

The Key to Commercializing Revolutionary Gene Therapies and Other Orphan Drugs:

High-Touch Services that Enhance Patient Outcomes



In today’s evolving, value-based environment for specialty drugs, high-touch services that enhance patient outcomes are playing an increasingly important role in market access and patient care delivery. Nowhere is this more apparent than in the world of orphan drugs and, in particular, the emerging technology known as cell and gene therapy. Using gene therapy as a specific example, this white paper will discuss many of the high-touch services that can help enhance patient outcomes such as patient safety, access, adherence, quality-of-life, and effectiveness. By focusing on high touch services that can help enhance patient outcomes, biopharma and life sciences companies can overcome the market access challenges faced by orphan drugs.

Gene Therapy

Gene therapy has the potential to revolutionize the treatment of serious and life-threatening diseases, including many cancers and rare diseases. By re-engineering a patient’s own immune cells into disease-fighting cells, or by introducing a new or modified gene into the body to help treat disease, each treatment becomes a personalized drug.

“We’re entering a new frontier in medical innovation with the ability to reprogram a patient’s own cells to attack a deadly cancer. New technologies such as gene and cell therapies hold out the potential to transform medicine and create an inflection point in our ability to treat and even cure many intractable illnesses.”¹ – Scott Gottlieb

The first of these therapies to be approved in the United States was Kymriah™ (tisagenlecleucel). Kymriah is a Chimeric Antigen Receptor (CAR) T-Cell therapy approved for the treatment of acute lymphoblastic leukemia (ALL) in pediatric and young adult patients. Each dose of Kymriah is a personalized treatment created using an individual patient’s own T-cells. The patient’s T-cells are collected and sent to a manufacturing facility where they are genetically modified to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) that now directs the T-cells to target and kill leukemia cells

that have a specific antigen (CD19) on their surface. These genetically modified T-cells are then infused back into the patient to kill the cancer cells.¹

Channel Optimization

Gene therapies present a number of complex logistical challenges that can potentially jeopardize patient safety and limit patient access if these challenges are not managed well. Whether the products are autologous or allogeneic in nature, understanding their transportation, distribution, and storage requirements is critical, especially since most products require real-time temperature monitoring and control. With CAR-T cell therapy in particular, a great deal of precision is required, and any delays in the process are unacceptable. T-cells are collected from a patient (through apheresis) at a hospital/clinic, transported to the manufacturing facility in a cryogenic chamber, re-engineered in the lab to be able to attack cancerous cells, transported back to the hospital/clinic in a cryogenic chamber, and then re-infused into the patient after thawing. Such a complex process requires special handling and a company that is able to meet all of these logistical challenges within precise timelines in order to help ensure patient safety and maximize patient access.

A simple checklist of requirements when it comes to the distribution and transportation of a gene therapy includes:



Temperature range requirements during transportation and storage



Storage logistics for the product throughout the product lifecycle



Education for providers regarding the product



Product viability timing from thawing to infusion

Beyond gene therapies, many other orphan drugs also have special needs with respect to handling, storage, transportation, and administration. Some may have shorter shelf lives than traditional medicines which, when combined with their high cost, makes it impractical to access these drugs through normal channels. As a result, biopharma and life science companies have had to re-think their distribution channels to avoid

delays in starting treatment and get these medications to patients at the right time and the right place. More products are now managed using a just-in-time approach that utilizes overnight delivery to fulfill next-day service to patients and providers.



McKesson’s distribution models optimize channels to reach a variety of healthcare providers and help ensure patient safety and access. With McKesson’s scale, best-in-class technologies, and breadth of service offerings, we are able to work with biopharma and life science companies to design just the right distribution model for each unique product. Moreover, our third-party logistics (3PL) services provide a seamless service model for patient and customer ease of access. By combining McKesson’s long-standing distribution services success with pharmaceutical experience, our 3PL services help biopharma companies deliver products accurately and on-time to more pharmacies, hospitals, clinics, and physician practices than any other health care services provider in North America.

Commercialization Strategies

CAR-T cell therapies highlight many of the market access challenges that are faced by orphan drugs. A successful commercialization strategy for a CAR-T cell therapy or an orphan drug must carefully consider how to:

- Execute complex logistical processes
- Maintain the quality and integrity of the product
- Minimize the risk of adverse events
- Achieve patient access to a very expensive drug
- Assist stakeholders with financial risk
- Enhance the customer/stakeholder experience
- Collect longitudinal data to prove clinical outcomes
- Access claims and outcomes data to gain reimbursement in a value-based environment

High-touch services are the key to addressing the above challenges and maximizing patient access. A comprehensive portfolio of patient support services is needed across the lifecycle of a product, but smaller orphan drug manufacturers often lack the resources and scale to be able to implement them. Without significant assistance, their life-altering drugs may not be prescribed, reimbursed, or dispensed; physicians and patients

may feel burdened by the access process; and payers may reject claims for orphan drugs. But by utilizing high-touch patient support services, such as those provided by McKesson, the stakeholder experience is significantly enhanced, and patients are far more likely to gain reimbursement for expensive products and avoid delays in treatment.

Integrated patient support programs need to be customized for different types of therapies, and are highly customized for orphan drug therapies.

These services are delivered by experienced health care professionals and case managers, and include the following services:



Traditionally, many of these services have been managed through brand-specific programs that utilize manual processes, including phone calls, faxes, and letters. But over the past several years, the industry has begun to shift to more technology-driven solutions to better leverage real-time, electronic transactions to replace manual intervention. This shift to e-services is the first stage of the transformation to a universal hub services platform designed to improve efficiency, reduce costs and facilitate patient access. McKesson is at the forefront of this transformation and today has a Patient Support Center that employs over 1,500 people to support the full spectrum of patient access and support services.

Another important aspect of commercialization, especially for orphan drugs, is understanding how the therapy will be utilized once approved versus how it was utilized during controlled clinical trials. The patient populations for orphan drugs are highly targeted and difficult to find. Physicians gaining early access to these drugs during the clinical trials will have better familiarity with the drugs, and drive faster adoption of these therapies post-FDA approval. These researcher physicians then become key thought leaders who drive education efforts for the therapy from a clinical, access, and adherence perspective.

Through McKesson’s clinical research services, Phase I-IV clinical trials are executed leveraging a centralized operational model that accelerates study start-up and patient identification. For example, we have participated in numerous immuno-therapy trials, driving clinical

education and administrative best practices that help prepare physicians for success. Additionally, our key opinion leaders (KOLs) serve as champions for immunotherapies, driving awareness and education across pre and post commercialization stages.

Real-World Evidence Generation

RWE now plays a crucial role in the funding of orphan drugs because the evidence generated from formal randomized controlled trials (RCTs) for drugs in this class may fail to meet payer or Health Technology Assessment (HTA) criteria for listing/reimbursement.^{4,5} For orphan drugs, small patient populations mean limited sample sizes which limit the interpretation of clinical outcomes. RCT trial periods may also not reflect the natural history of the disease.⁶

Real-world evidence (RWE) is the collection of post-marketing data that reflects the use of a drug in real clinical practice.^{2,3}

For HTA agencies in several jurisdictions, the solution is the collection of RWE which can augment clinical trial data and support pricing and coverage decisions. HTA agencies in Canada and the UK (CADTH and NICE, respectively) have recognized the value of RWE, particularly for drugs for rare diseases.^{7,8} CADTH, for example, in making reimbursement decisions for orphan drugs, has in many cases recommended drug reimbursement contingent on the generation of additional RWE to confirm clinical and cost outcomes.⁷ In addition, private payers in Canada and the US are beginning to request additional real-life clinical and economic data to support long-term reimbursement for orphan drugs.

RWE will also be essential for the future approval, pricing, and coverage decisions for gene-based therapies. At a recent Institute for Clinical and Economic Review (ICER) Policy Forum on gene therapy, three key categories of challenges for gene-based therapies were defined: evidence generation, assessing value, and affordability.⁹ These are the same elements that lead to doubt in approval and reimbursement of orphan drugs but they are magnified in the case of gene therapies for the following reasons:

- **Evidence generation:** Apart from the difficulties of carrying out classic RCTs on these therapies, gene-based treatments in theory provide a “cure” after a single therapeutic intervention. However, questions remain about how durable the cure is and whether or not there are any long-term consequences of the technology itself (i.e., does the process used to introduce the genetic material impact other cell functions over the long-term?). Short term clinical trials, regardless of their design, cannot address these outcomes.
- **Value:** How is the value of the therapy (expressed in terms of clinical or quality of life gain for the patient) and the price paid for this improvement to be assessed over the lifetime of the patient? In addition, is the value of the therapy durable over this time and, if not, how is the limited value of the therapy assessed? Again, such outcomes cannot be assessed through short-term clinical trials.
- **Affordability:** Although very few gene therapies have been approved, it is clear that the cost of therapy will be very high. It has been estimated that in the US even if only one in 10 patients with a genetic condition receives a gene therapy at a unit cost of US \$1-2 million, the budget impact could approach US \$3 trillion, which is currently the amount spent for all healthcare in the US.⁹ Novel reimbursement

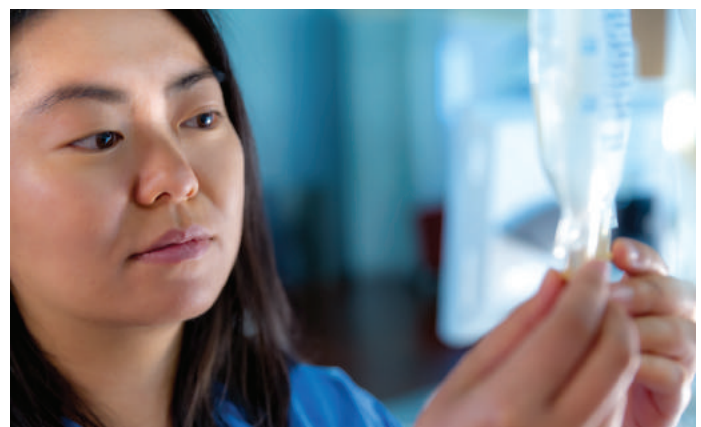
solutions to these expensive therapies have been proposed including value-based reimbursement, risk-sharing agreements, reinsurance (insurers take out insurance of their own to cover large pay-outs), or payment based on amortization (making small payments over a long period of time rather than one large initial payment).⁹

Generation of RWE may play an essential role in addressing these gene-based therapy challenges. Collection of long-term clinical and economic data after a gene-based therapeutic intervention could:

- Confirm the durability of the therapy
- Identify any long-term safety issues
- Be used to track timing of any failures of therapy and support value-based reimbursement strategies which may be relevant at failure
- Support ongoing cost-utility estimations over time
- Be used to assess revised economic and clinical burden of illness which in turn could be used to validate therapy cost assumptions

Various methods are available to collect RWE prospectively, including prospective chart reviews and observational studies. But, registries are emerging as one of the best ways to collect long-term clinical outcomes data.²

An excellent example of the potential of a RWE/registry database is McKesson’s large iKnowMedSM database.³ Based on study protocols developed by McKesson’s RWE experts, the iKnowMed database collects real world data from approximately 2,000 providers and 650 oncology sites across the US. This database can be used to track patient outcomes over time and the real world data can be used in different ways, including the advancement of FDA approval. For example, a novel therapy for Merkel cell carcinoma, a rare malignancy, has recently received FDA approval with supporting data from patients receiving conventional chemotherapy in The US Oncology Network. Real-world data was used to generate evidence on outcomes for patients receiving usual care for the disease confirming the efficacy of the new treatment, which was based on a single arm non-comparative trial.^{3,10}



In the future, national and international real world registries, like the iKnowMed database in the US and the Healthpoint database in Canada, will continue to play an important role in orphan drug market access and will be vital in the cost-effective support and expansion of gene-based therapies.

To learn more about McKesson's high-touch services that enhance patient outcomes, leverages clinical research services for the right clinical education, mitigates financial burden and generates data to align with value-based outcomes, please contact:

McKesson US

800.479.9546

AccessSolutions@McKesson.com

www.mckesson.com/pharmaceutical-manufacturers

McKesson Canada

800.576.2380

PharmaSolutions@McKesson.ca

www.mckesson.ca/mckesson-specialty



REFERENCES

- ¹ "FDA approval brings first gene therapy to the United States". FDA News Release. U.S. Food and Drug Administration. 30 August 2017.
- ² Tadros N, McCormick John. Enhancing market access for oncology drugs through real-world evidence. 2016. McKesson Canada. Available at: https://www.mckesson.ca/documents/1222016/0/WPager_EnhMarkAcc%2BConSer_EN-2.pdf/9f02ed9f-9852-4963-8684-68e7ddec6b7d.
- ³ McKesson Specialty Health. Real-world evidence: Leveraging electronic health records to improve patient outcomes.
- ⁴ Nason E, Husereau D. Roundtable on Real World Evidence: System Readiness – Are we ready to use routinely collected data to improve health system performance? Summary Report – September 2014. Institute of Health Economics. Available at: ihe.ca/download/real_world_evidence_system_readiness_summary_report.pdf. Accessed January 25, 2018.
- ⁵ Garrison LP, Neumann PJ, Erickson P et al. Using real-world data for coverage and payment decisions: The ISPOR real-world data task force report. Value Health 2007;10:326-35.
- ⁶ Lewis JRR, Kerridge I, Lipworth W. Coverage with evidence development and managed entry in the funding of personalized medicine: Practical and ethical challenges for oncology. J Clin Oncol 2015;33:4112-17.
- ⁷ Recommendation framework for CADTH Common Drug Review and pan-Canadian Oncology Drug Review programs: Guidance for CADTH's Drug Expert Committee. March 2016. https://www.cadth.ca/media/cdr/templates/pre-sub-phase/CDR_pCODR_recommendations_framework.pdf. Accessed January 25, 2018.
- ⁸ Bell H et al. The use of real world data for the estimation of treatment effects in NICE decision making. 2016. Available at: https://www.cadth.ca/media/cdr/templates/pre-sub-phase/CDR_pCODR_recommendations_framework.pdf. Accessed January 25, 2018.
- ⁹ Hampson G, Towse A, Pearson SD et al. Gene therapy: evidence, value and affordability in the US health care system. J Comp Eff Res 2018;7:15-28.
- ¹⁰ Cowey CL, Mahnke L, Espirito J et al. Real-world treatment outcomes in patients with metastatic Merkel cell carcinoma treated with chemotherapy in the USA. Future Oncol 2017. Epub.