

Building new business models to support high-cost cell and gene therapies



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13-06-2018 Comments (0)

Lev Gerlovin (pictured, left) and Walter Colasante are vice presidents at the life sciences division of Charles River Associates. Writing for The Pharma Letter, they seek to address the challenges posed to the existing biopharma business model by revolutionary, but prohibitively expensive, cell and gene therapies.

After many decades of both progress and challenges in clinical research, there is substantial evidence to indicate that we are entering a promising period in the development of new cell and gene therapies. There are now clinical-stage development programs in gene therapy targeting almost 50 different diseases, up from 10 only a few years ago, and many are reaching the later stages of regulatory review.

Development programs for cell and gene therapies are now underway around the world, with the largest share led by US and European Union companies (53% and 32%, respectively), and the remainder based primarily in China and South Korea.

Development challenges and costs

Development of cell and gene therapies is widely known to present some unique challenges that can both increase risk and drive up costs, including complex discovery paths and uncertainty about the effectiveness of chosen delivery mechanisms.

In many cases, the mode of drug delivery for gene and cell therapies cannot be fully determined until late in the development process, potentially putting the program in jeopardy. To advance these complex therapies, companies often require access to both specialized expertise and highly advanced manufacturing capabilities that are in short supply; consequently, very few biotechnology companies can produce their own viral vectors on site. As a result, production options to meet the challenging bioprocessing requirements of viral vectors typically have multi-year wait-lists and extremely high costs.

Additionally, the fact that many gene and cell therapies target very rare diseases can make it difficult to identify appropriate patients for clinical research. This can affect clinical development programs at every phase.

In the early stages, companies must often reach out globally to identify appropriate patients to participate in clinical trials and connect them with a limited number of available treatment centers.

At the commercial stage, limitations on clinical data, while sufficient to support approval, may raise some concerns among clinicians and limit adoption. In late 2017, the US Food and Drug Administration (FDA) issued guidance to help address the lack of available patients for research in rare diseases by encouraging extrapolation of data across different populations, increased use of models and simulations, and use of a single control group as the basis for more than one investigational drug.

While these modifications can help streamline some drug development programs, there is concern that they could also create an over-reliance on computer simulations or lead to research results that are less statistically sound than current industry standards.

The personalized nature of cell and gene therapies can also affect costs after drugs are launched and available commercially. With many small molecule drugs, the cost per unit will decrease as production scales up. But cell and gene therapies are typically developed individually for each patient. As a result, per-unit production costs remain relatively consistent at different production levels.

One example is seen in the emerging generation of CAR-T cell therapies. While drugs in this class have shown potential use in treating a range of cancers, they must be developed for each patient using a complex production process. It is therefore not possible to achieve significant economies of scale that can support commercial viability as production levels rise.

Existing drug development models are inadequate

With these challenges, there is now significant and justifiable concern that traditional business and financial models in drug development, many of which were engineered to support companies developing small molecules and monoclonal antibodies, may not be positioned to address the unique characteristics and costs of more complex and high-risk therapies.

There is widespread agreement that new financial models to support these therapies will require levels of innovation and stakeholder alignment that have not been tried previously.

While government action, such as the FDA's recent plan to expedite the review of gene therapies for certain disease areas, can help, the full range of issues associated with development, production, distribution, administration, and patient monitoring could still deter many companies from advancing promising early stage research and limit their access to capital.

New modes of collaboration and stakeholder engagement

To improve efficiencies and mitigate risk, drug developers are looking at new options in stakeholder engagement that may have seemed unthinkable even a few years ago. Expanded collaboration and risk sharing among stakeholders including manufacturers, academic research centers, payers, providers, and patient advocacy groups are essential.

These alignments can help promote knowledge sharing and allow for more rapid technological advances, and can potentially help companies identify new options to access capital. The involvement of groups located internationally can also support efforts in global access, marketing, patient and clinician education, and programs to monitor and collect real-world efficacy data.

Among the options in stakeholder collaboration, partnerships between manufacturers and academic research centers show strong promise in advancing many high-risk gene and cell therapy development programs.

Examples of this strategy are already emerging. Orchard Therapeutics recently launched a transformative gene therapy development program built from partnerships with several leading research organizations, including UCLA, Boston Children's Hospital, University College London, Great Ormond Street Hospital for Children NHS Foundation Trust, and the University of Manchester. The program will exploit ex-vivo autologous stem cell gene therapy technology for potential treatment of a range of primary immune deficiencies, metabolic diseases, and hematological disorders.

In the years ahead, more established cash-rich companies might also recognize the long-term benefits of partnering with and nurturing early-stage gene and cell therapy assets. As demonstrated by Celgene's (Nasdaq: CELG) decision to acquire Juno Therapeutics in 2017, licensing and acquisition agreements can help larger companies build their pipelines and access technology platforms to develop complex new drugs at an accelerated pace.

Developing new strategies for stakeholder alignment and identifying new options for financing are now widely considered to be essential to turn the promise of high-risk research efforts into drugs that are both commercially viable and broadly available to patients who can benefit from them.

Stakeholders will need to consider alignments that balance their individual concerns about risk and their commercial interests. Concurrently, regulators must continually work to improve efficiency and embrace the often significant differences in the development of cell and gene therapies compared to other drug development programs.

There is strong evidence indicating that the new business models necessary to support these clinical research programs will need to be as innovative and flexible as the drugs they are designed to support. If successful, the impact on global health systems and on patients could be transformative.

The authors wish to acknowledge the contributions of Pascale Diesel, Stephanie Donahue and Michael Krepps to this article.

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