Syner•G

WHITE PAPER

BioPharma Due Diligence in a Shifting Global Market

Libby Russell
VP, Pharmaceutical Development

Executive Summary

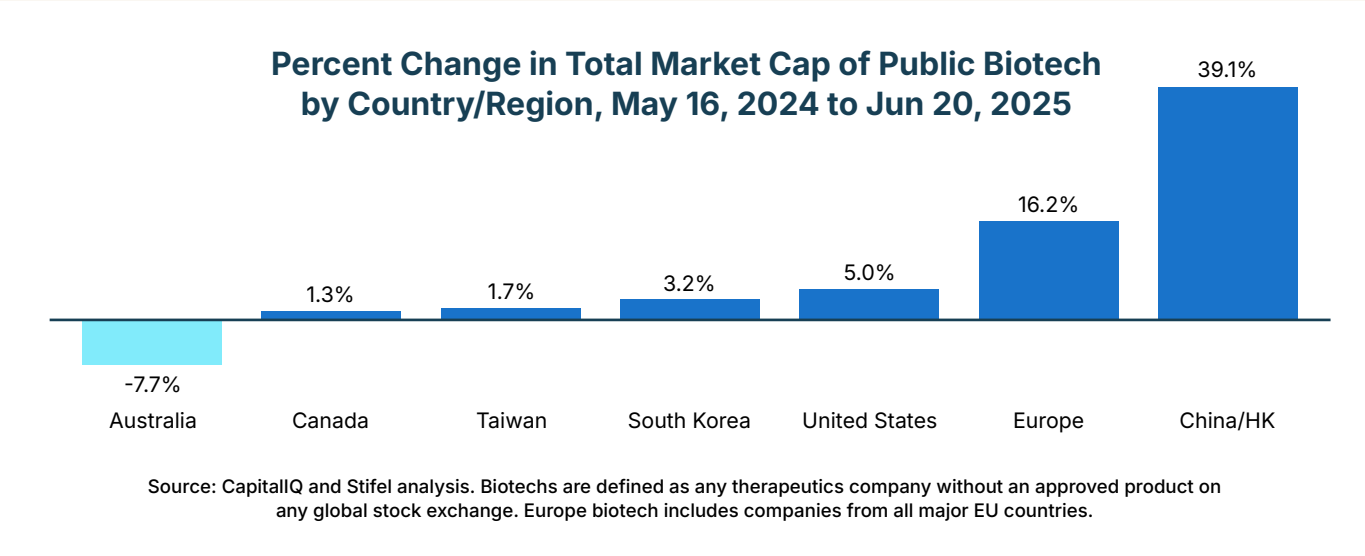
Biopharma deal-making is shifting, with Chinese companies now accounting for 30% of global licensing deals as of 2024. While Western markets face uncertainty, China's rapid growth in first-in-class therapeutics presents attractive acquisition opportunities for U.S. and EU buyers. However, key risks—such as differences in regulatory standards, quality systems, and data integrity—must be carefully assessed.

This white paper outlines a structured approach to CMC due diligence, including data review, risk assessment, and strategic recommendations. Three case studies illustrate common challenges in transitioning China-manufactured biologics for Western clinical trials. As interest in earlier-stage Chinese assets grows, robust due diligence is essential to ensure regulatory compliance and commercial viability.

Article

Despite ongoing uncertainty in the markets, including tariffs and FDA operations, biotech and pharmaceutical companies remain active in mergers and acquisitions. Recent activity includes both full company acquisitions—such as Sanofi's $9.5 billion purchase of Blueprint Medicines—and single-asset or licensing deals, like GSK's $1.2 billion acquisition of a Phase 3-ready liver disease drug from Boston Pharma[i]. A recent article in Nature Biotechnology, summarized the M&A landscape saying that it was a good start to the year with several multi-billion-dollar deals, but deals have stalled as "pharma buyer are sitting on their hands" due to uncertainties in tariff and policy. But as deals are stalling in most of the biotech industry, China is surging ahead moving beyond generics into first-in-class drugs at a pace and cost that is highly attractive. In 2024, China deals represent 30% of all the licensing deals[ii].

With enterprise values currently depressed, many assets are becoming more financially attractive. Notably, biotech markets in China and other Asian countries are outperforming those in the U.S. and EU. These regions have seen increases in both total market capitalization of public biotech companies and IPO activity. The figure below shows the side-by-side comparison on how China biotech market cap is stacking up against the EU and US. This represents just a snapshot of biotech growth in China but highlights the continued trend within the industry.



Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. Europe biotech includes companies from all major EU countries.

As of 2025 year-to-date, 37% of biopharma licensing deals valued at $50 million or more have originated from China—an exponential increase from just 6% in 2020[iii]. However, while Chinese companies are advancing therapeutic development under their local regulatory frameworks, key risks must be considered when acquiring Chinese assets—particularly due to differences between Chinese and U.S./EU regulatory standards. At a basic level, there are differences in compendial requirements for raw materials, drugs and analytical methods[iv,v]. In recent years, there has been an effort to harmonize compendial requirements across global regions, but China has been left out (or abstained) of these efforts resulting in a gap between ChP (China) compendia and Ph.Eur. (EU), JP (Japan) and USP (US) requirements [vi, vii, viii]. This poses an issue especially when filing a regulatory submission in the US as the Manual of Policies and Procedures for CDER, Acceptability of Standards from Alternative Compendia, is limited to BP (British), EP (European) and JP and excludes ChP[ix]. Secondly, there are differences in GMP requirements as China is governed by the National Medicinal Products Administration (NMPA) which has different GMP requirements compared to the US CFR, WHO and EMA[x]. There are also inherent differences in how drugs are manufactured, the quality culture and data integrity that, although not country specific, should be considered in asset due diligence.

This paper presents three due diligence case studies that illustrate how to evaluate the CMC (Chemistry, Manufacturing, and Controls) aspects of potential therapeutic drug acquisitions. The process and framework of the analysis enables a comprehensive assessment of the assets risks that would ultimately impact success, cost and timeline for commercialization.

Key Steps in the Due Diligence Process:

01 Define Buyer Intent and Acquisition Context

- Understand the strategic purpose of the acquisition
- Establish the timeline for due diligence and the deal
- Identify the first key CMC milestone post-acquisition (e.g., IND filing, clinical trial initiation, manufacturing)

02 Gain Access to Data and Source Materials

03 Conduct Comprehensive Data Review

04 Engage in Q&A with the Asset Owner and/or Buyer

Multiple iterative rounds to clarify gaps

05 Develop a SWOT Analysis

Summarize strengths, weaknesses, opportunities, and threats

06 Optional On-Site Visit

To validate key data or assess facilities

07 Generate Final Due Diligence Report

Deliverable includes findings, risk assessments, strategic recommendations and if needed, a realistic CMC budget and timeline

Each due diligence project is unique, shaped by the buyer's goals and the availability of technical information, type of asset, and stage of development. **However, the following areas are typically reviewed, assuming relevant data is accessible:**

Analytical and Quality Control:

- Analytical method readiness and validation/qualification
- Product characterization
- Product specifications
- Stability data
- Reference standard qualification and inventory

Drug Substance:

- Master Cell Bank (MCB) / Working Cell Bank (WCB) development, qualification and inventory
- Cell line licensing or royalty obligations
- Process development
- Manufacturing process robustness (e.g., transfer feasibility, lot-to-lot variability, scalability, yield)
- Raw material availability and compliance with pharmacopeial standards

Drug Product:

- Formulation development history
- Primary packaging compatibility
- Drug product in-use study results

Supply Chain:

- Inventory levels of drug substance and drug product and expirations

Regulatory Submissions and Correspondence:

- Filings, regulatory agency feedback and correspondence
- Facility inspection history
- Regional regulatory compliance (e.g., EU Annex 1)

Documentation

- Level of documentation
- Data integrity
- Language(s) of records and translation coverage

Typically, a targeted list of questions is compiled and shared with both the asset owner and the buyer. The response, along with the reviewed data, is synthesized into a formal SWOT analysis, which summarizes the asset's viability from a CMC perspective.

Case Study #1

Case Study 1: Bispecific Antibody for Phase 1 Clinical Trials in EU

Documents reviewed: IND Module 3 sections (except 3.2.S.3 and A.1)

The asset—a bispecific antibody—was developed and manufactured in China and had received approval to initiate a Phase 1 clinical trial there. The prospective buyer was evaluating its potential for clinical development in the USA and EU. The scope of the due diligence focused on all aspects of CMC, including the risks associated with using the China-manufactured drug product in EU clinical trials and the potential challenges of a technology transfer.

Strengths	Weaknesses
• Stability data does not show any concerning trends. • Two potency methods • Industry standard DS and DP manufacturing process, no red flags for ability to tech transfer (TT) – could require some raw material changes. • Facility stated to have been through QP inspection (no information on findings shared). • Re-supply batch at 2000L scale will use material grades meeting USP and compendial methods will meet USP. Cell line to be used for 2000L will be tested in accordance with USP.	• No stability indicating assay or forced degradation studies. • Tight release specifications may be a risk for tech transfer. • No appearance specification for DS. • Some critical raw materials sourced from China (cell culture basal medium) – could require change during TT. • HCP kit not qualified for host cell line (further development work needed for later phase). • Limited in-use compatibilities studies were performed. Additional studies could be needed.
Opportunities	**Threats**
• Cell culture titer on low end of industry standard. • Purification yield on low end of industry standard. • In-process bioburden sampling pre-filter in DS process.	• IND section 32S3 not shared. • No current GMP inventory of DS or DP, re-supply batch required. • Major changes between 200L and 2000L: cell line change and one column changed to bind-and-elute. Comparability study planned (release, extended, stability); protocol not shared. • Cell bank (200L scale cell line) characterization testing in accordance with ChP only. • 2000L batches will not have PUPSIT, risk to EU clinical use. • Bioburden specification is too wide. • No history with QP release. No US FDA or EU regulatory facility inspections.

Case Study #2

Case Study 2: IgG1 monoclonal antibody for multiple Phase 2 clinical trials in the US for new indications. Phase 1 clinical studies completed in Australia. Phase 2 clinical trials were on-going in US and China.

Documents reviewed: DS comparability, regulatory meeting minutes, IND Module 3

The therapeutic was initially developed and manufactured (Phase 1 material) at a CMO in China, then transferred to a larger CMO for Phase 2 clinical trial production. It was being considered for multiple indications in the U.S., with plans to initiate Phase 2 trials for these new targets.

Strengths	Weaknesses

• IND for phase 2 approved; do not appear to have been any non-binding CMC related topics.
• 1 prior successful tech transfer
• 2 chromatography step purification process (3 industry standard).
• Standard DS and DP manufacturing processes.
• Cell-based potency assay was developed and qualified and used for recent stability timepoints.
	• Full DP comparability not part of tech transfer evaluation.
	• Osmo specification is at upper limit of clinical acceptability, potential limits in future formulation work, potential clinical AE
	• Charge variant (IEF) thermal stability issue, need to understand cause and impact under stressed conditions
	• Cell culture titer is on the low end of industry standard (development planned).
	• Licenses required for cell line.
	• Future potential process modifications to consider:
	  • DS storage container (change from bottles to bags).
	  • High concentration formulation requires additional development and could be challenging (screening had high viscosity and osmolality)
	  • In-house proprietary cell culture medium

Opportunities	**Threats**
• Yield increase of 50% mentioned; outstanding question to evaluate feasibility. • Add parallelism evaluation to cell-based potency assay system suitability • Perform additional photostability following ICH Q1B guidelines	• Development timeline for autoinjector does not align with clinical trial timeline.

Case Study #3

Case Study 3: Bispecific antibody in pre-IND phase.

Documents reviewed: IND Module 3 sections (except 3.2.S.3 and A.1)

Documents reviewed: overview powerpoint, developability report, CMC summary, process flow diagram, draft DS specification, batch analysis data for one 500L drug substance batch.

This bispecific antibody was being considered for use in a Phase 1 US clinical trial. No IND had been filed yet. Due to lack of information available, much of the due diligence investigation occurred through Q&A with the CMO/asset owner.

Strengths	Weaknesses
• Good inventory of MCB and WCB • Cell culture titer moderate • Process scaled from 20L to 50L (only preliminary quality data available, but promising)	• Amount of information shared • Proposed timeline for IND submission does not align with stability study data availability • License fee for clinical and commercial batches
Opportunities	**Threats**
• Downstream purification process: atypical ProA resin with low binding capacity, intermediate depth filtration step (oftentimes designed out), somewhat atypical AEX resin	• None identified within the limited information

These three case studies illustrate the range of due diligence scopes involved in evaluating potential therapeutic assets. Each example focuses on assets manufactured in China, that are being considered by U.S. companies for use in U.S. or EU clinical trials. Transitioning these assets from China to U.S./EU is complex and requires careful risk mitigation to ensure the material meets regulatory expectations and quality standards.

As the industry evolves, more U.S. companies are seeking to acquire Chinese assets that have already demonstrated therapeutic potential. Purchasing an asset at an earlier stage of clinical development can save considerable time and cost on the path to commercialization. This approach is particularly appealing given the growing pace of innovation and cost efficiency within China's biopharma sector. A comprehensive CMC due diligence review is critical to evaluating such opportunities.

ABOUT

Syner-G

Syner-G brings extensive expertise in guiding biopharma companies through the complexities of global CMC due diligence. By leveraging our integrated services,including regulatory strategy, CMC development planning, quality and data integrity assessments, and technology transfer support, we help clients identify risks early and implement pragmatic solutions. Our experience with both U.S./EU and Asian markets allows us to bridge regulatory and cultural differences, ensuring that acquisition targets are positioned for successful transition and long-term commercial viability. In the context of the challenges outlined in this white paper, Syner-G provides the strategic insight and operational support necessary to mitigate risks, accelerate development, and maximize the value of biopharma investments.

REFERENCES

1. https://www.stifel.com/newsletters/investmentbanking/bal/marketing/healthcare/biopharma_timopler/2025/BiopharmaMarketUpdate_051925.pdf
2. Senior, M. “Biotech financing: divide and reset.” Nat Biotechnol 43, 1028–1034 (2025). https://doi.org/10.1038/s41587-025-02723-8
3. https://www.stifel.com/newsletters/investmentbanking/bal/marketing/healthcare/biopharma_timopler/2025/BiopharmaMarketUpdate_033125.pdf
4. Cundell, T. “Comparison between the Microbiological Testing Methods in 2015 Chinese Pharmacopeia and the United States” American Pharma. Rev. Sept (2018)
5. Zhang Sheng, LI Tiantian, QU Haibin. Comparison Study of the Content Uniformity Tests in Chinese Pharmacopoeia and United States Pharmacopeia Based on Monte Carlo Simulation[J]. Chinese Journal of Modern Applied Pharmacy, 2019, 36(19): 2405-2410. DOI: 10.13748/j.cnki.issn1007-7693.2019.19.008
6. Befir, F. “Comparing International Pharmacopoeias: Similarity and Differences.” Pharmacoeconomics 8 (2023):169.
7. Wiggins, J. “Harmonization Efforts by Pharmacopoeias and Regulatory Agencies”. BioPharm International Sept (2019).
8. Yujiro Kameyama, Maki Matsuhama, Chie Mizumaru, Rieko Saito, Tsuyoshi Ando, Seiko Miyazaki, Comparative Study of Pharmacopoeias in Japan, Europe, and the United States: Toward the Further Convergence of International Pharmacopoeial Standards, Chemical and Pharmaceutical Bulletin, 2019, Volume 67, Issue 12, Pages 1301-1313.
9. CDER Manual of Policies and Procedures, “Acceptability of Standards from Alternative Compendia (BP,EP,JP)” MAPP 5310.7 Rev.1
10. Petrelli F, Caraffa A, Scuri S, Grappasonni I, Magrini E, Cocchini A. The requirements for manufacturing highly active or sensitising drugs comparing Good Manufacturing Practices. Acta Biomed. 2019 May 23;90(2):288-299. doi: 10.23750/abm.v90i2.8340. PMID: 31125009; PMCID: PMC6776210.