to further demonstrate long-term outcomes post-launch

Introduction

Integrating Supply Chain and Logistics Strategy

Critical Success Factors for Market Access: Coding, Coverage, and Reimbursement

Managing Payment and Distribution

Manufacturing and cGMP

Securing Regulatory Approval

Creating a Differentiated Patient and Provider Experience

Conclusion

Overarching data management architecture delivers needle-to-needle insights

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CRITICAL SUCCESS FACTORS FOR MARKET ACCESS: CODING, COVERAGE, AND REIMBURSEMENT

Marrying innovation with commercialization

When bringing a cell and gene therapy to market, three key factors impact the therapy owner's approach to achieving successful coverage and proper reimbursement for their innovative product.

These include:

- **Production and administration**
- **The level of evidence/size of the study population**
- **The magnitude and duration of benefit**

In this section, we describe how these three factors can affect the coding, coverage, and reimbursement of a product, and therefore directly influence the product's commercial potential.

Coding

Planning for the unique requirements associated with the novel administration of these therapies not only presents potential logistical issues, but also several payment and reimbursement challenges, too. Therapy owners are paid for different components of the product (for example, apheresis, cell processing, infusion, etc) and the timing of each payment is informed by the reimbursement plan in place.

In the US, receiving payment from payer (whether government or private insurance) to therapy owner is contingent on how the product is coded. One of the few cell and gene therapies approved in the US, sipuleucel-T (Provenge), highlights the challenges of relying on legacy codes to assign these products.

The autologous cellular immunotherapy was approved in the US in 2010 for treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer.[8] It is administered via 3 infusions at 2-week intervals; leukapheresis is performed 2 to 3 days in advance.

Despite multiple rounds of coding requests to the **CMS HCPCS workgroup** for novel payment methodologies, only a specific **Q-code** was assigned, which placed sipuleucel-T into a traditional HCPCS drug-type coding process. In addition, existing **CPT® codes** were deemed appropriate for collection and administration by the provider.

Q-Code for Provenge	Description
Q20143	Sipuleucel-T, minimum of 50 million autologous CD54+ cells activated with PAP-GM-CSF, including leukapheresis and all other preparatory procedures, per infusion

Shortchanged

The Q-Code includes "leukapheresis and all other preparatory procedures" involved in producing a patient-specific infusion,

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CMS HCPCS workgroup
Centers for Medicare & Medicaid Services
Healthcare Common Procedure Coding System

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Q-Code for Provenge	Description
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Shortchanged

The Q-Code includes "leukapheresis and all other preparatory procedures" involved in producing a patient-specific infusion, meaning there is no separate code to account for cell processing

Q-code

Miscellaneous services on a temporary basis, including procedures, services, and supplies

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CPT® codes

Current Procedural Terminology codes are used to describe medical procedures, including tests, surgeries, and evaluations

The international perspective

Coding challenges for these novel therapies are not limited to the US. In the EU5 (UK, France, Germany, Italy, and Spain), hospitals typically receive funding on an annual basis from either a national or regional authority based on actual costs from diagnosis-related groups (DRGs) from previous years. Therefore, when introducing a costly new therapy, a funding gap may arise for hospitals, especially if that hospital is a select center that will provide care to patients with a rare condition from many different regions.

To address this financial gap, there are potential, unique funding mechanisms in each country. Understanding the intricacies of each of these mechanisms will be important to improve adoption rates of these therapies. For example, in Germany 2 funding mechanisms exist:

1. **NUB**, which is similar to a new technology add-on payment in the US and provides a supplemental funding source for the first 2 years after a therapy is launched
2. **ZE**, which provides a permanent update to the reimbursement for a DRG

The NUB application must be submitted by each hospital to secure additional payment for that hospital to the Institute for the Hospital Remuneration System.

In Italy, therapies that will present a funding gap must be included on an F file list. A local physician must initiate the application and receive backing from a hospital pharmacy director. Each region in Italy has its own F file list; therefore, there can be significant variation in reimbursement.

These examples highlight the importance of understanding the operational side of coding and reimbursement in each country to avoid barriers to reimbursement.

Coverage

When pharmacy and therapeutics (P&T), medical policy, and/or health technology assessment (HTA) committees evaluate coverage for a product, they assess not only the clinical efficacy and safety data, but the cost-effectiveness of that product, too.

Given the complexity, novel production, and administration of these cell and gene therapies, the type of committee responsible for assessing these therapies may vary. It is essential then to engage in discussions with payers early in the development process to glean invaluable insights into the possible evaluation pathways, associated steps and evidence packages required.

In addition, the criteria for assessing cost-effectiveness varies by country and by individual HTA/P&T committee; therefore, knowledge of the evaluation metrics and processes for these products target

Coverage

Coverage for a product refers to payers (government or private insurance) allowing access to a therapy.

meaning there is no separate code to account for cell processing by the manufacturer, and consequently, no separate payment for that service. This means that no reimbursement for the product is granted until the product is administered to the patient.

Therefore, if the patient can't receive the therapy in 2 to 3 days due to illness or another reason, the cost of producing that specific dose cannot be recouped by the manufacturer. In the case of sipuleucel-T, this is a dose-by-dose issue. However, for some pipeline cell and gene therapies, production of the full treatment course (several doses) will occur from a single extraction of patient-specific material.

Therefore, under a sipuleucel-T (Provenge)–like coding arrangement, a therapy owner may be required to absorb the cost of an entire treatment if therapy is discontinued.

"Many therapy owners think, 'If I build it, they will come,' and are not thinking about pricing and reimbursement. The consequences are that payers may choose not to reimburse the product, or will at least create long lag times because the therapy owners didn't engage soon enough."

– Former Board Member, multiple health plans

Strategize to monetize

The sipuleucel-T Provenge example highlights the importance of developing a coding strategy to determine if existing codes will be sufficient or if the therapy owner should apply for new payment codes.

Having the appropriate code set will not only affect the therapy owner's payment, but can also significantly impact a provider's ability to be reimbursed for administration of the product or extraction of the source material from the patient.

Without the proper diagnosis, procedure, and therapy codes, utilization of the novel therapy may be delayed or significantly reduced due to the inability of the provider to be appropriately remunerated in a timely manner—or at all.

Cracking the code

Developing a coding strategy should be carried out 2 to 3 years prior to launch while a product is in phase 2 or 3 for five key reasons:

1. It can take three or more years to apply for and secure the necessary codes
2. It can impact the site of care selected for a therapy because that site allows the most feasible path to payment; therefore, knowing this information early in development may impact the site of care selected in the trial design
3. Collecting the appropriate resource utilization data in clinical trials may increase a product's ability to secure certain new payment codes
4. A product's coding at launch and its potential evolution will determine what personnel and resources will be needed; often, hiring field reimbursement personnel and developing reimbursement tools to guide providers starts a year prior to launch
5. The level of evidence and magnitude of benefit may affect the willingness of a private or public payer to award new and/or product specific codes

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markets is necessary early in the development process. Market research, advisory boards, or other methods of collaboration with payers and HTA decision makers should be implemented while the product is in trials. In addition, seeking scientific advice in Europe or leveraging a pre-approval information exchange with US payers will allow dialogue to identify reimbursement and coverage barriers prior to launch. This will help ensure that the appropriate clinical and outcomes measures can be captured in the clinical or health economics study programs.

Complex care

Because many of the cell and gene therapies in the pipeline are being developed for orphan indications, trials are typically limited in length and held within small patient populations. This provides a reduced data set for decision makers to assess the product's true impact or value over time. To further complicate matters, many of these therapies will be administered over weeks to months, thereby front loading the cost to the payer and limiting the ability to avoid costs if the benefit in a patient isn't realized long-term.

Since several of these therapies may be curative or provide a substantial clinical benefit over standard of care, it is expected they will be priced based on this projected benefit. Therefore, the cost of therapy (perhaps in excess of USD 1 million) magnifies the issue of making coverage decisions based on limited data sets.

In single-payer systems, coverage decisions are complex; therapy pricing reflects the benefit to the entire health and social care system, which has multiple budget holders (primary, tertiary, and social care being major groups.) The budget holder responsible for cell and gene therapy costs may not reap the full benefit because avoided costs are realized by other budget holders.

Complicating this issue further are marketplaces like the US that do not have a single-payer system, patients often switch insurance plans; hence, the payer that paid for the cell and gene therapy may not receive all of the benefit if that patient leaves their plan. However, they may also inherit patients from other plans who have already benefited from receiving a therapy.

Managing multiple issues

This far-reaching range of issues means payers may need to re-evaluate the processes and criteria that determine coverage policies for cell and gene therapies.

For therapies that provide an incremental benefit above standard of care, it is anticipated that payers will evaluate them via the existing standard process and expect pricing reflective of the incremental benefit.

For therapies that are transformative, payers may ask for data beyond the clinical package to increase their comfort level with the upfront cost burden. Creating registries to capture resource utilization and burden of illness with the existing standard of care may be important to have a baseline for demonstrating the economic impact of these transformative medicines.

"With cell and gene therapies, it becomes more critical that a pharmaceutical company has a well-designed trial, clear clinical markers, and robust data. We need a clear story around efficacy."

– VP of Pharmaceutical Contracting, top 5 national health plan

Data targets

Capturing changes in resource utilization during the clinical program will also be critical. In addition, the emergence of value frameworks from provider-led organizations/guideline developers (especially in oncology) and the move toward value-based payment of providers, suggests that resource utilization data and outcomes data is becoming more relevant in provider marketing, as well. Including strategies to convey outcomes data to new audiences will be important, as will selecting a partner who can facilitate this from the data collection method design to the analysis of the data to make it actionable and applicable to all stakeholders.

Finally, the complexity of producing and administering a cell and gene therapy may involve multiple sites of care and multiple high-cost procedures. Such complexity may require split payments or new contracting agreements between entities, which dramatically increases the need for care coordination. This could also impact a payer's decision for coverage, as they may choose to require administration by certain specialists/centers or require providers to undergo training and certification before granting access.

By understanding the coverage scenarios early in development and coordinating between clinical and health economics plans, market access strategy, a distribution strategy, will help the development of an integrated commercialization strategy that increases the likelihood of a successful launch.

Creating a clear channel strategy

Access is contingent on developing an appropriate channel strategy when bringing a cell and gene therapy to market. It requires strategic thinking and has a significant impact on product uptake and commercial success.

Patient expectations and influence on their own treatment is growing. So, too, is provider demand for access to cell and gene therapies. That's why it is important that any brand team speak with channel stakeholders who are experienced in delivering the right product to the right patient at the right time. Understanding both the commercialization impact of distribution and customer channel decisions will help therapy owners evaluate channel strategy through the lens of patient access and product success.

Reimbursement/payment

Payment refers to reimbursement by the payer to the provider or manufacturer for the services or a product provided.

Although most advanced healthcare systems are evolving from a service fee system (or similar) to a value-based system, much of the existing payment modalities still reflect a service fee model.

The characteristics of cell and gene therapies magnify some of the limitations of the service fee model and will require a thoughtful strategy from the therapy owner based on proactive discussions with both providers and payers.

If a product is covered under the pharmacy benefit, then payment for any procedures associated with pre-production extraction of the biologic material from the patient or administration of the product by a provider must be paid for separately by the payer directly to the provider. It means that an understanding of the authorization process and payment levels/timeliness for these associated services will be critical to commercial success.

If a product is covered under the medical benefit, pre-production extraction may still require separate payment for services or the payer may dictate that coverage of those services be provided by using the drug-specific HCPCS code. Therefore, the administering provider may need to establish a contract with the provider(s) completing the collection of the patient-specific material.

Alternatively, if the payer determines a bundled payment is appropriate, then the logistics of providing that bundled payment may fall on the payer, manufacturer, or one of the providers along the supply chain. A thorough understanding of the payment logistics will be required by the therapy owner to ensure that any one provider along the payment continuum is not disincentivized to complete their part of the process. Data transparency along the supply chain supports the analysis.

Breaking down barriers

Additionally, because of the expected cost of these therapies, a traditional buy-and-bill method for these products would require the administering provider to invest significantly to purchase the product. This alone may be a barrier to prescribing and administering the product; however, the risk is compounded if multiple providers are required to complete various steps of the process. Any misstep along the process may put the administering provider at further risk of recouping their financial outlay.

From the payer and patient perspectives, paying for the therapy or the coinsurance for the therapy upfront may be cost-prohibitive, depending on the cost of the therapy. In either case, a new payment mechanism with both the payer and patient may be needed, such as outcomes-based contracts, licensing agreements, or loans that gradually write off the cost over the expected benefit's duration—or at least a portion of that time.

This will not only impact the type of contracts put in place with payers or patient assistance strategies for patients, but may require a novel relationship with distributors; after all, they could play a pivotal role in delivery of these therapies and are in a position to address several of the potential reimbursement and logistical barriers that exist for these products.

"Many of these therapies have 7-figure 1-time costs. We have to cover them and we need to figure out alternative reimbursement arrangements."

– VP of Pharmaceutical Contracting, top 5 national health plan

Proactivity with payers

Cell and gene therapy owners need to reach payers to communicate the product's value messages and clinical and economic data. Evidence-based guidance is required to facilitate meaningful discussion between owner and payer, particularly as product portfolios change and as value-based reimbursement models evolve. For cell and gene therapy owners without this capability in-house, selecting a partner who can offer outsourced managed care resources is key to accessing influence payer knowledge and perception of the product.

REIMBURSEMENT COMPARISON: SPECIALTY INFUSED DRUGS AND BIOLOGICS VS CELL AND GENE THERAPIES

	Specialty Infused Drugs and Biologics	Cell and Gene Therapies
Coverage	▪ Established coverage paradigms; typically managed under a medical benefit ▪ Coverage is usually based on product label and treatment guidelines	▪ Benefit categories are likely to vary; multiple or new categories may be needed ▪ Coverage may be based on label and treatment guidelines
Coding	▪ Drug/biological coding follows well-established processes ▪ Existing codes for drug administration services are usually sufficient	▪ Likely to generate significant uncertainty about coding, since it may not fit into established processes for product and administration coding ▪ Codes may not allow for separate payment of all services (eg, preparation, storage, etc) ▪ Need to modify or create new codes to facilitate appropriate payment requires significant effort and time on the part of manufacturers
Payment	▪ Typically fee for service, with separate payment for the drug and for the drug administration ▪ Bundled and value-based payment models are becoming more prominent	▪ Multiple scenarios possible, including "split" payments for multiple phases of therapy or greater potential for combined or bundled payment ▪ Multiple providers and sites of care may result in need for new contracting between different stakeholders ▪ Manufacturers will need to explore alternate payment models that spread economic risk in order to overcome payer hesitancy

The reach of coding, coverage, and reimbursement decisions

It's essential to understand that coding, coverage, and reimbursement decisions will impact all other aspects of cell and gene therapy program creation:

- Optimal coding arrangements will be influenced by a clear, early view of supply chain and manufacturing processes; these processes may be adjusted as manufacturers aim to minimize risk exposure to unreimbursed treatment courses
- Supply chain design, with the requirement to serve the specialists/centers as determined by the payer
- The site of care selected for a therapy in trial design is informed by the most feasible path to payment, which, in turn, impacts the creation of patient programs based on the site selected

Production and administration, level of evidence/size of study, and magnitude and duration of the benefit are the three key factors that shape a therapy owner's approach to achieving successful coverage and proper reimbursement for their cell and gene therapy product.

The approach to, and demonstrable results from, each of these factors informs the creation of a fully formed coding, coverage, and, ultimately, reimbursement strategy that will optimize access for therapies in which the patient is in the supply chain.

Coding, coverage, and reimbursement: KEY TAKEAWAYS

Coding, covering, and reimbursement strategies are essential to the development and commercialization of cell and gene therapy products and must be proactively managed. In summary, therapy owners should:

- Begin discussions early in the development process with providers, payers, and distributors to understand the payment logistics and possible pathways that will address their product's specific needs
- Develop a coding strategy 2 to 3 years prior to launch while a product is in phase 2 or 3
- Investigate and implement the right channel strategy to ensure access in all the appropriate channels to minimize complexity for patients and healthcare providers
- Examine the patient affordability issues to gain a true understanding of the holistic out-of-pocket costs to the patient; this will help guide not only a patient assistance strategy, but also potentially several aspects of the commercialization
- Launch with the right logistics and payment mechanism in place, which may lead to a reduction in overall funding needs for a patient assistance program
- Consider the requirement for health economics and outcomes research to provide evidence-based strategies to communicate the product value story at launch, and to extend commercial opportunities later in the life cycle by uncovering new evidence that demonstrates comparative effectiveness

AmerisourceBergen®

CREATING A DIFFERENTIATED PATIENT AND PROVIDER EXPERIENCE

Navigating the patient and provider partnership together

A wrap-around service is needed to meet the high level of coordination required by the patient, provider, and other stakeholders in the supply chain.

As a product moves into commercialization, the focus will inevitably turn to product access within the supply chain and most importantly, on the patient and provider experience. Vital to this transition is the ability for the patient to successfully navigate through the many potential challenges relating to payer coverage/reimbursement, affordability, and ongoing treatment.

Analyzing clinical trial protocols that encompass both patient and trial site experiences is essential to this process, with the caveat to understand there may be critical differences. It should cover all aspects of the treatment journey, from initiation to the course of the therapy itself, and serve as a benchmark that will drive the development of a therapy owner-branded commercial patient and provider support program.

The end goal is to position the program as a single point of contact for the provider and patient, and aid in the coordination of product and treatment insurance coverage, and logistics and/or distribution services. This will help mitigate the challenges often experienced at the initial launch and as the product matures, aid in the ongoing coordination of all key stakeholders including the provider, patient, manufacturer, and logistics and/or distribution partners.

Addressing cell and gene therapy specifics

The key difference between cell and gene therapy provider/patient support services and traditional specialty pharmaceuticals is the need for a wrap-around service that fully addresses the high level of case management coordination required for patients. The service plan should cover the entire process, beginning with the providers' decision to treat the patient through to therapy completion and perhaps beyond, to further support prospective studies. The planning should also include a range of timing requirements, such as tissue samples and transport, as well as the management of complex dosing regimens.

CELL AND GENE THERAPY PATIENT SERVICES ACCESS, COORDINATION, AND ADHERENCE SUPPORT

Designing a patient and provider program

A critical element of commercialization and patient support services is the ability to create a proven and tested process for patient access that offers a consistent experience for both the patient and the prescriber.

In preparation for commercialization, there are several recommendations for the design of a cell and gene therapy patient support solution to ensure success. Firstly, the patient support program provider should serve as the point of intake and referral in the patient enrollment process. The provider should also secure reimbursement coverage, offer financial assistance, and provide initial and ongoing stakeholder education.

Key features of a patient support solution

The patient support model should be based on a case management model—this typically features a dedicated point of contact assigned to each patient who is geographically aligned with field sales/educators and has the necessary expertise in regional payer management. A qualified patient support provider should be deployed, as well, to strategically manage and administer the cell and gene therapy program. In the event of denials for coverage, the patient support case management group will also serve as the trigger to notify the managed care team of the denial and to determine the appropriate strategy to support the appeal and overturn the payer decision.

In addition, looking at aggregated coverage/denial data on a regional- or payer-specific level can help guide a therapy owner on deployment of payer account management or field reimbursement personnel. For complex therapies, both account management or field reimbursement managers can serve as a highly effective extension of a patient support solution. For cell and gene therapies with ultra-orphan populations, it may be beneficial or required for a field representative to be both payer facing and physician facing so that they can optimally bridge the reimbursement logistics gap between both parties.

Other critical roles to consider include an experienced strategic account lead to take responsibility for supporting the partnership, as well as dedicated operational leads to serve as daily contacts for program operations and activities.

To ensure effective data and systems integration with supply chain providers, a suitable patient support services provider who can secure a seamless transition into the commercial space should be sourced. This ability to collect data throughout the patient journey will also help evolve the program over time and is critical to the rollout and ongoing development of a successful cell and gene therapy product model.

Ultimately, the provider should help create an invaluable toolset for the patient support case manager to coordinate each program step, as well as offer the opportunity to analyze the time variances in the overall patient experience.

> *"Creating a team that understands the patient disorder and empathizes with what the patient is undergoing is important. If the patient doesn't understand and doesn't want to take the therapy, all the access work you've done is null and void."*
>
> – Former Senior VP of Patient Programs, orphan indication company

Patient and provider experience as the differentiator

Across cell and gene therapy there are likely to be competing products, as there are in the Chimeric Antigen Receptor T-Cell Therapy (CAR-T) space. Efficacy and side effects will be paramount, but those being roughly equivalent to the provider and patient experience will be the differentiator. Key benchmarks will include:

- Comprehensive data capture of the patient journey to include identification of potential barriers and variances within the commercial market to inform the build and design of the support program

- Effective enrollment of the patient into the support program leveraging technology to improve the need for signatures for authorization of services
- Ease of status tracking for manufacturing and estimated return for provider's ability to coordinate with patient preconditioning
- Knowledge and expertise of the case manager supporting their patients and their practice
- Efficient and timely apheresis scheduling
- Flawless logistics supported by a quality framework to track performance and variances to ensure there are no missed manufacturing slots or lost shipments
- Timely turnaround with defined key performance indicators

Fewer, not more, integrated partners with substantial experience and volume are more likely to succeed.

Preparing the provider

Cell and gene therapies have specific requirements relating to handling, storage monitoring, and treatment procedure—all of which will incur significant planning, communication, and coordination between the therapy owner and health system caregivers.

Does an existing facility need to be modified? Is the necessary equipment available? Are site personnel qualified to administer the therapy or is additional training needed? Is upskilling of existing teams a realistic option or do they need to be hired on a temporary basis?

Site staffing requirements could lead to the creation of specialized treatment teams that follow administrations from site to site, trained and/or maintained by the therapy owner and subcontracted by the provider.

These scenarios could lead to fiscal realities that the health system may not have considered. The therapy owner should identify as many of the change factors required and recommend solutions ahead of identifying potential treatment sites with health system customers.

Emphasize education

There is a critical need for patient and clinician education in all aspects of cell and gene therapy. Such education should be customized for all key stakeholders and delivered in a variety of settings and at key points throughout the process.

The patient and their caregiver will require education support as well and they should be given the opportunity to ask questions and access the case manager resource assigned to them throughout the treatment. The education of the patient and their caregiver should also be tailored to meet their level of understanding and segmented based on their ability to manage their own care, as well as the next step in the treatment process that the patient and their family members are about to experience.

Collaboration with patient advocacy groups gives the therapy owner an opportunity to educate, advocate, and actively engage with, and reiterate their commitment to the patient and their community.

As access to these therapies expands to the community setting, therapy owners should explore the benefits of partnering with a specialty physician group purchasing organization (GPO), particularly in oncology. Partnership with a GPO offers access to a network of prescribers through contracting services, as well as analytics to understand prescriber utilization and an array of marketing solutions to support clinical education and product performance. Advisory boards, clinical education, and marketing solutions can be deployed to the GPO's members before the product launches commercially and throughout the product life cycle.

Keep sight of core processes

It is critical that essential processes and practices are rolled out and monitored; for instance, effective patient enrollment via leveraging technology, efficient and timely apheresis scheduling as required, flawless logistics to track performance and variances to ensure there are no missed manufacturing slots or lost shipments.

Timely turnaround is also critical with defined key performance indicators put in place and a "design a center of excellence" approach taken for cell and gene therapy program implementation; key milestones should be created within a detailed project plan and timeline—and include all key stakeholders delivering services.

IMPLEMENTATION PHASED METHODOLOGY

	T-120 Days	T-90 Days	T-30 Days	Launch/Post-launch
Assess	**Design**	**Implement**		**Operate**
▪ Program Awarded ▪ Contracting ▪ Internal Kickoff ▪ Project Plan ▪ Prepare for Design Workshop	▪ Client Kickoff and Design Workshop ▪ Process Flow and Business Rules ▪ Integrated Program Design Document ▪ Program Design Approval ▪ Initiate Program Staffing ▪ Finalize SOWs	▪ Implementation Kickoff ▪ Standard Operating Procedures (SOPs) ▪ System Configuration - CRM - Telecom - Reporting - Data Feeds ▪ Legal Review and Approval ▪ Staffing and Facilities	▪ Team Training ▪ User Acceptance Testing ▪ Executive Business Simulation	▪ Program Launch ▪ Ongoing Quality Monitoring ▪ Effective Business Review ▪ Ongoing Communication Regarding Program Changes, New Innovations, etc

Engagement Approach

Kickoff and Program Design
Workshop to review program strategy, deliverables, and develop program design

Program Status
Checkpoints to review project status and deliverables (weekly)

Executive Status
Status report of project accomplishments and a look ahead (monthly)

Ad Hoc
Discussions and meetings as needed

Focus on the future

Future **care pathways** will exist in multiple forms; for some diseases, there will be a continued need for regular chronic treatment with therapies, while for others, there may be opportunities for lifetime one-time treatments but continued follow-up with the patient. It means clinicians will need to be supported in both pathways with centers of excellence based on disease states ultimately prevailing because of the increasing complexities surrounding treatments.

The reach of decisions related to the patient and provider experience

It's essential to understand that decisions related to the patient program setup will impact all other aspects of cell and gene therapy program creation, such as:

- The supply chain, notably the requirement for needle-to-needle data collection and actions to trigger supply chain activities
- Manufacturing and logistics integration with the centers of excellence for therapy administration
- Manufacturing capacity to scale to a number of global sites; designing a burdensome manufacturing and supply chain process can impact product viability and adoption

Introduction
Manufacturing and cGMP
Integrating Supply Chain and Logistics Strategy
Securing Regulatory Approval
Critical Success Factors for Market Access: Coding, Coverage, and Reimbursement
Creating a Differentiated Patient and Provider Experience
Managing Payment and Distribution
Conclusion

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Care pathways

Clinical pathways, also known as **care pathways**, critical pathways, integrated care pathways, or care maps, are one of the main tools used to manage the quality in healthcare concerning the standardization of care processes. It has been shown that their implementation reduces the variability in clinical practice and improves outcomes. Clinical pathways promote organized and efficient patient care based on evidence-based practice. Clinical pathways optimize outcomes in the acute care and home care settings. Generally, clinical pathways refer to medical guidelines; however, a single pathway may refer to guidelines on several topics in a well-specified context.

Creating a Differentiated Patient and Provider Experience

KEY TAKEAWAYS

The high level of coordination and interdependency between the various components in the cell and gene therapy supply chain is well documented.

As the product moves toward market launch, the spotlight turns to access, key stakeholder coordination, and how the interlinking parts can combine to prioritize the patient and provider experience through the creation of robust, appropriate patient programs.

It is vital that the solution works for both the prescriber *and* the patient based on the results of pre-launch surveys and advisory boards with key opinion leaders and community practices. These findings should be applied to the design process with accompanying feedback from field sales on how any service messaging will be delivered.

> The patient program will be paramount to the success of a cell and gene therapy product, so it must be proactively planned and managed. In summary, therapy owners should:

- ☑ Analyze clinical trial protocols that encompass both patient and trial site experiences throughout all stages of treatment journey and the impact of transitioning the experience into the commercial real-world setting
- ☑ Anticipate and plan for a wraparound service that fully addresses the high level of case management coordination required for patients
- ☑ Consider the overarching data architecture to ensure that effective systems integrate and data is collected to support and evolve the program
- ☑ Prioritize patient and clinician education and support, given the novel nature of the products
- ☑ Be cognizant of the fact that patient and provider experience are ultimately going to be the differentiator in a market where there are likely to be competing products

Overarching data management architecture delivers needle-to-needle insights

AmerisourceBergen®

Contributors & cell and gene therapy working group

References

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MANAGING PAYMENT AND DISTRIBUTION

Developing dynamic distribution

Because cell and gene therapy products evolve differently than traditional specialty pharmaceutical products, therapy owners will need to overcome several significant obstacles to create a truly optimized distribution strategy.

Cell and gene therapy products require a variety of paths for effective delivery, primarily because the patient can be part of the manufacturing process and the products cost more to develop and produce than traditional specialty products. Additionally, such products often require temperature-controlled handling, are more expensive to purchase, and are designed for a smaller patient population. They may also have rigorous requirements for safe administration.

There are several models that can be tailored to meet such exacting distribution considerations, whether via a standard approach or a highly customized model. Understanding the differences between various models and the impact on customers and patients is critical to ensure a successful cell and gene therapy product launch. Regardless of the approach that is ultimately adopted, the final distribution strategy must be able to deliver "the right dose of the right drug for the right patient at the right time."

The role of the distributor

Understanding the commercialization impact of distribution and customer channel decisions will help manufacturers evaluate the channel strategy that is right for their product.

It can be easy to think of a drug distributor as the entity that moves a product from point A to point B, but in reality it's the unseen services within the distributor's infrastructure, such as financial management, supply chain security, customer experience, and more, that add value to partnerships between therapy owners and distributors. In addition, the right distribution partner can help evaluate how channel strategy will affect customers and their patients. As product value increases, so does the value of the distributor and the many services they provide.

Given that cell and gene therapies are expected to launch with particularly high price points, there is benefit in the financial management services the distributor provides. The distributor plays a critical role in the supply chain by taking on financial risk for the therapy owner's receivables. Whether from health systems or other customers, the distributor insulates the innovator company from risk; both logistics risk (if product is broken or lost in transit), as well as attributable risk when a customer can't pay on time. Given the prime vendor agreements that are used to manage pharmaceutical purchasing between health systems and a distributor, the distributor model provides manufacturers with reliable cash collection.

MANAGING PAYMENT AND DISTRIBUTION

Developing dynamic distribution

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Channel strategy

Access to cell and gene therapies is contingent on developing an appropriate channel strategy when bringing a product to market. It requires strategic thinking and has a significant impact on product uptake and commercial success.

Read the "Creating a Differentiated Patient and Provider Experience" chapter to find out more.

Distributors are purpose-built to drive efficiency and continuous improvement in the supply chain—scaled and staffed to deal with logistics, customer experience, accounting, and more. Why would an attributable risk cell and gene therapy owner want to turn their focus away from developing life-saving medicines to instead build out a complex and costly financial plan, supply chain security, and customer service infrastructure? Some have actually explored it—they've done the math of investing in "self-distribution" and concluded that it would be much more costly and inefficient than the distribution partnerships they have today.

As product value increases, so does the value of the distributor and the many services they provide; it's far greater than pick, pack, and ship services.

Defining distribution models

Specialty and full-line wholesale distribution channels include:

- **Open distribution:** Therapy owners establish distribution agreements with a wide group of distributors—both traditional and specialty
- **Limited distribution:** Therapy owners only sell the specialty drug through a select, relatively small list of traditional distributors, specialty distributors, and specialty pharmacies
- **Exclusive distribution:** Therapy owner chooses a single distributor to carry its product
- **Title model:** An enhanced 3PL distribution solution, is an exclusive distribution model in which a third-party logistics provider takes title of the product and handles full order-to-cash management on behalf of the manufacturer

THE ROLE OF THE DISTRIBUTOR[9]

The Banker
- Accounts receivable management, taking on attributable risk and logistics risk for themanufacturer— and scaled and staffed to do so

The Storefront
- Contract, order, and pricing management

The Distributor
- Distributions of high-value products, ability to scale logistics offerings, and make investments in customer experience

The Intelligence Provider
- Essential, aggregated data on pricing and inventory across all commercial off-the-shelf manufacturers and products

The Guardian
- Protecting the healthcare supply chain against fraudulent activities that harm patient care deliveries

The Industry Builder
- Customer service and sales outreach to tens of thousands of healthcare organizations
- Strategically investing to grow key markets

To achieve "the right dose of the right drug for the right patient at the right time," therapy owners should consider the individual characteristics, needs, and preferences of the patient population during all stages of care to gain vital insights into the level of customization the product will require. Therapy owners should also consider how certain aspects of distribution will correlate with specific product requirements.

To inform the distribution model choice, there are several questions that must be addressed as part of the overall strategy definition. These include:

Price and reimbursement

- Will reimbursement and financial assistance services be needed?
- How will credit worthiness of customers be assessed?
- How will data be captured for milestone or value-based payments?

Customer experience

- How easy is it for customers to order the product?
- How easy is it for customers to access any support required to enable the transactions related to product usage?

Access

- How easy is it for patients to access the therapy, taking into account availability and network reach?
- Will the therapy need to flow through specific **classes of trade ?**

Ordering process

- What level of customer service is required?
- What are the associated diagnostics requirements, if any?

Data collection

- What data needs to be collected?
- How quickly does that data need to be accessed?
- What is the requirement for customized data?

Level of customization

- How important is the tailoring of all aspects of ordering and operations to the therapy owner's manufacturing preferences (eg, ordering platform, customer service, payment terms, etc)?

Integration

- What processes should be put in place for financial management, customer service, and other aspects to guarantee effective integration with other commercialization services such as patient support and logistics?
- How can a high degree of coordination with logistics be achieved—delivery triggering revenue recognition?

Starting material and product attributes

- What are the temperature-control requirements?
- What are the time constraints?

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Classes of trade

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Customer experience

"Customer" is defined as hospital, research institute, or other provider.

Security and safety

- What is the chain of custody and is it traceable across every touchpoint in the supply chain?
- What are the serialization requirements?

Patient population size

- How big is the patient population?
- Are they located in specific geographic concentrations?

Sites of care

- Where will the product be administered?

PAYMENT AND DISTRIBUTION TABLE

ATTRIBUTES	SCALE	
Price and Reimbursement	Lower	Higher
Customer Experience/Convenience	Standard	Customized
Access	Wide	Limited
Ordering Process	Standard	Complex
Data Collection and Access	Low	High
Level of Customization	Low	High
Integration	Low	High
Product Attributes	Simple	Complex
Patient Population Size	Large	Small
Sites of Care	Many	Few
STANDARD		HIGHLY CUSTOMIZED

Coordination counts

To ensure successful outcomes to the questions posed, a coordinated approach between all key supply chain stakeholders is essential—from manufacturing sites and sites of care (including research facilities, apheresis centers, hospitals, and clinics) to logistics partners and patient support partners—and must be part of any channel strategy development.

An integrated third-party logistics partner can provide proven expertise and processes for product storage and distribution, and offer comprehensive accounts receivable management, including account setup, invoicing, collection, and cash application efforts. In cases where the definition of distribution means never even touching the product itself, an integrated third-party logistics partner can manage

functions like order-to-cash, financial management, and customer service. Because the complexity of this therapeutic category is so immense, all of these services must be flexible and customizable based on business model and product, provider, and patient need.

Taking the strain

Manufacturers choose to partner with distributors to access an established and market-leading provider/customer base. Even for therapy owners who seek to launch in a select group of centers of excellence, a distributor partnership can create several key advantages:

- Distributors reduce the operational burden on customers because they do not require a new account and separate processes. Less time spent on work-arounds, means more time for patients, which leads to better patient outcomes.
- A distributor partnership means the therapy owner will not face the unenviable position of having to cut off access if a major academic center is late on payment. After all, no therapy owner wants to stop serving the customer, as this would only harm patients. Having to take such a step could also impact the therapy owner's financial reporting, as well as the long-term relationship with its customers.
- Distributors improve cash collection for the therapy owner. Given the provider's dependency on the distributor, particularly for those customers who have a high-volume purchasing relationship with the distributor, the advantage of the distributor's financial management services is key.

The reach of payment and distribution decisions

It's essential to understand that decisions related to payment and distribution strategy will impact all other aspects of cell and gene therapy program creation, such as:

- Supply chain and logistics designed to meet product storage and shipping attributes
- The site of care selected for a therapy in trial design is informed by the most feasible path to payment
- Patient programs, based on the location of site selected and designed to meet hub model requirements where actions trigger supply chain activities
- Data architecture created to fulfill payment and distribution requirements

Payment and distribution: KEY TAKEAWAYS

There are a number of reasons a therapy owner might consider different distribution strategies—downstream customer pressures, patient population, product shipping requirements, and more. But there are also aspects that can become very costly if overlooked. For example, while therapy owners may want to explore exclusive distribution models, the long-term costs and negative implications of such a restrictive access strategy should be fully understood.

Therapy owners are challenged to meet an important goal (with their commercialization partner); to carefully manage the patient's treatment journey and related data insights. Given the potentially curative benefits of cell and gene therapies, innovators and their partners have an opportunity to create a healthier future for each patient, should this goal be achieved.

Cell and gene therapies are continuing to push the level of innovation in each area of the supply chain—from production, to uncovering different ways to manage logistics, and making therapies more affordable and accessible to patients. Because of this, therapy owners and their partners must be open to exploring new models and strategies. These will lead to the creation of the innovative processes required to achieve commercialization goals —and critically, to truly create healthier futures for patients and their families.

The payment and distribution strategy will be paramount to the success of a cell and gene therapy product, so it must be proactively planned and managed. In summary, therapy owners should:

- ☑ Consider the requirements of the provider and the patient population prior to payment and distribution strategy design; these include patient sites of care and access, data provision, chain of custody and the integration of payment with the supply chain to drive a seamless experience
- ☑ Consider payer requirements for data, particularly for milestone-based or outcome-based payments
- ☑ Determine whether a standard distribution approach or customized model is needed to meet the therapy's bespoke requirements and to deliver "the right dose of the right drug for the right patient at the right time"
- ☑ Choose a distribution partner with an established provider base to reduce the burden on sites, improve cash collection, and reduce risk in terms of payment collection

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CONCLUSION

Face the risks, reap the rewards

Complexity and risk both feature as factors when we consider the process of bringing a cell and gene therapy product to market. But with an integrated approach, the future remains bright for both commercialization prospects and patient outcomes.

Cell and gene therapy owners face many challenges, during pre-trial setup and the early trial and through later phases to commercialization and product launch:

- **Manufacturing setup and the ability to scale up , scale out or scale up and out**
- **Transportation, distribution, communication and data integration, and access**
- **Unique patient treatment and therapy requirements**
- **Regulatory complexities**
- **Reimbursement challenges**
- **Providing the optimal patient and provider experience**

Any solution to meet these challenges will only ever be as strong as its weakest link—and with so many potential points of failure, an integrated solution is essential to minimize complexity and remove risk.

Threats include pooling partners who have not worked together before—even if they are perceived to be strong in their individual role. This may result in a solution that is less than the sum of its parts; failing to create an integrated supply chain or benefit from the leveraging of established relationships within health systems to support availability at launch. And later, as the product's utilization may extend to community practice physicians and GPOs, market potential could be limited by a failure to bring on board specialty distributors who will be necessary in the event the provider prefers to have the product shipped by the manufacturer, but billed by their preferred specialty distributor.

Therapy owner action points

To ensure that any cell and gene therapy program is optimally set up to transition from clinical trials into a commercial reality, therapy owners must:

1. Set up **manufacturing** to coordinate with logistics to optimize throughput and turnaround and have the potential to be automated and maintain sufficient capacity to handle expected peak demand.
2. Facilitate manufacturing coordination, validation, and documentation of all required steps with health system stakeholders.
3. Create a **supply chain** that can scale up to serve an increasing number of patients.
4. Develop a full understanding of the **interdependencies** between components such as ordering, manufacturing, and payment.
5. Formulate new **reimbursement models** that share risk and address payer concerns about budget impact.
6. Pull together compelling evidence that demonstrates product value and secures/retains **coverage**, both at product launch and over time.
7. Design a **patient-services hub** that offers a consistent experience for prescribers while removing any barriers to access and affordability.
8. Check that **channel and product access strategies** are balanced enough to take into account the needs of established centers of excellence and other potential prescribers.
9. Roll out educational support for health systems that focus on ordering and obtaining payment for therapy services, plus raise awareness of sponsored patient support programs.
10. Create an **optimized distribution strategy** by considering patient population characteristics and product requirements.
11. Build a valid process model that considers impacts to health system stakeholders, including equipment and infrastructure investments, state and federal regulatory compliance including cGMP support, staff training and competency verification, and health system risk mitigation.
12. Construct a framework for an overarching data management architecture that offers a single view of the patient/product journey.

The way forward

By having the end state in sight as cell and gene therapies are in early development, therapy owners will benefit from a truly integrated model for their operations; one where silos are torn down, weak links in the supply chain are removed, and manufacturing is customized for the needs of both the product and the patient.

Ultimately, an integrated model will support the potential of cell and gene therapy as the medicine of the future, securing the prospects of a sector that has the potential to transform global healthcare—and the lives of the patients long into the future.

"An integrated solution would have been very valuable. This service would be vital to standardizing the variables between manufacturing and patient treatment. It gives you the confidence that variations between trials are not due to the quality of the drug, temperature deviation, or shipping location."

– Former Head of Clinical Research, clinical stage gene therapy—biotechnology company

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12. Construct a framework for an overarching data management architecture that offers a single view of the patient/product journey.

The way forward

By having the end state [illegible] development, therapy owners will benefit from a truly integrated model [illegible] in the supply chain, delivery, and manufacturing processes that are fit for the needs of both the product and the patient.

Ultimately, an integrated model will support the potential of cell and gene therapy as the medicine of the future, securing the prospects of a sector that has the potential to transform global healthcare—and the lives of the patients long into the future.

> *An integrated solution would have been very valuable. This service would [illegible] variables between manufacturing and patient [illegible] confidence that variations between trials are not [illegible], temperature deviation, or shipping location."*
>
> —Former Head of Clinical Research, clinical stage gene therapy—biotechnology company

Manufacturing

There is no established handover from clinical to commercial manufacturing of cell and gene therapies; this means decisions made during clinical development will influence the product's future viability to an unprecedented degree.

Read the "Manufacturing and cGMP" chapter to find out more.

Therapy owner action points

To ensure that any cell and gene therapy program is optimally set up to transition from clinical trials into a commercial reality, therapy owners must:

1. Set up **manufacturing** to coordinate with logistics to optimize throughput and turnaround and have the potential to be automated and maintain sufficient capacity to handle expected peak demand.
2. Facilitate manufacturing coordination, validation, and documentation of all required steps with health system stakeholders.
3. Create a **supply chain** that can scale up to serve an increasing number of patients.
4. Develop a full understanding of the **interdependencies** between components such as ordering, manufacturing, and payment.
5. Formulate new **reimbursement models** that share risk and address payer concerns about budget impact.
6. Pull together compelling evidence that demonstrates product value and secures/retains **coverage** both at product launch and over time.
7. Design a **patient-services hub** that provides [illegible] for prescribers while removing any barriers to access and affordability.
8. Check that **channel and product access strategies** are balanced enough to take into account the needs of established centers of excellence and other potential [illegible]
9. Roll out educational support for health systems that focus on ordering and obtaining payment for therapy services, plus raise awareness of sponsored patient support [illegible]
10. Create an **optimized distribution** [illegible] to patient needs, characteristics and product requirements.
11. Build a valid process model that considers impacts to health system stakeholders, including equipment and infrastructure investments, state and federal regulatory compliance [illegible] reimbursement.
12. Construct a framework for an overarching data management architecture that offers a single view of the patient/product journey.

The way forward

By having the end state in sight as cell and gene therapies are in early development, therapy owners [illegible] model for their operations; one where silos are torn down, weak links in [illegible] for [illegible]

Ultimately, an integrated model will support the potential of cell and gene therapy as the medicine of the future, securing the prospects of a sector that has the potential to transform global healthcare—and the lives of the patients long into the future.

"An integrated solution would have been very valuable. This service would be vital to standardizing the variables between manufacturing and patient treatment, [illegible] confidence that variations between trials are not [illegible], temperature deviation, or shipping location."

[illegible] clinical stage gene therapy—biotechnology company

X

Supply chain

Given the interdependencies between each stage in cell and gene therapy, bespoke and integrated supply chain elements are essential. Personalized medicine requires a personalized supply chain; complicated from the outset and only growing in complexity as studies move rapidly through the clinical phases to market.

Read the "Integrating Supply Chain and Logistics Strategy" chapter to find out more.

Therapy owner action points

To ensure that any cell and gene therapy program is optimally set up to transition from clinical trials into a commercial reality, therapy owners must:

1. Set up **manufacturing** to coordinate with logistics to optimize throughput and turnaround and have the potential to be automated and maintain sufficient capacity to handle expected peak demand.
2. Facilitate manufacturing coordination, validation, and documentation of all required steps with health system stakeholders.
3. Create a **supply chain** that can scale up to serve an increasing number of patients.

X

Interdependencies

The dependencies between each touchpoint in cell and gene therapy are far greater than in traditional specialty pharmaceutical production—and the coordination needed to manage them effectively demands true connectivity.

Read the "Integrating Supply Chain and Logistics Strategy" chapter to find out more.

Ultimately, an integrated model will support the potential of cell and gene therapy as the medicine of the future, securing the prospects of a sector that has the potential to transform global healthcare—and the lives of the patients long into the future.

Therapy owner action points

To ensure that any cell and gene therapy program is optimally set up to transition from clinical trials into a commercial reality, therapy owners must:

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4. Develop a full understanding of the **interdependencies** between components such as ordering, manufacturing, and payment.
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6. Pull together compelling evidence that demonstrates product value and secures/retains **coverage** both at product launch and over time.
7. Design a **patient-services hub** that offers a consistent experience for prescribers while removing any barriers to access and affordability.
8. Check that **channel and product access strategies** are balanced enough to take into account the needs of established centers of excellence and other potential prescribers.
9. Roll out educational support for health systems that focus on ordering and obtaining payment for therapy services, plus raise awareness of sponsored patient supp[illegible]
10. Create an **optimized distribution strategy** by considering patient population characteristics and product requirements.
11. Build a valid process model that considers impacts to health system stakeholders, including equipment and infrastructure investments, state and federal regulatory compli[illegible]ation.
12. Construct a framework for an overarching data management architecture, that offers a single view of the patient/product journey.

X

Reimbursement models

The characteristics of cell and gene therapies magnify some of the limitations of a service fee model and will require a thoughtful strategy from the therapy owner based on proactive discussions with both providers and payers.

Read the "Reimbursement/payment" section to find out more.

The way forward

By having the end state in sight as cell and gene therapies are in early de[illegible] mo[illegible] in the supply chain are removed, and manufacturing is customized for the needs of both the product and the patient.

"An integrated solution would have been very valuable. This service would [illegible] variables between manufacturing and patient [illegible] confidence that variations between trials are not due to the quality of the [illegible], temperature deviation, or shipping location."

—Former Head of Clinical Research, clinical stage gene therapy—biotechnology company

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Introduction
Manufacturing and cGMP
Integrating Supply Chain and Logistics Strategy
Securing Regulatory Approval
Critical Success Factors for Market Access: Coding, Coverage, and Reimbursement
Creating a Differentiated Patient and Provider Experience
Managing Payment and Distribution
Conclusion

Therapy owner action points

To ensure that any cell and gene therapy program is optimally set up to transition from clinical trials into a commercial reality, therapy owners must:

1. Set up **manufacturing** to coordinate with logistics to optimize throughput and turnaround and have the potential to be automated and maintain sufficient capacity to handle expected peak demand.
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X

Coverage

It is essential to engage in discussions with payers early in the cell and gene therapy development process to glean invaluable insights into the possible evaluation pathways, associated steps, and evidence packages required.

Read the "Coverage section" to find out more.

The way forward

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11. Build a validated process model that constitutes a guide to health system stakeholders, including equipment and infrastructure investments, state and federal regulatory compliance, [illegible].
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Patient-services hub

The end goal is to position the patient-services program as a single point of contact for the provider and patient, and aid in the coordination of product and treatment insurance coverage, and logistics and/or distribution services.

Read the "Creating a Differentiated Patient and Provider Experience" chapter to find out more.

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Channel and product access strategies

Access to cell and gene therapies is contingent on developing an appropriate channel strategy when bringing a product to market. It requires strategic thinking and has a significant impact on product uptake and commercial success.

Read the "Creating a Differentiated Patient and Provider Experience" chapter to find out more.

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— Former Head of Clinical Research, clinical stage gene therapy—biotechnology company

Optimized distribution strategy

Because cell and gene therapy products evolve differently than traditional specialty pharmaceutical products, therapy owners will need to overcome several significant obstacles to create a truly optimized distribution strategy.

Read the "Manufacturing and cGMP" chapter to find out more.

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Thank you to all authors and contributors to *Commercializing Cell and Gene Therapies*, who bring a wealth of experience in specialty pharmaceutical production, logistics, and commercialization to the perspectives outlined in this paper.

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Peter Belden is President of ICS, part of AmerisourceBergen's global specialty logistics business. In this role, Peter is responsible for the strategic and operational oversight of the ICS business unit. Peter joined ICS in August 2014 and prior to this role spent 11 years with the AmerisourceBergen Packaging Group where he held roles of increasing responsibility across sales, marketing, and general management leading the US and UK pharmaceutical contract packaging units. Prior to joining AmerisourceBergen, Peter was with Avery Dennison, Reynolds Metals, and Printpack in sales and marketing leadership positions. Peter holds a BS in Commerce from the University of Virginia and an MBA in Strategic Management from DePaul University.

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Albert Cooksey is Vice President of Business Development for ICS. Al joined ICS in 2007 and is a seasoned third-party logistics (3PL) veteran with over 12 years of experience managing various aspects of 3PL operations. His responsibilities encompass managing all business development activities, including overseeing the RFP process, as well as all contracting and pricing for new manufacturer clients. He also works with existing clients on logistics solutions and new product introductions into the ICS 3PL support model, providing consultation throughout the process. In his previous role, Al managed all client-facing operations for ICS, including account management, A/R operations, customer service, and business development. Al holds a Bachelor of Science in Agri-Economics from Texas A&M University where he graduated in 1996.

Alex Guite – Director of Strategy

Alex Guite is Director of Strategy at World Courier, part of AmerisourceBergen's global specialty logistics business. As strategy lead, Alex is responsible for developing and executing key strategic initiatives, including World Courier's cell and gene therapy offering. Alex is based in World Courier's global headquarters in London. Before joining World Courier in 2013 as Head of Pricing, Alex spent nearly 3 years with Oliver Wyman as a consultant in the Health and Life Sciences practice. Alex holds a PhD in Experimental Solid State Physics from Imperial College, London.

Sam Herbert – President

As President of World Courier, part of AmerisourceBergen's global specialty logistics business, Sam Herbert leads a business spanning more than 140 company-owned offices in 50+ countries. Prior to his role as President, Herbert was Chief Operating Officer, responsible for World Courier's global functions. Before joining World Courier in 2013 as Vice President of Strategy, Sam was a partner in Oliver Wyman's Health and Life Sciences practice where he advised some of the world's leading pharmaceutical, healthcare, and pharmaceutical services companies, including AmerisourceBergen. Sam holds an AB of Economics, cum laude, from Harvard College and is based in World Courier's global headquarters in London.

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Lisa Vocat is Global Content Marketing Manager at World Courier, part of AmerisourceBergen's global specialty logistics business. Lisa is responsible for World Courier's content marketing strategy and thought leadership development. She led the editing and production of Commercializing Cell and Gene Therapies. Lisa joined World Courier in 2016 after eight years with a global, FTSE-listed recruitment business, latterly as regional Head of Digital, and an early career as a journalist in South Africa.

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Derek Cothran is the Vice President and Lead for Strategic Account Management at Lash Group, AmerisourceBergen's patient support services business. Derek partners closely with manufacturers to create a comprehensive access strategy, as well as facilitate the evolution of this strategy throughout the product or program life cycle. He proactively incorporates market trends and industry capabilities to help manufacturers create a service offering to meet patient and provider needs. In his previous role as Vice President of Operations, Derek provided strategic direction to multiple clients for their specialty medications across a range of disease states and provided direct operational oversight into manufacturer programs.

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As a Director of Business Development for Lash Group, AmerisourceBergen's patient support services business, Nancy Pilcher is responsible for establishing new manufacturer relationships, and conducting program development efforts to create a comprehensive program offering administered by Lash Group on behalf of the manufacturer. She plays a key role in business development efforts, and has participated in numerous new program launches. Throughout her 20-year career, Nancy has supported operational management, as well as the expansion of specialty pharmacy operations, clinical services, and development of patient support programs on behalf of pharmaceutical and biotech manufacturers.

Strategic Consulting

Matt Sarnes – SVP, Commercial Consulting

Matt Sarnes, PharmD, is Senior Vice President at Xcenda, AmerisourceBergen's market access business, which focuses on helping the biopharma industry innovative strategies and tactics to overcome barriers to product access. Matt has consulted for numerous manufacturers, managed care organizations, and health systems, and has led the commercialization strategy for both new and in-line products across several therapeutic areas. Matt's expertise is founded on more than 15 years of experience across several disciplines, including market access, health economics, reimbursement, quality improvement, marketing, and distribution strategy.

Mitch Wood – Managing Director, Pharmacy Healthcare Solutions

Mitch Wood is Managing Director of the Consulting Practice at Pharmacy Healthcare Solutions, AmerisourceBergen's consulting solutions company for health systems. Mitch has more than 32 years of administrative pharmacy practice experience, with a focus on administrative pharmacy leadership, staff education and development, information and automation systems, medication safety, pharmacy care practice models, financial performance and analysis.

Strategic Global Sourcing

Joseph Cappello – VP, Global Specialty Branded Planning and Integration

As Vice President of Planning and Integration within AmerisourceBergen's Strategic Global Sourcing team, Mr. Cappello leads operations and strategic initiatives, driving growth and strengthening partnership between the Brand/Specialty Category team and both AmerisourceBergen's customers and trading partners. Prior to joining AmerisourceBergen, Joe spent his career with pharmaceutical manufacturers such as Centocor/Johnson & Johnson, Sanofi, and Endo Health Solutions. At those organizations, Joe worked in areas of demand creation and strategy, with roles in brand and strategic marketing, as well as sales and sales leadership, focusing on product and service commercialization.

AmerisourceBergen Partners

Invetech

For nearly 30 years and across the globe, Invetech has been helping clients turn important projects into commercially successful products. Our passion and enthusiasm, combined with our full spectrum of product development expertise, has made us the clear choice for those who demand the highest standards from their product realization partner.

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Brian Hanrahan has more than 15 years of product development experience across the biomedical and cell therapy industries. In his current role, Brian is the Manager of Invetech's Cell Therapy Group in San Diego, CA, USA, helping cell and advanced therapy companies across the globe realize clinical and commercial-scale cGMP manufacturing solutions. Brian has been a key contributor in building Invetech's cell and advanced therapy capabilities and continues to have a deep involvement in projects ranging from the development of cell separation instruments to single-use, automated cell therapy production systems. Brian has a Bachelor's Degree in Applied Science from RMIT University in Australia.

Richard Grant – Global VP, Cell Therapy

Richard Grant has 33 years of product development experience across various industries including cellular therapy automation, medical devices and instruments, commercial valving and fluidic systems. Since 2000, Richard has played an instrumental role at Invetech in managing the development of many products, from drug discovery and cell separation, to automated cell therapy production systems. Richard managed Invetech's first cell therapy project and has subsequently been involved in over 20 more cell therapy projects across the globe. Richard assumed the role of Global Vice President of the Cell Therapy group at Invetech in 2011 and continues to support the rapidly growing field of cell and gene therapy.

David Kneen – Program Manager

David is a Program Manager in Invetech's Cell Therapy group. He supports Cell and Advanced Therapeutics clients worldwide with the industrialisation and commercialisation of their therapeutic products. He has more than 11 years' experience in bringing new biomedical technologies to market, including strategic business case preparation, operations planning and leading development teams in custom automation, manufacturing, and product design. David holds a combined BE (Mechanical)/BSc (Applied Mathematics & Physics) from the University of Melbourne, and an MBA from Melbourne Business School.

TrakCel

TrakCel delivers a suite of integrated technologies to effectively and easily orchestrate the cell therapy supply chain for autologous and allogeneic therapies—ensuring safe, scalable, and affordable products. Developed in collaboration with industry leaders, TrakCel delivers the visibility and control required to safely manage cell, gene, and immunotherapies from clinical trials through to commercial scale on a global basis.

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Matthew Lakelin – VP, Scientific Affairs

Matthew Lakelin is the VP of Scientific Affairs at TrakCel. Using his knowledge of handling and distribution of ATMPs, Matthew has assisted with the development of TrakCel's technology platform. He provides a technical bridge between the software development side of the technology platform and the GxP application of the system. He is also a member of the company's Quality Unit to ensure that development and configuration of TrakCel's technology platform adheres to a GAMP-5 framework. Prior to TrakCel, Matthew worked as Head of Technical Support for a specialist clinical supplier company where he was responsible for identifying, assessing, and verifying new equipment for use in GMP pharmaceutical manufacturing including temperature-controlled shipping, storage, and labelling systems for cell therapy products.

Ravi Nalliah – Chief Executive Officer

Ravi Nalliah is the Chief Executive Officer at TrakCel, a clinical orchestration platform designed to efficiently safeguard patients and orchestrate processe across regenerative and cell-based therapies. Prior to joining TrakCel, Ravi was Finance Director at PCI Services, Inc., a US-headquartered global leader for drug development services and a trusted partner to the world's largest and most successful pharmaceutical firms. Ravi was also a key member of the team that, in 2010, led the management buy-out of Biotec Services International, a leading UK-based clinical trial services and supply group specialising in clinical trial services for phase 1 to 4 trials. He was Chief Finance and Strategy Officer of the business and its subsidiaries before leading the sale of the business to PCI Services, Inc., in 2014. Ravi is a qualified Chartered Accountant and also holds a Bachelor of Science (BSc) in Biochemistry & Molecular Biology.

AmerisourceBergen Integrated Commercialization Solutions

We continue to expand our business in key markets across the world to support the growth of pharmaceutical-led care and improve global health. AmerisourceBergen offers integrated commercialization solutions in core markets across the world.

Profarma Specialty
AmerisourceBergen

Profarma Specialty is a joint venture between Profarma and AmerisourceBergen that caters to patients, healthcare providers, as well as the pharmaceutical and biotechnology industry in the Brazilian market. With over $300M USD in annual revenue across three business units, 100% territory coverage, and 500+ employees, it is a market leader and the only player in the Brazilian specialty market to have an integrated service offering that includes specialty distribution, patient support services, and specialty pharmacy.

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Innomar® Strategies
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Innomar Strategies, a part of AmerisourceBergen, is the leading patient support provider in the Canadian specialty pharmaceutical market. Since 2001, hundreds of industry leaders have trusted Innomar Strategies to optimize their product and improve its performance, while delivering superior results to their patients and stakeholders. Through our integrated services, Innomar Strategies delivers customized, scalable solutions to manufacturers of specialty pharmaceutical and biotech products. Strategic consulting, patient support programs, clinics and nursing services, and specialty pharmacy and distribution services are just a few of our key areas of specialization.

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- Supporting manufacturing services commercialized through our partner, Invetech

Manufacturing and cGMP

Integrating Supply Chain and Logistics Strategy

- Integrated global specialty logistics
- Inventory management solutions
- Supporting software management and tracking services though our partner, TrakCel

- Global health economics consulting

Securing Regulatory Approval

Critical Success Factors for Market Access: Coding, Coverage, and Reimbursement

- Market access consulting
- Global health economics consulting
- Real-world evidence studies
- Health policy insights
- Stakeholder insights
- Payer strategy and communications

- Hub model design
- Patient education
- Patient access & affordability services
- Adherence support
- Product administration support
- Customer engagement and insights
- Field reimbursement support

Creating a Differentiated Patient and Provider Experience

Managing Payment and Distribution

- Product-aligned distribution models
- Third-party logistics
- Outsourced billing
- Data analytics

Overarching data management architecture delivers needle-to-needle insights

As a committed partner for your cell and gene therapy, AmerisourceBergen will design a customized strategy that integrates proven solutions to deliver a superior customer experience for patients and providers.

Start a conversation:
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