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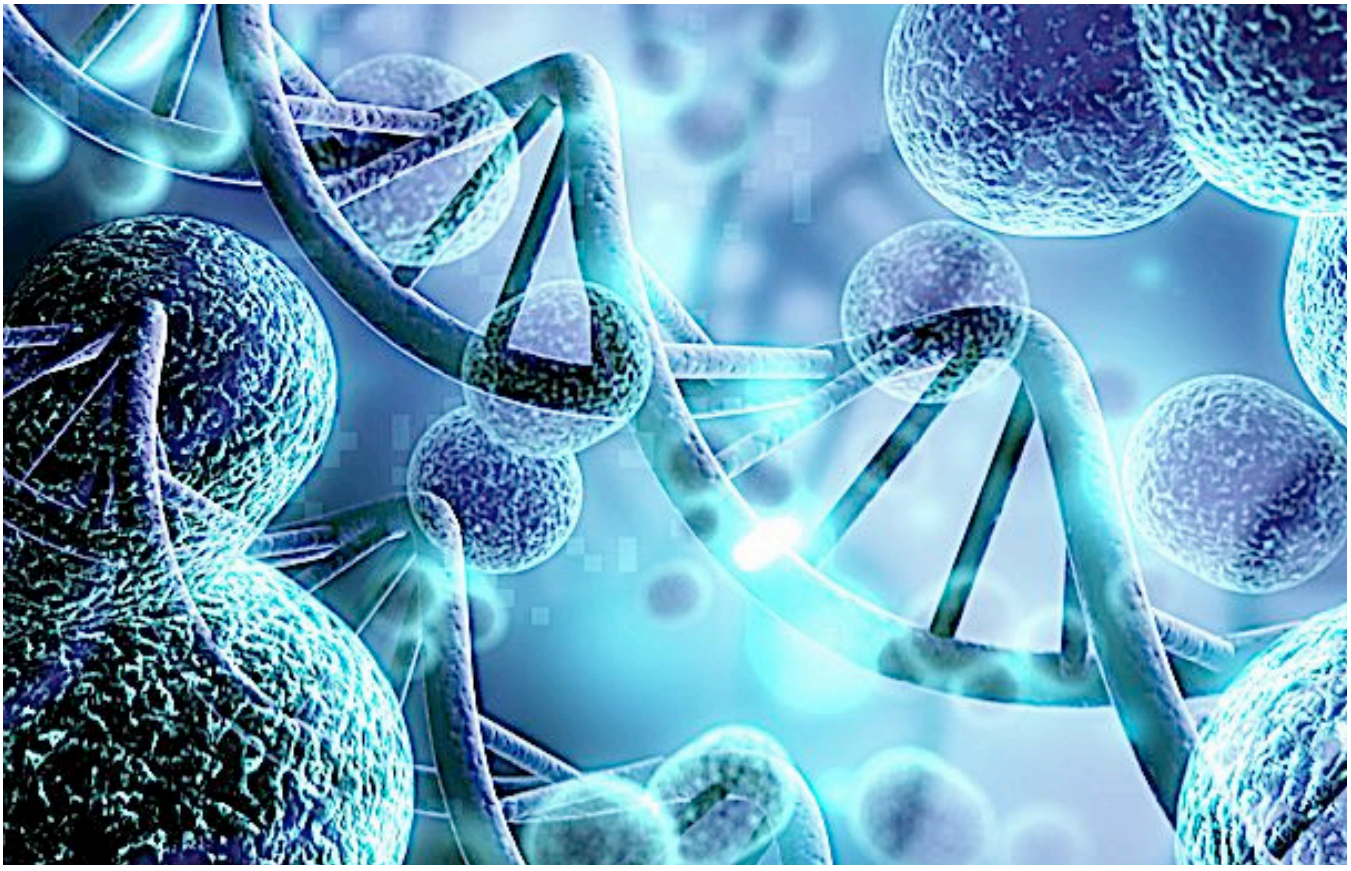
# Cell and Gene R&D in Cancer Care: Increasing Patient Access



With more than $185 billion in global investment in research and development, global oncology drug development is leading the way in clinical trial activity and in the launch of novel medicines. In addition to the emphasis on survival, stakeholders are focused on improving the current quality of life for patients and strengthening the overall cancer care paradigm, as highlighted in the notable industry trends below.

## THE LATEST IN CAR-T THERAPIES

With six chimeric antigen receptor, or CAR, T-cell therapies currently approved by the U.S. Food and Drug Administration for treatment of hematological malignancies (i.e., leukemia, lymphoma and multiple myeloma),stakeholders are expanding the reach of this groundbreaking therapy in other therapeutic directions, including novel hematological malignancy targets and solid tumor indications. As such, understanding the current opportunities for and challenges to CAR-T access is key.

## LOCALIZED ACCESS TO CAR-T THERAPIES

In the U.S. alone, there are more than 100 CAR-T therapy centers. Closer proximity to treatment helps reduce logistical burdens on patients and families and increases patient access to these potentially life-changing therapies. With increased access, it is critical that care teams at all centers engage patients and families with patient-friendly educational information to guide them throughout the entire process, from how CAR-T works to post-visit steps. Also, some centers are safely administering CAR-T therapy in the outpatient setting, which can help reduce healthcare costs and the need for patients' continuous onsite surveillance. However, there is a significant checklist of safeguardsthat care teams and patients should meet in order for outpatient care to be viable. For example, centers need to consider restructuring their CAR-T program with appropriate support, including a standard procedure to monitor post-infusion complications and adequate staffing of trained nurses for cell infusion in the clinic. Centers also need to account for thorough patient guidance as well, such as providing instructions for post-infusion complications and more.

As CAR-T assets become more approachable in terms of center burden, it will allow for more patient access to these promising therapies.

## CAR-T MANUFACTURING, STORAGE AND SUPPLY CHAIN

Current manufacturing of CAR-T and other cell therapies is laborious, intricate and costly, especially when considering logistics, sup-

ply chain, cold storage and stringent regulatory guidelines. Sponsors and therapy centers have to account for variabilities throughout the manufacturing process, which can influence the number of patients receiving treatment and cause access delays. Some variables include:

- High cost and limited availability of production materials (e.g., cell-culture media and good manufacturing practices-grade cytokines), potentially affecting the final product's safety and quality.
- Risk of contaminated, lost or inconsistent cell batches due to human error or not having appropriate equipment and assays for monitoring during development.

The industry is working to resolve anticipated and unanticipated process holdups and enhance consistency in providing high-yield end products by:

- Using multiple qualified suppliers to expand supply chains, ensuring materials are available when needed.
- Creating several lines of parallel production within one manufacturing facility to help increase product and potentially decrease variability, so more patients receive quality therapy.
- Opening local/regional manufacturing sites to better maintain GMP-grade materials across facilities, bringing the process closer to patients.
- Developing manufacturing equipment specifically designed for cell therapy, including increased automation capabilities to reduce human error.

Additionally, to combat challenges associated with autologous CAR-T therapies and to evaluate broader use of CAR-T for solid tumors, there is an intense spotlight on the safety and efficacy of allogeneic (donor-derived) CAR-T therapies. Currently available autologous CAR-T therapies show limited efficacy against solid tumors. Though some manufacturing processes would remain complex and time-intensive, allogeneic therapies may offer less batch variability and stronger cell quality because donors are healthy and unexposed to other taxing cancer treatments (e.g., chemotherapy). Furthermore, use of healthy donors can potentially help meet therapy demands and minimize delays in CAR-T therapy administration.

## DOSE OPTIMIZATION IN EARLY PHASE ONCOLOGY

The FDA Oncology Center of Excellence, through its Project Optimus initiative, is aiming to reform the dose optimization and dose selection model that has shaped decades of oncology drug development. The mindset that higher drug dosage leads to greater antitumor activity, which is based on cytotoxic chemotherapeutics, is being challenged. There is growing emphasis on patient tolerability and maximizing efficacy while minimizing treatment-related morbidity and mortality.

During a critical workshop at the 2022 American Society of Clinical Oncology annual meeting, the FDA gathered key oncology stakeholders to discuss strategies to improve dose optimization. Project Optimus urged companies to explore dose optimization earlier in development and addressed perceived challenges to pre-marketing dose optimization trials (e.g., randomized dose finding may slow down development and dose finding can increase patients' exposure to sub-therapeutic doses in trials).

An early phase setting allows sponsors to build evidence, using safety, pharmacokinetics/pharmacodynamics analysis, efficacy data and patient-reported outcomes for dose selection in registration trials, including as combination use. Identifying a dose that allows for improved tolerability with preserved efficacy increases treatment compliance and reduces patients' exposure to unnecessary toxicities to improve their quality of life. If not addressed early in development, regulatory authorities may request additional studies, causing approval delays or denial or additional post-marketing evaluations.

## OPERATIONAL CONSIDERATIONS FOR CLINICAL TRIAL STAKEHOLDERS

To effectively optimize early-phase dose identification, sponsors need to plan for the added operational load of increased data collection, assessments of varying datasets and stricter turnaround times for labs conducting assay work to collect and analyze samples. Given the FDA's strong push for earlier dose optimization, keeping lines of communication open with the agency throughout the trial lifecycle is also beneficial.

## CANCER CARE OUTLOOK

With the extreme growth in oncology R&D, it is clear that stakeholders in cancer care are committed to evaluating groundbreaking treatments to resolve some of the longstanding issues in care. Through the development and use of oncology cell therapies, the industry and stakeholders beyond are combining their collective insights to optimize cancer care globally. Looking ahead, the focus is multi-pronged, aiming to not only advance innovative medicines but to also ensure they reach patients quickly, safely, with quality and at lesser cost while integrating patient perspectives into their development. **CP**

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