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WHITE PAPER



Investigator-Initiated Trials in China

Charting the Accelerated Path to Clinical Proof of Concept

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Introduction

Every cell and gene therapy (CGT) company approaching the clinic eventually confronts a version of the same question: what is the fastest, most capital-efficient path to a clinical proof-of-concept (PoC) result compelling enough to secure the next round of investment? For much of the industry's history, the assumed answer ran through a single jurisdiction and a single regulatory body. To use the United States as an example this could look like filing an IND with the FDA, initiating a Phase 1 study, and hoping that the safety and early efficacy signal is strong enough to carry the program forward.

That assumption is changing. Investigator-Initiated Trials (IITs), clinical studies sponsored not by a company but by an individual investigator at a single hospital site, usually with oversight by a local/hospital specific ethics committee, have existed for decades and have long offered developers a (sometimes) leaner, (sometimes) faster route to early human data. In fact, a great many CGT therapies have begun via a US-based IIT path.

What has changed is where that route is proving most valuable, and why. China's streamlined regulatory path for IITs, rapidly maturing hospital infrastructure, expanding CDMO capacity, large and diverse patient population, and comparatively significantly lower cost of clinical operations have converged to make it an increasingly attractive and increasingly common venue for a CGT program's first-in-human trial, in the form of an IIT.

That convergence has been reinforced by a wave of new Chinese regulatory guidance culminating in State Council Order No. 818, which took effect May 1, 2026, and, for the first time, established a national framework governing clinical research and clinical translation of new biomedical technologies in IITs, providing a streamlined path for Chinese and foreign sponsors.

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In this white paper, we describe why an IIT in China has become a strategic option worth serious consideration for CGT developers, when in a program's life cycle that decision should be evaluated, and how Dark Horse Consulting Group ("DHCG" or "the Group") helps sponsors pursue this path in a manner that protects, rather than compromises, their future global development plans.

What Is an Investigator-Initiated Trial?

An Investigator-Initiated Trial, or IIT, is a clinical study sponsored not by a pharmaceutical or biotech company but by an individual clinical investigator: typically, a physician at a hospital or academic medical center. Unlike a standard developer-sponsored trial, an IIT is usually, but not necessarily, conducted at a single site, under the direction of one investigator who is responsible for the conduct of the trial. In many (but not all) countries, IITs are not regulated directly by the national health authority, but through a separate process at the clinical site.

IITs are not a new concept. They have existed for years in the United States and elsewhere, and the underlying logic has always been the same: because the investigator (rather than a company) conducting the study at their own hospital is the trial's legal sponsor, an IIT can often proceed with a leaner data package than is typical for a corporate-sponsored, multisite trial. Though in the US, the FDA still reviews and approves the INDs for IITs, in China, the decision to proceed has rested with the individual hospital's scientific review and ethics committees rather than with a national regulator, with a subsequent informational filing to the National Health Commission (NHC), a meaningful difference that has led to increasing use of this path for sponsors to efficiently conduct first-in-human studies. Until recently this has made the requirements for a China IIT vary considerably from one hospital to the next, particularly with respect to the CMC and quality expectations attached to the investigational product.

That variability is what China's new Order No. 818 framework is designed to resolve, and it is worth understanding that background before addressing why so many CGT developers look at China first.[1]



Why China, Why Now?

A Familiar Concept, an Unfamiliar Opportunity

If the IIT itself isn't new, what has changed? In the US, many IITs have been driven more by individual clinician-investigators pursuing their own research questions, sometimes with the ultimate goal of licensing a promising asset to a company, but just as often in service of advancing knowledge, research, or publication, often of existing products, rather than a defined commercial development plan. What is comparatively new is the number of CGT companies now actively choosing to run their first-in-human (FIH) study as a China IIT by design, as a deliberate development strategy, rather than as an opportunistic byproduct of academic research.

That shift reflects where China's biotech ecosystem has arrived. Over roughly the past decade, China has built the infrastructure that makes this option genuinely competitive: a large network of premier hospitals with deep clinical experience in CGT modalities, a rapidly maturing CDMO base capable of cGMP-quality manufacturing, and a patient population whose scale allows many studies to complete enrollment considerably faster than would be possible at a single US or European site. Combined with a materially lower cost of clinical activities and manufacturing, and, in many cases, a comparatively leaner preclinical data package required to open an IIT, the result is a path to clinical PoC data that is frequently faster and less expensive than the traditional Phase 1/2 route through an IND.

Order No. 818: From Regulatory Ambiguity to a National Framework

Until recently, one real constraint on this strategy was the unevenness described above: what one hospital's ethics committee expected in a data package could look nothing like what another hospital required, and CMC expectations in particular were, by most industry accounts, applied inconsistently and without a common national standard.

State Council Order No. 818, formally titled the Regulations on the Administration of Clinical Study and Clinical Translation and Application of New Biomedical Technologies, took effect May 1, 2026, and established, for the first time, a unified national framework governing IITs for technologies operating at the cellular or molecular level: squarely encompassing CAR-T, gene editing, gene therapy, and stem cell products.[1]

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The order and its subsequent implementing rules, a series of "Detailed Rules" issued by the National Health Commission and the China National Center for Biotechnology Development between April and May 2026, accomplish several things directly relevant to CGT sponsors:[3]

- They create a national filing framework, requiring a hospital to file an approved IIT with the NHC within five working days of clearing academic and ethics review.[1]
- They restrict eligible clinical sites to Grade A Tertiary Hospitals, China's highest-tier medical institutions: thus raising, rather than lowering, the baseline quality bar for where these trials can be conducted.[1]
- They require the clinical research sponsor to be a legal entity established within China; for foreign sponsors, the right structure (a wholly owned entity, joint venture, or licensing arrangement with a domestic partner) depends on China's foreign investment restrictions and remains an actively evolving area of practice.[1,2]

This does not eliminate the complexity of CGT drug development but may provide opportunities for simplification of development. Since the law was only instituted in May of 2026, it is not yet clear exactly how it will translate in practice. A foreign sponsor's ability to directly access the Order 818 translation pathway remains genuinely unsettled given China's continuing restrictions on foreign investment in CGT development, and the framework carries its own obligations around human genetic resources and technology export controls that must be structured correctly from the outset.[2] These are precisely the kinds of questions where the regulatory and legal nuance benefits from deep, current, in-market expertise: DHCG's bread and butter.

The takeaway: Order No. 818 has converted what was once a patchwork of local hospital discretion into a defined, navigable national system, and in doing so, has made the China IIT pathway a considerably more credible and predictable option for foreign CGT sponsors than it was even a year ago. DHCG has extensively reviewed Order 818 and authored a detailed white paper on the Order, its associated regulations, and their implications (reach out to bd@darkhorseconsultinggroup.com to obtain). The Order may also improve a sponsor's ability to take IIT data to other jurisdictions. And, with DHCG's 12+ years of global consulting experience, a team that brings unmatched rigor to CGT consulting, and now a dedicated team in China, we are perfectly positioned to assist drug developers in navigating their IIT strategy and implementation (see The DHCG Approach below for more on this topic).

The Strategic Case for an IIT

Given that backdrop, when does an IIT make sense, and when does it not? In our experience, the decision comes down to a handful of core considerations, of which cost and speed to clinical PoC data are consistently the primary drivers. Compared to a Phase 1/2 study conducted under an IND, an IIT frequently allows a sponsor to reach the same milestone, i.e. human safety and early efficacy data sufficient to support the next investment decision, with a leaner preclinical package, lower manufacturing and clinical operations costs, and, in China specifically, considerably faster enrollment given the scale of the eligible patient population (for the majority of diseases).

But cost and speed are not the only variables worth weighing. A program's current status and future plans also weigh in. Most companies' development strategies are squarely focused on the US market, potentially global markets, and reaching a commercially marketed product there as quickly as possible. If the product is already IND-ready, well-funded and/or focused on a disease state that is facile to enroll or more common in the US, it may make more sense to proceed directly through a US IND and Phase 1 or Phase 1/2 study rather than adding a China leg to the plan. Indication and enrollment feasibility matter too. For a rare disease where patient identification is already difficult, a larger population base may be the deciding factor regardless of cost; for a more common indication, the calculus may tilt differently. And manufacturing complexity is a real, practical consideration. In most cases, a China IIT will require manufacturing the drug product in China, which means tech-transferring a process into a China-based CDMO, running the trial, and, in many cases, eventually tech-transferring the process back out again for global development: a sequence that adds coordination costs even as it reduces others.

Manufacturing transfer is only part of this complexity. Research provided by Converge Consulting, a division of Dark Horse Consulting Group, highlights that unlike the US and EU, where clinical trial authorization generally also enables shipment of investigational material, China treats importation of investigational product as a separate regulatory and customs process overseen by Chinese Customs (GACC); shipments can be held at port pending complete and consistent documentation. Therefore, import strategy needs to be planned as a critical-path activity from the outset rather than handled as a downstream logistics detail.

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For CGT products specifically, sponsors should also be aware of an emerging expectation that importation be tied to patient-specific informed consent, which can place international shipping and customs clearance directly on the treatment administration timeline.

There is one further consideration that cuts both ways: patient population. A larger potential patient pool can be a genuine strength for particular indications, as could an eastern-specific demographic representation that may differ from those available in a single-site westernized trial. But, representativeness of the population has to be evaluated against the specific disease being studied, and the locations in which a sponsor may hope to eventually commercialize the product. The underlying drivers of a given condition can differ meaningfully by population and geography; for example, the leading causes of certain liver diseases differ between the US and other regions, while a disease such as sickle cell disease is concentrated in specific population groups that may not be well represented in every geography. Additionally, the available or standard-of-care treatments may differ in other countries, making the population that would be treated in China (and resulting data) less relevant to the subsequent US population or expectations. Evaluating whether a given patient population is the right population for a specific product and indication, not simply the fastest one to enroll, is part of getting this decision right, and it is exactly the kind of cross-disciplinary judgment that benefits from DHCG's broad development experience across regulatory, clinical, and translational disciplines.



Beyond Proof of Concept: Ensuring Forward Compatibility

Reaching clinical PoC data is often framed as the finish line for an IIT, and for many sponsors, it is treated as such: get the safety and efficacy signal, bring it to investors, and move forward. But treating an IIT purely as a standalone milestone leaves real value on the table, and done carelessly, can actively work against a program's future.

The risk is straightforward. If an IIT is conducted without appropriate quality oversight, or with drug product manufactured or tested in a manner that does not enable forward comparability, the resulting clinical data may be effectively unusable outside of China. A sponsor in that position has generated PoC data but has not necessarily built anything that can carry forward into a US IND, an EMA filing, or any other jurisdiction's registration pathway. We think of the alternative, designing an IIT so that its data and manufacturing history remain usable for future global development, as ensuring that the program is forward-compatible.

Achieving forward-compatibility comes down to two connected decisions. The first is quality oversight of the trial itself: working with a clinical research organization whose operational standards, data management practices, and safety monitoring processes meet the bar that future regulatory reviewers, wherever they are, will expect to see. The second is the choice of manufacturing partner: selecting a CDMO whose quality systems, documentation practices, and process controls are built not just to support a single IIT, but to survive a subsequent tech transfer without requiring the process to be substantially redesigned.

Done well, this approach doesn't just protect the value of the PoC data; it can meaningfully change what an IIT is capable of delivering. The most instructive example remains Legend Biotech's LEGEND-2 study, a multi-center, first-in-human IIT conducted in China evaluating what would become ciltacabtagene autoleucel (cilta-cel).[4] The early response data generated through that investigator-initiated trial were compelling enough to support a global collaboration and license agreement with Johnson and Johnson and ultimately underpinned the product's approval in the US as Carvykti. Programs executed at that caliber have not been universal, but they illustrate what a properly executed China IIT can achieve. Ideally it is not simply an inexpensive way to generate initial safety and efficacy data, but, when designed with forward-compatibility in mind from the outset, a genuine on-ramp to an accelerated global, pivotal-ready development program.

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The time savings can be substantial. A typical CGT clinical development campaign, from preclinical/nonclinical development through to an initial Phase 1 study, a Phase 2 expansion, and a pivotal study, can span roughly a decade. Compressing the early proof-of-concept work into a single, well-designed China-based IIT has the potential to meaningfully shorten that timeline, though the precise magnitude depends heavily on program specifics.

Navigating Trust and IP

One further consideration: for years, a meaningful barrier to running clinical work in China was a legitimate, well-founded concern that a sponsor's technology or intellectual property might be appropriated by the Chinese government or competitors in China. That concern has shaped how many companies (including our own) approached working relationships and data security around China-based activity.

However, our view, based on discussions with our legal partner in China, is that the picture has changed materially over the past five years, and for a structural reason rather than a cosmetic one.

The most important shift is that Chinese pharma and biotech companies have become net exporters of intellectual property. China now accounts for roughly a third of global licensing spend. Companies that are licensing assets to Western pharma at that scale have a direct commercial interest in a system that enforces IP rights, because they are now on the receiving end of infringement risk themselves. The legal framework has moved forward with the Fourth Amendment to the Patent Law taking effect in 2021; however the alignment of incentives is a much more durable driver of strict enforcement.

The risks of IP infringement have not disappeared, but they have become manageable rather than prohibitive.

Site Selection

Under Order 818, IITs are now restricted to Grade A Tertiary Hospitals, and different hospitals continue to vary meaningfully in both their procedural expectations and their clinical specialization. A hospital with a leading team focused on a particular disease or modality is simply a better fit for a program targeting that indication than a generalist site would be. Matching a sponsor to the right hospital is as much a clinical decision as an operational one.

Furthermore, research provided by Converge Consulting has found that hospitals will frequently decline to serve as the importer of record for investigational material due to regulations, tax, and liability concerns, which means the importer-of-record relationship is itself one of the agreements that needs to be resolved before a program begins, not discovered as a gap once product is already in transit.

The DHCG Approach

DHCG has spent the past year building the infrastructure necessary to guide clients through the China IIT pathway with confidence, not simply pointing sponsors toward opportunity, but standing behind the path we recommend. That work includes:

- **A growing physical presence in China**, including a dedicated office in Shanghai with locally-based staff, allowing us to maintain direct, ongoing oversight of client programs rather than managing relationships remotely.
- **Direct regulatory intelligence**, including in-depth analysis of Order No. 818 and its subsequent implementing guidance by our APAC-based, Mandarin- and Cantonese-fluent staff, so that clients receive current, first-hand interpretation rather than secondhand summary.
- **A vetted network of premier hospitals and investigators**, developed through direct engagement, allowing us to match sponsors with the hospital best suited to their specific indication and clinical profile.
- **Partnerships with clinical CROs and CDMOs** that we have personally audited for quality systems, documentation practices, and, critically, forward-compatibility with future global development, and, increasingly, for import and customs execution experience, since strong clinical capability does not always come paired with experience navigating GACC and China's investigational product import requirements.
- **Global regulatory strategy expertise** ensures that a China IIT is designed from the outset to generate data and manufacturing history that will be capable of holding up under FDA, EMA, or other regulatory scrutiny later in a program's life cycle.
- **The ability to offer guidance on routing shipments** through major ports of entry such as Shanghai or Beijing, where customs pathways tend to be more predictable than at smaller ports.

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That network is already producing tangible partnerships. In April 2026, DHCG announced a Memorandum of Understanding with Porton Advanced, a premier ATMP-focused CDMO with two GMP sites in Suzhou, China and a track record that includes 24 IND clearances across the NMPA and FDA and support for more than 30 IITs to date, a partnership designed specifically to give DHCG clients a streamlined, trusted path into China IIT-enabling manufacturing. It complements a broader set of China-based collaborations, including with KunTuo, an IQVIA-owned clinical research organization with a dedicated cell and gene therapy clinical team, reflecting the same principle on the clinical operations side of the equation: sponsors should not have to build these relationships alone, or discover their quality after the fact.

The result is a unique value proposition for DHCG. The Group has spent more than a decade building a reputation grounded in scientific rigor and regulatory precision across the CGT industry, having supported more than 500 CGT clients to date. Bringing that same standard to bear in China, vetting partners, building relationships in advance, and holding a consistent quality bar, means the path we recommend to clients is one we are prepared to stand behind.

Conclusion

The Investigator-Initiated Trial has existed, in one form or another, for a long time. What has changed is the strategic calculation around where (and why) to run one. China's combination of clinical infrastructure, patient population scale, manufacturing capacity, and cost-efficiency has made it an increasingly compelling venue for CGT developers seeking clinical proof-of-concept data, and the arrival of Order No. 818 has, for the first time, given that pathway the kind of national regulatory clarity that had previously been missing.

For sponsors, the opportunity is real, but so is the need for careful navigation. Cost and speed are genuine advantages, but they are only advantages if the resulting data and drug product remain usable for the global development plan that comes after the IIT, and that requires the kind of quality oversight, manufacturing partner selection, and regulatory foresight that doesn't happen by accident. Done well, a China-based IIT is not merely a cheaper first step. It can be, as Legend Biotech's experience demonstrates, the foundation of a program's entire global development strategy.

At DHCG, we believe the sponsors best positioned to take advantage of this moment are the ones who treat their China IIT as forward-compatible from day one, and we have built our China presence, our partner network, and our regulatory expertise specifically to help our clients do exactly that.

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