cell & gene

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Part 2: Getting The System Ready: Enabling Investment In Community Hospitals To Improve Patient Access To Cell And Gene Therapies

By Dr. Sanjay Srivastava, Managing Director, Cell & Gene therapy lead; Rahul Mirchandani, Senior Analyst, Life Sciences at Accenture Life Sciences, and Joe De Pinto, Head of Cell, Gene & Advanced Therapies at McKesson Pharmaceutical Solutions and Services

Second in a two-part series

Patient access remains a key challenge for CGTs. The healthcare system is already constrained, and the emergence of advanced therapies and CGT 2.0[1] will only increase the severity of this problem. While "there is such hope created by these innovations, there is a gap that continues to develop and widen for those who have access to the discoveries. Because we know that your best chance of a cure is your first chance," Roger Stone, CEO of City of Hope. We must focus on how we get the right treatments to the right individuals at the right time and at the right place that is accessible to patients.

To effectively navigate the complexity and operational challenges associated with delivering cell and gene therapies at community hospitals, the biopharma industry must evaluate the strategic questions we identified in the previous article in this series. The key questions relate to geographic considerations that could influence patient access and clinical outcomes; establishment of cross-functional teams to assess patient eligibility for CGTs; overcoming the necessary capability- and infrastructure-related challenges mentioned in Part 1 of this paper to get patients through treatment; and implementation of robust mechanisms to secure timely reimbursement.

Determining where to start is critical for bringing CGTs to community hospitals. Precisely defined entrance criteria across various domains, including location, patient access, partnerships, medical and operational capabilities, and financial/business considerations, serve as indispensable guides for selecting the ideal network of community hospitals for CGTs. The following themes could provide a framework for setting up community hospitals to deliver CGTs. They can then be used advantageously to counteract the five barriers mentioned in Part 1:

1. **Access and Location** to maximize access to eligible patients as well as place them within reach of network partners (e.g., Academic Medical Centers, or AMCs, and ecosystem partners). This criterion helps address the barrier of patient identification and could improve clinical outcomes in underserved communities as well.
2. **Infrastructure and Capabilities** to safely administer therapies to patients, while meeting regulatory requirements. This criterion helps to address the barriers of infrastructure, capabilities, and capacity.
3. **Financial and Investment** to fill any capability gaps and address the barrier of finances and cash flow to maximize patient access to these innovative therapies.

Access and Location

When determining the community hospitals that are most appropriate for CGTs, it is important to consider ease of patient access to the center and profiles of eligible patients. Due to the nature of their conditions, some patients are unable to, or simply would prefer not to, travel significant distances to access care. They end up choosing alternative care methods instead of available therapies. Additionally, diversity in clinical trials is an ongoing and important consideration. There is a need to prioritize diversity in access to treatments as well. Historically underserved communities often lack the socioeconomic mobility to afford these treatments or travel to hospitals where they can receive them. A helpful use case through which to test and prioritize access to diverse and underserved patient populations will be the upcoming therapies for sickle cell disease. These upcoming product launches will expand the typical available population that get CGT. Community hospitals could help larger patient populations get care locally for this debilitating disease.

Another important factor when determining the right location is a center's ability to deliver desired clinical outcomes. It has been reported that cancer patients treated in community hospitals experience poorer outcomes compared to academic medical centers or National Cancer Institute (NCI)-Designated Cancer Centers. However, when a community hospital is located near an AMC(s), the clinical outcomes tend to be better[1].

While geographic location near an AMC is key to selecting a community hospital, other considerations such as therapy type, label indication, and patient availability within the community must also be considered. A health system must examine their referral network and patient catchment area when it comes to delivery of CGT. Cell and gene patients continue to be diagnosed in the community setting. These patients must often navigate a complex and often challenging referral network to gain access to these scientific breakthroughs. When the referral network is further challenged by a big geographic distance between the community location where the patients are

diagnosed and the treatment location at a regional academic center, there is more risk of patient dropout. Patients lost in the referral network is a pain point that stakeholders, healthcare professionals, biopharma, and payers must solve for. Initial patent consideration of treatment options in socioeconomically depressed areas may limit commercial and clinical trial inclusion if treatment sites do not exist in the local community. Conversely, community centers with poor referral rates can be a good source of eligible patients and a great candidate to expand the treatment center network to include those community centers. Tracking patient eligibility through case management can be done through various groups in the treatment center to hub services. This must happen with clinical case management and social work to assure success in resourcing these patients appropriately. A digital platform to track patient need and commercial and clinical CGT availability would be an excellent tool for all stakeholders to leverage.

Infrastructure and Capability Considerations

Once identified, the treatment center needs to be onboarded and certified. We must determine what it takes to get semi-equipped centers to deliver advanced therapies. There are infrastructure challenges at community hospitals both in inner cities and rural areas. As noted in an Accenture analysis (**Figure 1**), this issue is sometimes as simple as lack of space for required temperature-controlled shipping, preparation, and handling of CGT material—a challenge for both major cities and rural hospitals. To effectively deliver CGT, there needs to be a solid understanding of and process governing how temperature-controlled product will be received, stored, and delivered to patients. This brings multiple passive and active temperature controlled shipping apparatus into consideration depending on the product requirements. Community hospitals may want to consider regional or local storage of these materials through outsourced vendors with extensive storage and logistics capabilities in CGT. These storage and delivery mechanisms need to be able to store, charge, and set up appropriate delivery of these complex CGT interventions. Utilizing a rubric to conduct in-depth analyses of community hospitals across several capability categories will help CGT developers identify impediments and required attention to enable a community hospital to administer these advanced treatments. Intensive assessment will provide the know-how to figure out which hospitals can be made ready to deliver these products, and the level of investment needed from the hospital's partner network.

Training and medical management:

The community hospital must deploy training resources to allow the center to bring on CGT products and coordinate with biopharma companies. These training resources must take a multidisciplinary approach looking at all professional departments involved in delivery of these complex products in the hospital. In addition, training resources must be deployed to patients and caregivers regarding expectations during the treatment process and long term follow up.

Training and education resources provided to patients and caregivers post therapy are critical to optimize and report outcomes. Community hospital engagement closer to the patients' home may allow for more consistent and convenient short term and long term follow up. This could facilitate the appropriate data collection and real-world evidence reporting.

The medical and nursing staff must be able to address and manage adverse events post therapy delivered in the community hospital. The community hospital must be able to manage side effects and the need to be equipped with the ability to manage diverse side effect profiles that may include severe grade 3/4 events post therapy. Common side effect profiles may include neurologic toxicities like CRS cytokine release syndrome and ICANS Immune effector cell associated neurotoxicity syndrome. Depending on the patient and the therapy selected adverse event profile differ in severity and duration. These side effects can typically last up to a week post therapy with varying onset.

Community hospitals will need to be able to develop and follow cellular therapy pathways. These will vary based on the type of cell therapy—allogeneic, autologous, in vivo, ex vivo, etc. For those community hospitals that are part of a larger academic medical center system it may be as easy as adopting their pathways and SOPs with some modification.

A community hospital must be able to embrace a cross functional care team approach to treatment and delivery of CGT. This team must be able to follow a documented process and record progress and report outliers as this may be included as part of the CGT product and companies. For some autologous products the manufacturing process starts with apheresis in the hospital and continues through the delivery back to the hospital for patient treatment.

FACT (Foundation for the accreditation of cellular therapy) is important accreditation standard to explore for a community hospital looking to optimize delivery of cellular therapies.

Physical Infrastructure

A review of appropriate community hospital infrastructure including space, cold chain requirements, storage, and treatment areas are an important consideration when expanding into CGT. The facility must be able to accommodate the appropriate ordering, delivery, acceptance of product, as well treatment in the appropriate fashion.

Infrastructure needs in CGT will also include appropriate documentation ad required technology to track, trace and report progress of the product during the patient journey. This could include chain of identity and chain of custody COI/COC and coordination between departments like apheresis, cell lab, pharmacy, inpatient and outpatient care units.

Biopharma will need to certify or qualify community sites prior to delivery of their commercial or clinical CGT therapy. This process takes time and resources. The lack of a consistent process causes treatment centers to deploy personnel and engage in multiple month engagements simultaneously with various biopharma companies. There is a need to streamline this process and qualify treatment centers locally and regionally that have proven they can engage in a consistent and quality patient and product experience.

As noted, there are a few considerations that must be considered when getting a community hospital ready for delivering CGTs. A non-traditional approach has a potential to simplify onboarding of a community hospital. The approach takes advantage of existing infrastructure and capabilities at already accredited AMCs and assumes that the potential community hospitals will be within CGT certified AMC regions and/or networks. When these conditions are met, the AMC can serve as a center of excellence (COE). The COE serves as a regional hub; it facilitates onboarding of community centers to expand the treatment delivery network. COEs can add other hospitals to their network, managing onboarding, infrastructure, and treatment, thereby easing the burden on CGT developers. Such a network mimics a Hub and Spoke model, where COE is the Hub and community hospital is a spoke within the model. Complex CGT specific capability requirements are met by COE and the spoke alleviates infrastructure and capability constraints in the system. The CGT developer or the sponsoring organization can assess quality controls across the network to ensure certification standards are maintained. The sponsoring organization in collaboration with COE invests in infrastructure and capabilities gaps to boost inter-hub collaboration and standardization of care. For example, transport between hub-spoke centers, supporting patient logistics. Latter will add credibility to existing structures in the Hub-spoke healthcare system.

Figure 3. Hub-and-Spoke Model

Such examples already exist as evidenced by UPenn; a hub-and-spoke model with Lancaster General Hospital within UPenn network. Lancaster Hospital was recently certified to deliver Kymriah for Diffuse Large B Cell Lymphoma (DLBCL) patients in the Philadelphia metro area. Having an AMC as a Center of Excellence with several nearby community hospitals within its network and benefit from an exchange of patients, information, and investment. It enables access to a number of patients with diverse backgrounds who otherwise may not have access to this care. Additionally, it lends the community hospitals the beginnings of capabilities and finances with which to increase their ability to offer advanced therapies and alleviate healthcare system constraint.

Financial and Investment Considerations

The price of CGT treatments has received a lot of attention from the world's medical and economic thought leaders. As they reach the early stages of development, cell and gene therapies have costs that are significantly higher than biologics and other products. Because of the distinct patient populations are, more challenging to treat like hematologic malignancies and rare and orphan diseases, the CGT market was first seen as the anti-scale market. The highest level of finance administration has been engaged in AMCs to assure a thorough understanding of costs and net cost recovery for these products. Hospitals have begun to take advantage of increasingly available longitudinal clinical outcomes data to work with payors on showing their quality of care. We are seeing an increased number of current CAR-T treatments centers delivering CAR-T in the out-patient setting to address capacity and patient access challenges. Outpatient treatment enables different reimbursement pathways, then inpatient treatment reimbursement.

Regardless of increase in outpatient CGT delivery, we know that CGT treatments come at a considerable cost. Large hospital systems and AMCs traditionally have the funds available to front the cost of such treatments while receiving reimbursement from payers later. As more products hit the market, though, the amount of financial risk involved greatly increases—and large hospitals will no longer be able to carry all that risk. Smaller community hospitals are already not poised to hold the current financial risk and will certainly not be able to handle the financial risk of the future state of CGT.

For community hospitals to be a viable option for CGT delivery, the system needs to de-burden the centers from the high-cost basis of CGTs. We believe that several potential pathways exist to de-risk financial liability so that community hospitals can invest in increasing their CGT capabilities. In the event of a hub-and-spoke model with centralized AMCs, the larger hospitals can assist in de-risking. However, given the future state where the financial burden is even greater than that which large hospitals can carry, it is important to turn to third parties such as specialty pharmacies and wholesalers that can partner with hospitals to carry the risk of the CGT investment and that can effectively influence reimbursement from health payers. It is, however, unclear if any shared cost structure (and shared data structure) will require regulatory review and compliance. We may need to investigate if such a review will be required when implementing cost sharing structures.

Figure 4 depicts multiple reimbursement and distribution models where specialty pharmacies and wholesale distributors can potentially play a significant role to ease the burden on the healthcare system. The first option – Center's Burden option is the current model being utilized by CAR-Ts. In this scenario, centers bear the financial risk and manage aging account receivables. The next three model options offer a shift in financial risk from treatment centers to specialty pharmacies or wholesale distributors

One of the biggest challenges with high priced cell and gene therapies is the significant financial risk taken when providing these therapies. If the treatment center pays the manufacturer upfront, they risk not getting reimbursed by the payer. While this risk won't bankrupt a treatment center for less expensive therapies, with CGT this can cause a significant disturbance to a hospital, even with a few CGT patients. Currently, larger treatment centers may be comfortable accepting that risk upfront. With the explosive growth of allogeneic therapies in coming years, and the significant increase in patient volume, even larger centers are likely to be uncomfortable carrying that risk.

With CAR-T's, where specialty pharmacies don't currently operate, that risk is in fact carried by centers. Opportunity exists for 3rd party players (such as distributors or specialty pharmacies) to alleviate some of that risk, especially with the right level of financial incentives. Outside of CAR-Ts, Specialty Pharmacies are playing in an increasing role in carrying that risk either alone or together with distributors

(see columns 2-4 in **Figure 4**). As CAR-Ts move to smaller centers that will have more difficulty carrying risk, there is need to re-arrange the payment flow and risk carrying in that space.

Figure 4. Options to shift the financial risk away from treatment centers.

Improving logistical and access challenges

The current and projected cell and gene therapies development pipeline and the anticipated commercial demand are further exacerbating the healthcare ecosystem and creating significant constraints in the overall system to deliver potentially transformative therapies to the market. The industry is experiencing unprecedented change, presenting opportunities for industry incumbents, who must rethink their current approach to commercialization and to improve patient access. We believe the next phase in this evolution is administrating CGTs in community hospitals. However, many key opinion leaders and key stakeholders rightly believe that that there are barriers to bringing these therapies to community centers. Expanding beyond FACT centers is challenging due to the required reporting, care management infrastructure, and lack of integrated specialties. This is a capability issue that needs to be solved before we can consider expanding to non-FACT accredited community hospitals.

The incumbents have choices to make about the role they want to play and how to address the impediments for expanded access of CGTs. They could adopt and expand their capabilities, use M&A transactions, and/or collaborate with traditional or new players to meet the anticipated demand. The proposed approach, enabling community hospitals to alleviate system constraints, would be a significant departure from today's approach and would usher a change in the future of CGT therapy delivery. The growth of a network of robust treatment centers will increase the emphasis on delivering standardized quality care with consistent outcomes, regardless of where a patient is treated, and will further accelerate the development and commercialization of more personalized CGTs.

References

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7854809/

[1]CGT 2.0 marks a defining shift in the Cell and Gene Therapy field, especially with the advancement of allogeneic therapies to replace autologous ones.