Regulatory Reforms Enhance China's Biotech Trial Potential

Lina Feng, Director,
Global Regulatory Affairs, ICON China

Qing Liu, Senior Director,
Project Management, ICON China

China has rapidly established itself as an attractive option for clinical trials, with activity trending upwards year on year over the last decade. In fact, for the first time in 2021 China overtook the US as the top destination for trials, with 3,795 new clinical trials initiated there compared to 3,310 in the US.[1]

There has long been great potential for international biotech companies that pursue studies in China, with its large population facilitating reduced patient recruitment timelines and lower study start-up (SSU) costs. However, the complex regulatory environment may have dissuaded some sponsors from considering China as a study location for multi-regional clinical trials (MRCTs). Now, following significant reforms and the Chinese National Medical Products Administration (NMPA) becoming a regulatory member of the International Council for Harmonization (ICH) of Technical Requirements for Pharmaceuticals for Human Use, there is a renewed opportunity for biotechs to reap the benefits of trials in China.

OPTIMIZED CLINICAL TRIAL APPLICATION & REGISTRATION PATHWAYS

Once a clinical trial application (CTA) has been accepted for review, timelines for approval have been standardized to 60 working days under the new regulatory framework. This is a notable improvement on the two- to three-year period it could previously take. Moreover, sponsors are permitted to initiate studies if no objection is received from China's Center for Drug Evaluation (CDE) in that timeframe, placing the burden on review bodies under a tacit approval model.

The CDE also offers multiple channels to support sponsors with studies and marketing authorization application (MAA) submissions, including communication meetings to clarify any uncertainties. These meetings are free of charge, which is particularly helpful for biotechs looking to manage their financial resources carefully.

Additionally, restrictions on registering imported medicinal products for use in clinical trials have been reduced, enabling sponsors to conduct research in China much earlier. Previously, in order to be used in a study in China, the product needed to have already commenced Phase II or III trials in other countries. However, under revised guidance, sponsors can now start Phase I studies in China in parallel with those in other locations. As a result, biotech companies can capitalize on the advantages China can offer their studies in early development and expedite progress.

There are also further benefits for overseas sponsors wishing to access the Chinese market after their products progress through clinical studies. The prior requirement stipulating an imported product must be authorized in its country of origin before MAA submission in China has now been removed. NMPA has also introduced measures to encourage the development of innovative products and those for unmeet clinical needs (e.g. rare disease and pediatric indications) such as breakthrough procedures, conditional approval and priority review processes. As China is the second largest health care market, this is valuable for companies looking for commercial success and it also increases prospects for Chinese patients looking for improved treatment options.

SOLUTIONS EXIST FOR REMAINING CHALLENGES

While the reforms made to clinical trial processes in China are very encouraging for biotech sponsors, there are underlying distinctions to studies carried out here that may dissuade companies from considering the location. Nevertheless, there are ways to overcome these obstacles.

Local treatment practices and guidance

There are local nuances to treatment practices and guidance in China that international sponsors may not have an in-depth understanding of, especially if conducting trials in the region for the first time. For this reason, it is very important to involve key opinion leaders (KOLs) as early as possible. These experts can provide suggestions on protocol design, support communication with the CDE, recommend principal investigators (PIs), help with site identification, and accelerate SSU timelines.

When identifying sites, biotechs must note that in China most are independent and, consequently, their requirements differ. Even the same site may change their conditions from one year to the next, so it is critical that sponsors check before any submission. Again, KOLs and local expertise are very helpful when navigating these complexities.

During the trial, it is also best to assign a medical monitor based in China, as they can uphold trial efficiency by removing language and time-zone barriers to quickly address any questions that may arise from the PI. If sponsors have local presence this could be a member of their own team, but as many US- or Europe-headquartered biotechs do not have such workforces, contract research organizations (CROs) can assist.

Competing trials

While the exponential growth of trials in China has greatly increased site and PI experience, as this continues some sponsors may find themselves competing to secure availability. One strategy is to target more sites in what may be referred to as "Tier 2/3" cities instead of highly oversubscribed "Tier 1" cities. While these sites may not have as much direct experience, training can be provided to ensure studies still run effectively and they will likely have untapped patient pools which can accelerate enrolment.

There are also recruitment and retention services available for sponsors should they struggle with enrolment. Partners have their own databases and networks of community hospitals and clinics which biotechs would otherwise not be able to access. Many CROs now have this capability in-house, but they can also form local partnerships with specialist providers to build targeted strategies for recruitment, depending on the therapy and patients required.

Communication and time zone differences

One of the key concerns from US- and Europe-based biotech companies when considering trials in China is the lack of control and communication they may have, due to significant time zone differences and language barriers. As a result, it is recommended that all trials have a China-based clinical trial manager (CTM) who is familiar with local practices, culture, and dialect, whilst also having a project manager (PM) in the sponsor's own time zone.

PMs can facilitate ongoing cross-functional conversations easily with the local CTM to ensure there is no breakdown in communication, while ensuring dedicated resource in the location of the trial to maintain progress. As part of this, there should also be clear escalation pathways in the event that challenges arise and other stakeholders need to be pulled in.

BENEFITS AWAIT FOR BIOTECHS

While there are no doubt challenges to conducting trials in China for biotechs based in the US and Europe, for those that persevere there are clear benefits to be realized. China is the most populous country in the world, but it has relatively untreated patients in a number of key therapeutic areas such as immuno-oncology and chronic diseases.[2] This leads to recruitment timelines that are estimated to be around two to three times faster, which is critical for biotech companies racing to generate positive clinical data and secure further investment.

Costs are also lower than in the highly competitive US and European markets for trial start-up and enrolment. Generally, even at top urban medical centers, direct costs are around 30% lower than in the US.[2] For early-stage sponsors progressing one of their first assets to the clinic, every bit of financing needs to stretch as far as it can, so savings such as this could be pivotal to move through development.

Most of the barriers to achieving these advantages can be overcome with understanding of the Chinese trial environment and requirements. For biotechs without a local presence in China, it is highly unlikely they will already have this in-house, so partnerships with specialists are the way forward.

Established CROs can utilize their experience and expertise to guide international sponsors through the nuances of China's regulatory and clinical processes, to avoid any delays or errors that require rectifying at a later stage. As China continues to gain momentum as a key study location and requirements continue to evolve, this will be key to ensuring trial success.

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