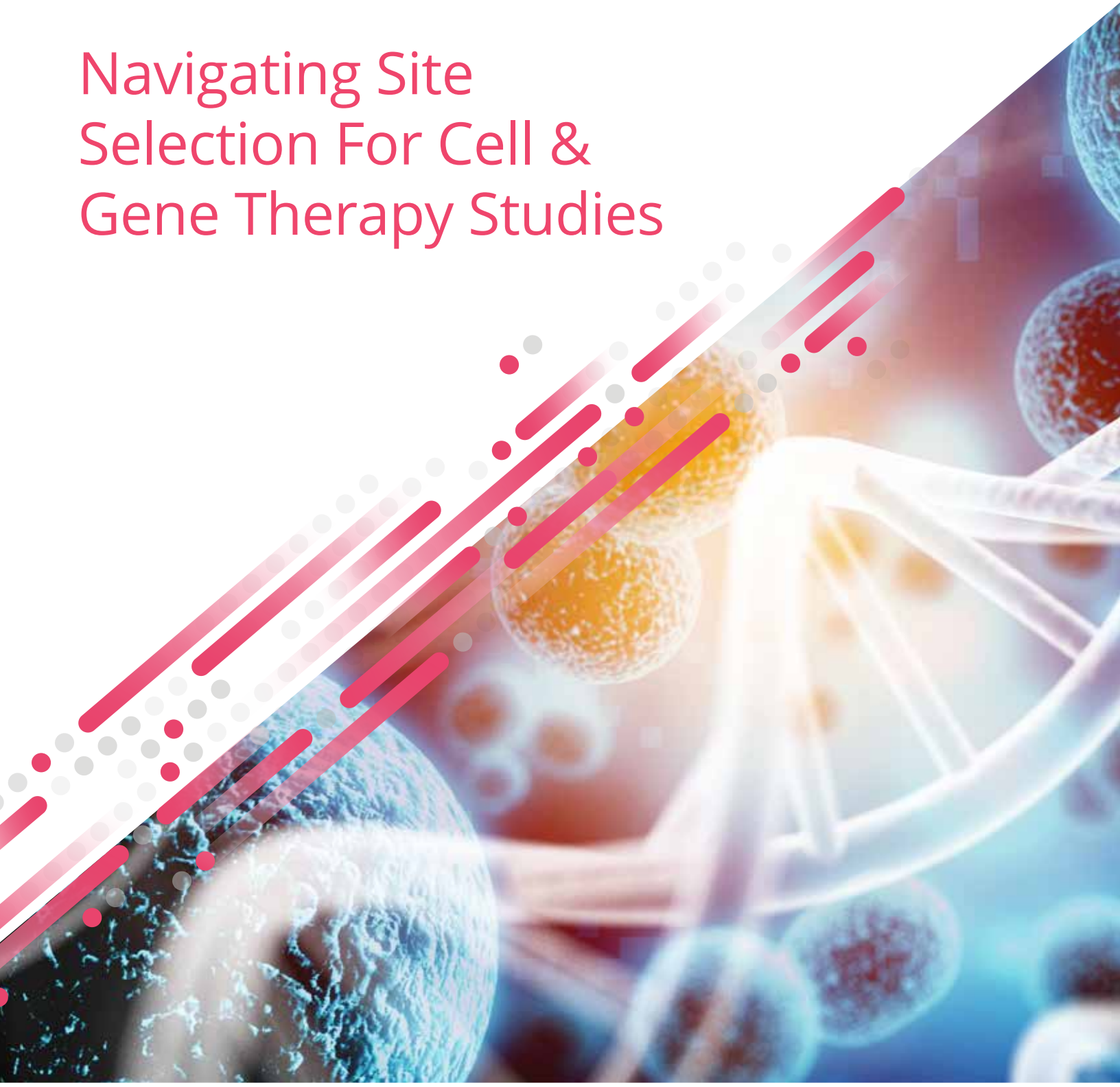
CITELINE

Navigating Site Selection For Cell & Gene Therapy Studies



BROUGHT TO YOU BY SCRIP

IN ASSOCIATION WITH caidya™

Navigating Site Selection For Cell & Gene Therapy Studies

Cell and gene therapy (CGT) studies are some of the most complex in life sciences, with the need for specialist expertise, highly advanced infrastructure, and meticulous care in delivery to ensure patient safety. Every product and trial are unique, so it is critical that biopharma companies partner with sites and investigators that meet their specific requirements. Identifying which are the most suitable is by no means an easy task for sponsors, as different sites have their individual advantages and disadvantages, with varying sizes, locations, and services.

Complex Therapies Require Specific Capabilities

At the close of 2022, 84 CGT products were approved globally for clinical use, with a notable 3,726 in development stages.[1] The space is gaining significant momentum, and with even more treatments in preclinical stages, clinical trial numbers will likely continue to grow. Nevertheless, there are currently limited blueprints to follow compared to small molecule drugs, so it can be challenging for sponsors to know what to look for when making site decisions.

Many of the criteria sponsors look for in non-CGT trials are still very important. These include whether the site has adequate resourcing, relevant experience in the indication and if they have access to patients. However, Adam Marsh, director of clinical development at contract research organization (CRO), Caidya notes that there are a number of nuances to these studies that require more from sites. “During the qualification process, it’s not just as simple as sending a feasibility questionnaire out with ten questions and hoping for the best. We must think about every aspect of what will be happening at the site,” he states.

Such considerations specific to CGT trials include whether there needs to be leukapheresis, surgical intervention, and the logistics of handling cellular and/or GMO material.

Genetic testing for patient screening is another key element of many gene therapy trials, which not all sites will be able to facilitate. While it is possible to get such testing with alternative providers, there are clear benefits to having this as an integrated option on-site. Marsh continues, "Centers where genetic testing is done as part of standard care is definitely advantageous, rather than having to send samples elsewhere to those without the background on the genetic characteristics of that patient. Moreover, if you can find centers that can identify specific mutations, then obviously that's going to put you in better stead."

Jorge Galvez, medical director at Caidya, notes that there are two main phases when assessing a site's ability to conduct a CGT trial. "We start by establishing an understanding of the complex science, processes and technologies, then eventually move on to confirming that the infrastructure is there." Galvez refers to centers that satisfy both as "quality treatment centers" (QTCs) and partnering with these can determine the success of clinical studies.

Industry accreditations are a good indicator of whether a site has the necessary facilities for CGT studies, and one key example is the Foundation for the Accreditation of Cellular Therapy (FACT). FACT currently covers Europe, United States, Canada, Australia, and New Zealand, and lists over 300 institutions deemed to meet the required international standards to administer CGT therapies to patients. It also includes information on the testing, collection and processing sites can do, providing a reliable starting point when shortlisting sites.

"Industry accreditations are a good indicator of whether a site has the necessary facilities for CGT studies."

Increased Demand Requires A Flexible Approach

Every site is different, meaning it can be difficult for biotech companies to identify which will be most effective for their study. The most obvious route to sponsors in the first instance is often the path most trodden, which in CGT cases tend to be major academic centers with esteemed reputations. These are often referred to as 'Tier I' sites in the US.

Marsh recalls that when the first CGT products were reaching the clinic, so long as a Tier I site had relevant infrastructure and experience, it was highly likely they would accept a new trial. Nowadays, these centers are highly subscribed and under-resourced for the number of therapies hitting the clinic. This demand could also be the result of an investment surge into biotech companies, many of which focus on CGTs. However, recent drops in biotech financing may make this a temporary problem for industry. "We're seeing venture capital funding unwind, and layoffs in some CGT companies. So, while this period of investment created a wave of trials which were making these sites extremely busy, it might level off," Marsh notes. Indeed, the final quarter of 2022 saw $200m less in start-up financing than 2021 for CGT products,[1] so while it might take some time for the impact of this be reflected in site demand, it is reasonable to expect a decline in the future.

Nevertheless, such projections do not solve the problem for today's sponsors, who are having to work much harder to gain buy-in from sites and investigators to partner on their trials. Marsh observes that even in instances where a study is accepted by a Tier I site, the work is by no means over, as the trial may not be prioritized over others at the facility. "Keeping the momen-

tum and those sites engaged is critical, to ensure they actually recruit patients into the studies as well," he states. The cost of delays to recruitment are well noted and can be devastating for biotechs operating under investor pressure and on limited resources.

As a result, sponsors should consider expanding their short-lists to include less famous, well-equipped 'Tier II' sites. These are usually still academic institutions, but they may not yet be certified as medical centers or have the same level of direct CGT experience as their Tier I counterparts. Typically, they have more availability to take on studies or might be trying to grow CGT at their institution, so principal investigators (PIs) may be more willing to say yes to these trials.

"Patient-centricity is key to successful studies, as enrollment difficulties and lack of adherence once recruited are stumbling blocks in most trials."

Is Balance Better?

While sponsors likely have to take a more flexible approach to site selection for high demand CGT trials, Marsh asserts that achieving a mix can actually be optimal. "In a site mix, you would ideally include some large, Tier I, academic centers, to gain access to key opinion leaders (KOLs) and give your trial credibility. They also have world-class doctors that can handle any kind of adverse event, so you would feel safe having your first patient dosed there. Then you might have what we call 'quick-start centers', which are sites that can get going and assist with early recruitment into a study. Then your Tier II centers will probably do the bulk of the enrollment, as we've seen that Tier I sites sometimes don't actually recruit that many patients."

Putting effort into less experienced sites from the beginning can lead to advantages later in the trial. While a Tier II site may not have as much historical experience as larger centers, through early involvement they will soon gain an in-depth understanding of the individual CGT and the infrastructure needed. This is critical during larger-scale Phase III studies and creates efficiencies for an expedited path towards commercialization.

Finally, expanding site selection to include Tier II facilities provides opportunities to be closer to patients, making clinical trials much more accessible. This has clear benefits for the diversity of participants, which is area of increasing focus following recent US legislation requiring study sponsors to submit diversity action plans to the FDA.[2] According to Galvez, the benefits also extend to patients themselves. "Most clinical trials are not offered at every single center in the US, so patients have to mobilize themselves. When we are talking about expanding Tier II programs, these very well recognized institutions, but maybe not in CGT, are very eager to learn, educate themselves, and make treatments available for their patients so they don't have to travel thousands of miles," he states. By marrying accessibility with well-established centers – such as those featured on the FACT registry – and conducting a robust risk evaluation, sponsors can be confident they are optimizing their trial strategies.

Improving The Patient Experience

Patient-centricity is key to successful studies, as enrollment difficulties and lack of adherence once recruited are stumbling blocks in most trials. Since the COVID-19 pandemic, decentralized clinical trial (DCT) models have attracted significant interest from sponsors and patients alike, offering a much less intensive study experience for participants. While the

treatment period of CGTs simply cannot be conducted remotely, there is potential for such approaches to be utilized in follow-ups. Marsh notes that this is particularly relevant for gene therapies, which offer a 'one-stop-shop' treatment. "Really, you're just waiting for the treatment to take effect or ramp up over a number of years. There's a regulatory requirement to have long-term follow-ups for patients that have had gene therapies, and COVID-19 really boosted the remote environment in which we work." This also lessens the financial, resource and logistical burdens on sites themselves, enabling them to accept studies they otherwise would not have the bandwidth to support.

Marsh also stresses that these follow-ups are largely standardized assessments, with an opportunity to adopt a 'hub and spoke' model for site selection. "Your 'hubs' would be centers of excellence who have the expertise to administer the treatment itself, and the facilities to keep patients in as long as needed. Then the 'spokes' are for your follow-ups, such as physical exams, getting back to the patient-centric approach of having satellite centers much closer to patients. You don't need a center of excellence to do these tests."

CROs Hold The Key To Optimal Site Strategies

As CGT trials could be considered relatively new compared to other modalities, discerning between sites can be a monumental task for sponsors. This is especially the case for early-stage biotech companies entering clinical studies for the first time. Rather than spending vast amounts of human resource and time compiling all the necessary information, sponsors may consider gaining support from specialist CROs with experience in the field.

Service providers like Caidya are equipped with clinical research associates (CRAs) that liaise with sites on a daily basis, with expertise on which are best equipped to handle specific indications. They are also specially trained to identify potential hurdles to enrollment, logistics and study management in CGT trials. Marsh asserts that there are real benefits to gaining objective feedback from a neutral third party at the feasibility and qualification stages of site selection. "Sponsors sometimes find when approaching investigators directly that they get quite a different, normally very optimistic, answer, compared to what a CRO representative might find when they get to the facility and start to ask the right questions," he states.

Moreover, CROs often have strong relationships with individual investigators and KOLs, which can make a substantial difference in a top-tier site considering a study at all. "You cannot overstate the importance of having those connections, and gaining investigator buy-in to be the true advocate of the trial," states Marsh. By giving sponsors the opportunity to have their study considered by the very best sites, they safeguard the prospects of their trial and CGT product, making it much more likely to have a successful outcome. Galvez concludes, "we must, of course, ensure the safety of the patients, but also the work that has been put into the therapy itself. We are the shield of these innovative treatments, which have the potential to benefit many people."

References

1. ASGCT & Citeline, *Gene, Cell & RNA Therapy Landscape: Q4 2022 Quarterly Data Report* (Feb 2023) https://pharmaintelligence.informa.com/asgct-report
2. Pink Sheet, *Clinical Trial Diversity Action Plans Required Under US Funding Bill* (Dec 2022) https://pink.pharmaintelligence.informa.com/PS147484/Clinical-Trial-Diversity-Action-Plans-Required-Under-US-Funding-Bill

Scrip Pharma Intelligence

caidya™

About Caidya

Caidya is a multi-therapeutic clinical research organization (CRO) serving innovators worldwide. Focused on delivery excellence and an elevated customer experience, Caidya offers a wide range of clinical services and vast therapeutic expertise, supporting its partners from pre-IND strategy, through clinical development to submission and post-marketing surveillance. Caidya leverages industry-leading and proprietary clinical technology to ensure trial transparency and data-driven decision-making.

For more information visit caidya.com