Toshiaki Nagafuji – Executive Officer, CTO, Head of Innovative Drug Development Business, Linical

Mid-sized CROs like Linical can be suitable partners for relatively small pharmaceutical and biotech companies that are searching for flexibility and true collaboration

28.05.2026

Tags: Japan, Linical, APAC, Clinical Trials, CRO, Cell & Gene Therapy

Dr Toshiaki Nagafuji leads the Innovative Drug Development Business (IDDB) at Linical after a career spanning discovery and research at Chugai and clinical development, project management, and business development at Shionogi. At Chugai, he also served as a visiting professor at Brain Research Institute, Niigata University and a visiting researcher at University of California San Francisco. At Shionogi, he also worked at its US subsidiary in New Jersey. With experience in both Japan and the US, he shares insights on Japan's evolving regulatory landscape, the rising complexity of cell and gene therapy trials, and Linical's positioning against global CROs.

Before we discuss Linical specifically, could you give us a sense of where Japan sits in the global clinical trial landscape today, and how you see that picture changing?

According to a report, in 2025 clinical trials conducted by companies headquartered in Japan accounted for only 4% of all clinical trials conducted worldwide. US companies ranked first (35%), followed by Chinese companies (32%) and European companies (20%). European companies held the top spot globally in 2009 with a share exceeding 40%, but their share has been declining steadily since then. Japanese companies held a share exceeding 10% until 2014, but this has been gradually decreasing.

In contrast, while Chinese companies held only a 2% global share of clinical trials in 2009, their numbers surged rapidly starting in 2016, and since 2023 they have been competing on equal footing with US companies. For the past three years, the US and China have continued to account for more than 60% of global clinical trials.

However, 88% of clinical trials conducted by Chinese companies are carried out solely within China, and their global expansion remains limited. While Chinese companies account for 77% of clinical trials conducted in China, their share stands at just 2% in the US and 5% in Europe. Although the global market share of clinical trials conducted by companies headquartered in the U.S., China, Europe, and Japan is expected to follow a similar trend over the next five years, Chinese companies are anticipated to accelerate their global expansion beyond domestic trials.

Can you tell us about Linical's footprint today, and the role you were brought in specifically to build?

Linical is headquartered in Osaka, Japan, and has an office in Tokyo. In addition, we have subsidiaries in South Korea, Taiwan, China, the US, and Europe, with a total workforce of 641 employees as of the end of April 2026. While we are a mid-sized CRO, I believe we are the most globalized among CROs headquartered in Japan.

Since its founding in 2005, Linical has grown by providing clinical monitoring services, a key component of clinical studies, to major Japanese pharmaceutical companies and the Japanese subsidiaries of global pharmaceutical giants. When I joined Linical in 2017, I set out to expand this client base to include biotech companies. Major pharmaceutical companies have all the functions necessary for drug development – such as non-clinical, CMC, regulatory affairs, medical writing, clinical development, pharmacovigilance, data management, statistics, and marketing, etc. – internally. However, biotech companies possess only some of these functions. Furthermore, when these companies are based outside Japan, they are often unfamiliar with Japanese regulatory requirements, so they require support in formulating regulatory and development strategies, as well as in discussions with the PMDA. In addition, since the exit strategy for many biotech companies involves licensing out their products rather than selling them directly, we also need to support their licensing activities. Therefore, I established the IDDB Unit at Linical and initially started these consulting services alone. Although the IDDB Unit is not yet large enough, the number of contracts with biotech companies both in Japan and outside Japan is gradually increasing. Currently, approximately 44% of the IDDB Unit's clients are companies based outside

Japan.

How does your service offering differ when the client is a biotech company rather than a large pharmaceutical company?

Major pharmaceutical companies possess all the functions necessary for drug development. Therefore, they approach Linical after having already determined the country or region of development, the target indication, the endpoints, the expected competitive advantage over other products, and the regulatory and development strategies. The clinical trial protocol encapsulates all these strategies. In most cases, the sponsor creates it and then requests that Linical handle only the clinical monitoring aspect of the trial.

In contrast, the situation is entirely different for biotech companies. They do not necessarily possess all the functions required for drug development. Foreign companies are often unfamiliar with Japanese regulatory affairs. Therefore, in order to conduct clinical trials in Japan, they typically request a gap analysis to evaluate the adequacy of their existing non-clinical and CMC data, an assessment of eligibility for accelerated review systems such as Orphan Disease Designation, Conditional Time-limited Approval, or Pioneering Drug Designation (formerly SAKIGAKE), as well as support for PMDA/MHLW consultations and the preparation of necessary documentation. Regarding clinical trials, in addition to clinical monitoring, if the company does not have a subsidiary in Japan, they will also require support for the role of In-Country Clinical Caretaker (ICCC) as defined by GCP, as well as the drafting and submission of the CTD for subsequent marketing authorization applications. Furthermore, as part of their exit strategy, they often consider licensing out their products, so they also seek support for licensing activities. In this way, they require a wide range of support, spanning from initial development feasibility studies to the licensing-out phase of their exit strategy.

Many biotech executives outside Japan describe it as complex, difficult, and something of a black box. When you are speaking with a biotech that is conducting trials elsewhere but has not considered Japan, how do you make the case?

This comes up constantly. The reasons for this include misunderstandings on the part of foreign biotech companies, as well as the fact that notifications issued by the PMDA can be difficult to understand. The notice is sometimes difficult to understand even in Japanese, and this is even

more true in English.

I had a meeting just yesterday with a biotech company that had been conducting Phase I and Phase II trials outside Japan, using non-Japanese subjects, and they wanted to know whether they could simply include Japanese patients from Phase III onwards in a multi-regional clinical trial (MRCT). My short answer was: in most cases, no – not without prior work.

The PMDA's position, when you approach them without Japanese Phase I or Phase II data, is to ask the applicant to explain why the dose level and administration route planned in the Phase III study can be expected to be safe and efficacious in Japanese patients. That requires scientific justification or prior data from the perspective of extrinsic and intrinsic ethnic differences. The traditional approach was a bridging strategy: after completing Phase I and Phase II in non-Japanese subjects, you would conduct a Phase I pharmacokinetic (PK) study to compare PK profiles between Japanese and non-Japanese populations, followed by a Phase II bridging study in Japanese patients to see the efficacy and the dose-dependency. Only after confirming PK similarity and dose-level equivalence would the PMDA agree to include Japanese patients in Phase III.

However, this has changed meaningfully in the past two years, precisely because drug lag and drug loss have become a serious policy concern in Japan. The PMDA has introduced new strategies to address this. One significant change is that even if Phase III pivotal studies were completed entirely outside Japan, if the results are positive and the target indication involves a serious condition with no available treatment – a rare disease, for example – the PMDA may now agree that an applicant can submit an NDA directly, without any Japanese-specific data. That is a very significant change, and it reflects how seriously the Japanese government is taking the drug lag and loss problem.

Furthermore, as part of the PMDA's efforts, I would like to add that it has established offices in Washington, D.C., in the US, and Bangkok, Thailand, to facilitate dialogue and provide consultation to local biotech companies.

In any case, it is wise for biotech companies outside Japan unfamiliar with Japan's pharmaceutical regulations and regulatory pathways to enter into a consultancy agreement with a reliable CRO at an early stage to resolve any questions and receive proper guidance.

Have you seen companies beginning to take advantage of that change?

Yes. For example, many companies involved in regenerative medicine products (RMPs) such as cell-based products and gene therapies have approached us expressing interest in utilizing the “Conditional Time-limited Approval System.” However, since this system involves both benefits and risks, we make a point of carefully explaining the details in advance, especially to clients who anticipate changing their manufacturing sites or who are considering licensing out their products for commercialization.

Cell and gene therapy trials bring specific regulatory and technical challenges. What are the particular pressures you face as a CRO supporting these programmes in Japan?

The key difference compared to small molecules, biologics, and antibodies lies in the focus of PMDA’s consultations. For small molecules, biologics, and antibodies, especially if the applicant has no other concerns to raise, 70–80% of the consultation time with the PMDA is typically devoted to clinical protocols and trial design. In contrast, for RMPs, this ratio is almost reversed, with 70–80% of consultations with the PMDA often focused on CMC (quality).

This poses a challenge for CROs. This is because there are few CMC regulatory consultants in the CRO industry with solid practical experience in RMPs. While there is no issue with CMC regulatory consultants for small molecules, biologics, and antibodies – who have retired from pharmaceutical or biotech companies where they previously worked and are now at an age where they have established their own consulting firms or joined CROs – the problem lies with RMPs.

Most CMC regulatory experts for RMPs belong to a generation that is still working at pharmaceutical companies, biotech companies, or CMOs, and they have not yet entered the CRO market in sufficient numbers. Consequently, finding a suitable CMC regulatory consultant for RMPs can sometimes be difficult, and due to the supply-and-demand dynamics, their fees tend to be relatively high. At Linical, we select the most suitable experts from our network of partner companies based on the modality of the client’s development project and the details of the Request for Proposal and assign them to the project as needed.

Linical was recognised as Best CRO in 2025. To what do you attribute that recognition?

The Global Excellence Awards recognize companies and individuals for outstanding achievements across a broad set of categories, with winners selected on criteria such as innovation, quality, customer service, and global footprint. Linical’s recognition as CRO Company of the Year

underscores our enduring commitment to scientific rigor, operational excellence, and client-focused solutions. Our 20+ year legacy in clinical research has been built on a foundation of integrity, collaboration, and continuous improvement across hundreds of clinical trials worldwide. Being recognized with this award affirms the dedication of our global teams, the trust of our clients, and the positive impact of the medicines we help bring to patients

While Linical has a particularly strong track record in oncology and CNS diseases, the clinical studies we conduct cover a wide range of diseases. I believe this is the result of a combination of factors, including the fact that we are the most globalized CRO headquartered in Japan, as well as the results of inspections by regulatory authorities in various countries and high client satisfaction with the quality of our work.

You face competition from very large global CROs – IQVIA, ICON, PPD – that also operate in Japan and Asia. How does Linical compete and retain clients against those organisations?

Linical is nowhere near the scale of the top three global CROs you mentioned. However, our goal is not to be the “biggest,” but to be the “strongest.”

Let me give you a specific example. A few years ago, we were contacted by a European biotech company. They were already partnering with a large global CRO and were conducting a Phase II MRCT outside of Japan. Although they did not have any Phase I/II Japanese data, they reached out to discuss including Japan in their Phase III MRCT. I asked them frankly: “Why don’t you ask your existing global CRO partner to handle the work in Japan?” The company replied, “We are not satisfied with the quality of the services we are currently receiving, and we heard that your company has a good reputation.” We took on the project, proceeded as scheduled, and successfully reached an agreement with the PMDA to include Japan in the Phase III MRCT even without Japanese Phase I/II Japanese data.

I’ve heard that large global CROs tend to charge high fees. I believe that mid-sized CROs like Linical can sometimes be more suitable partners for relatively small pharmaceutical and biotech companies that are searching for flexibility and true collaboration.

AI is reshaping drug development across the industry. How is Linical engaging with these technologies, and how do you see them changing the CRO’s role?

Linical is focused exclusively on clinical development – we do not provide non-clinical or discovery services. In the pharmaceutical and CRO industries, AI is already involved in various aspects of our work. Japanese pharmaceutical companies are using AI in target validation, discovery and in predicting efficacy and safety signals in clinical trials. We are undergoing training and applying AI tools in our own clinical operations as well. The technology is deeply embedded in the industry and evolving rapidly.

A final message to biotech executives outside Japan who are reading this and considering whether to include Japan in their clinical development strategy?

Japan is the world's fourth-largest pharmaceutical market among individual nations and is internationally renowned for its exceptionally high standards of data quality and rigor – a reputation that is well-deserved. Data generated in Japan is trusted by regulatory authorities around the world.

On the regulatory complexity that often deters companies: I understand the perception, but I would push back on it a little. The Japanese system for clinical development is not fundamentally so different from the US or Europe. The PMDA is making active efforts to communicate more openly with international companies. They have opened a subsidiary office in Wahington D.C. specifically to meet with biotech companies in the US market and make the process more accessible. The Japanese government is clearly committed to reducing drug lag/loss and making Japan a more open and attractive destination for clinical development. Furthermore, Japan's patent extension framework offers specific advantages worth understanding – I have recently published a position paper on this on the Linical website. The paper explains that Japan's patent term extension system differs from both the US Hatch-Waxman system and the EU's Supplementary Protection Certificate framework in one critical respect: in Japan, patent term extensions of up to five years apply not only to the initial approval but also to subsequent additional approvals – new indications, new dosage forms, and new methods of administration. Unlike the US, where the total effective patent life is capped at fourteen years from FDA approval, and the EU, where protection is capped at fifteen years and applies only to the first marketing authorisation, Japan imposes no fixed upper limit on total patent term following approval. The practical implication is that ongoing development activity – pursuing additional indications or formulations – can generate successive extensions, creating the potential for substantially prolonged market exclusivity. For originator companies weighing whether to develop and commercialise in Japan, this is a meaningful commercial consideration that is frequently overlooked. The complexity is manageable. The opportunity is real.

Finally, my practical recommendation to any biotech executive considering Japan is to start the conversation early and to work with a partner who knows the system and the market.

See more interviews