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The role of expanded access in cell and gene therapy

In this white paper we set out how to achieve success in cell and gene therapy, considering the important role of expanded access, go-to-market models, and what's required for organisational success.

THE RISE OF CELL AND GENE THERAPIES

Few cell and gene therapies have reached the market over the past decade. In 2022, there were seven approved in the US and fewer than 10 in Europe[1].

By their very nature as some of the most complex and advanced medical treatments under development[2], cell and gene therapies face steeper challenges at launch than traditional drugs, potentially limiting their adoption.

However, judging from the pipeline of products currently in Phase III clinical trials, the number of approvals is likely to rise dramatically in the near future[3]. There are over 2,000 clinical trials happening today, with 200 in Phase III – offering hope for patients waiting on durable, possibly curative treatments. But bringing them to market poses obstacles including investment, policy, and regulatory challenges[4].

With over 237 regenerative medicines companies headquartered in Europe, the region is seen as the favourite destination for cell and gene therapy manufacturing[5].

There are now six approved CAR-T cell therapies available to patients in both the US and Europe to treat various blood cancers. However, they are but one part of a growing set of promising cell and gene therapies to address rare and prevalent conditions[4].

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Of the seven cell and gene therapies approved by the FDA last year, five were CAR-T cell therapies. The remainder were gene therapies to treat two rare diseases: spinal muscular atrophy and inherited retinal diseases such as Leber congenital amaurosis or retinitis pigmentosa[1].

Development is progressing as 13 new therapies could be approved in the US, Europe or both by the end of 2023[4]. And in 2024, up to 21 cell therapy, and as many as 31 gene therapy launches – including more than 29 adeno-associated virus (AAV) therapies – are expected[3]. By 2030, 50–75 new therapies are anticipated to be approved in the US[1].

Although cell and gene therapy has the potential to treat or even cure life-limiting diseases and infections, the full impact can only be realised if it is delivered for the benefit of everyone[6], as opposed to widening the existing gap in health inequalities between different countries.

The current cost of licensed gene therapies makes widespread availability in low- to middle-income countries (LMICs) a particularly difficult challenge. Examples of this include the cancer immunotherapy chimeric antigen receptor T cell (CAR-T) product Kymriah, which was originally priced at $475,000 and Zolgensma for spinal muscular dystrophy, which, with a price tag of $2.125 million, was the most expensive drug ever placed on the market[7].

Aside from cost, there are other barriers to the access of cell and gene therapies in LMICs, including manufacturing technologies, research and development and policy and regulation. How to confront such challenges when it comes to global access is something our cell and gene therapy insights will explore.

GO-TO-MARKET MODELS

With so many new therapies coming to market, there is great opportunity. But timely access can be difficult.

By their very nature, they target rare diseases where there is a large unmet need within the patient population. But many of these patients need access quicker than it currently takes to gain approval. Added to this, their complexity means they can be used in fewer healthcare institutions, and healthcare professionals (HCPs) need training to administer. And, in addition, they also carry a large price. As such, regulatory agencies and payors are reworking their practices to manage these complexities.

But as a company bringing a new cell and gene therapy to market, it's necessary to rethink your go-to-market model, moving away from traditional approaches and focusing on more innovative approaches.

Outcomes-based models offer an opportunity to overcome some of those complexities however, you must engage all parties early; regulators, payers, even intermediaries, such as pharmaceutical distributors who can act as a risk-sharing vehicle, as well as writing a complex set of contracts[3].

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To put this into context, the market access team of one gene therapy launch began monthly meetings with payers three years before approval.

This approach of engaging early with payers and providers on payment models, disease and therapy information means you can get a head start on assessing the cost-benefit ratio of your cell and gene therapy[3].

However, while you're managing this complexity, expanded access programs (EAPs) offer an opportunity for patients to access much needed medications prior to commercialisation in their country. There is also an opportunity for you to gain additional insights and data to support approval. This is where Uniphar can alleviate the burden from the sponsor when widening access, allowing them to build awareness, gather valuable real-world data and access market demand.

EXPANDED ACCESS IN CELL AND GENE THERAPY IS DIFFERENT FOR MULTIPLE REASONS

As discussed, there are complexities with cell and gene therapies. For EAPs it means that standard ways of operating are often not appropriate. Regardless of whether expanded access will be offered by the sponsor, the policy dictated in the 21st Century Cures Act under[8] which requests are considered may well need to be amended to ensure suitability for cell and gene therapies.

The rare or complex nature of diseases covered by cell and gene therapies, how they are diagnosed or treatment administered, means not all HCPs or institutions are able to handle the therapies. Some require specialist training to ready them to treat patients. And for the patients themselves, they may have to travel out of their area, and even internationally, to receive therapy.

Although many products are one-time therapies, for the safe administration, follow up treatment and monitoring are often required. Ensuring adherence is important for all patients and it is even more complex for those patients who are treated away from their usual place of care under a different Physician.

Manufacture, storage and transportation requirements mean the supply chain needs special thought compared to more conventional therapies, and there are often additional complexities in order to meet customs and regulatory requirements for importation.

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MAKING ACCESS WORK

The most successful organisations working in this space have recognised the need for new ways of working and have embraced the opportunity to do things differently. But to do so, you must take on some important considerations when planning your EAP.

Most companies have an EAP policy which describes their approach to expanded access and advice on how HCPs can get in touch with them to request access. It is a requirement to have an internal process and external communications plan that is followed to assess each request as they are received. However, from our experience, many policies and communication plans currently in place for other therapeutics are not suitable for cell and gene therapies so you may need to adjust them accordingly.

PATIENT JOURNEY

Patients that may benefit from cell and gene therapies are commonly suffering from life threatening, life limiting or very serious diseases. Therefore, there is a large awareness within the patient population of products in development, leading to increased pressure for pharma and biotech companies to provide access.

The patient journey is complex with diagnostics and other testing requirements to determine if the patient is suitable for therapy. And if the patient has to travel for treatment, the stay away from home can be lengthy, especially when factoring in post-treatment monitoring and follow up requirements. The cost of treatment is also a burden on patients if it is not sponsored so can have a significant impact on a patient accessing treatment. Our cell and gene therapy insights explore how to navigate these hurdles.

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HEALTHCARE PROFESSIONAL JOURNEY

As with pharma and biotech companies, cell and gene therapies create new ways of needing to work for HCPs and their institutions. There has been a mixture of excitement and nervousness with some HCPs around the utilisation of cell and gene from our experience.

Due to the need for significant training on the use and handling of cell and gene therapies, there is a great opportunity for early engagement. Pharmacy staff also need to be considered in any site readiness program as they will be receiving delivery of, and handling, the product. If a HCP or site is not suitable for treating patients, then they may have to refer patients to another place of care. This causes complexities in the treatment pathway meaning it is essential that responsibilities for pre- and post-treatment activities are defined and potential treatment sites are identified early and well supported in their centres for treatment.

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PRODUCT JOURNEY AND REGULATIONS

The supply chain challenges are numerous for cell and gene therapies with extreme cold temperatures required in addition to regulatory and customs requirements not yet well defined. However, our experience of expanded access has seen sponsors benefit greatly from the knowledge gained within an EAP ahead of their commercial launch.

For cell therapies, cells from the patient and/or a donor may need to be collected and sent to the manufacturing site before the product can be manufactured. Many cell and gene therapies are manufactured to order and, as such, are shipped from the manufacturing site directly to the treatment site, although we do have experience with a GTx that can follow a more traditional supply model.

Complex and distinct regulatory frameworks define the global expanded access landscape, often presenting planning and implementation challenges. Regulators are yet to fully adapt their ways of working for cell and gene therapies. As a result, in 2020 six cell and gene therapy programs were forced to delay their development timelines after the FDA asked for more information about their production processes. Requests for additional data delayed one cell therapy company's program by four to six months[9].

At Uniphar, we have had positive discussions with regulators and governments in various countries in terms of importing cell and gene therapies and the amendments to their processes required to accommodate them. Partnering with an experienced organisation brings you a wealth of experience which means you're not starting afresh with your program.

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THE FUTURE IS NOW

As we approach a critical point in the commercialisation of cell and gene therapies, the landscape is primed for early access success, not only to allow for faster patient access to critical treatments, but also to pave the way for regulatory approval.

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