Kingchem's Role in Clinical and Commercial Small-Molecule Supply

1. Executive Summary

Kingchem is a U.S.-founded and US majority owned, global CDMO with over 30 years of experience supplying clinical- and commercial-stage small molecules, specializing in challenging chemistries and both non-GMP and cGMP manufacturing for regulated pharmaceutical markets worldwide.

Founded in New Jersey in 1994, Kingchem brings more than **30 years of experience** in the fine chemicals and pharmaceutical industries, with a demonstrated track record of enabling reliable scale-up, regulatory readiness, and long-term supply continuity.

Key highlights include:

- **Late-stage and commercial focus:** More than **52% of Kingchem's pharmaceutical projects support Phase II–III and commercial drugs**, reflecting deep experience beyond early development.
- **Differentiated chemistry expertise:** Kingchem supports challenging chemistries across R&D through commercial manufacture that relatively few CDMOs offer, including **fluorination and phosgenation**.
- **cGMP manufacturing for regulated markets:** Clinical and commercial cGMP manufacturing is conducted at **Kingchem Laboratories in Milwaukee, Wisconsin**, which has been **recently audited by the FDA (no Form 483 observations) and PMDA**.
- **Trusted long-term partner:** Kingchem serves as a **priority vendor** to customers ranging from emerging biotechnology companies to large pharmaceutical companies, as well as other CDMOs around the world.

Kingchem's commitment to technical execution, responsiveness, and customer partnership has earned its reputation as a **reliable supplier of complex APIs, cGMP intermediates, and regulated starting materials (RSMs)**. Customers consistently cite Kingchem's ability to rapidly resolve technical challenges and deliver at scale where others struggle.

> *"I initially worked with a reputable, significantly more expensive European CDMO that struggled to get the process running even after three months. When I transferred the project to Kingchem, it was running successfully on the third reaction."*
>
> **— D. P., Customer Testimonial**

2. The Evolving Small-Molecule Supply Landscape

Despite sustained investment and innovation in biologics, small molecules continue to dominate pharmaceutical development and commercialization by volume. Over the past decade, small-molecule drugs have consistently represented the majority of annual regulatory approvals worldwide, accounting for approximately 65% of novel drug approvals in the United States.[1] This trend is driven by their well-understood development pathways, oral bioavailability, scalable manufacturing, and broad applicability across therapeutic areas. As a result, demand for reliable small-molecule manufacturing capacity remains strong across the industry.

At the same time, the **outsourcing model for small-molecule development and manufacture has continued to mature**, particularly for late-stage clinical and commercial programs. Pharmaceutical companies increasingly rely on external partners not only for early development activities, but also for **Phase II–III scale-up, process validation, and long-term commercial supply**. This shift reflects both internal capacity constraints and the recognition that experienced CDMOs can reduce technical risk, accelerate timelines, and support regulatory compliance across global markets.

Increasingly, sponsors are evaluating CDMOs based on **technical depth, regulatory maturity, and global operational footprint**, rather than geography alone. The ability to provide continuity from late-stage clinical supply into commercial manufacture—while maintaining consistent quality systems and regulatory readiness—has become a critical differentiator in CDMO selection.

The COVID-19 pandemic further reshaped expectations around **supply-chain resilience and continuity**. Sponsors now place greater emphasis on manufacturing partners that demonstrate robust quality systems, reliable raw-material sourcing, and the ability to maintain uninterrupted supply during periods of disruption. Geographic diversification, transparent change management, and proven operational execution have become essential criteria—particularly for commercial products with limited tolerance for supply interruption.

Within this evolving landscape, **CDMOs with strong technical teams and manufacturing footprints in Asia** have assumed an increasingly important role in small-molecule supply. Advances in chemistry expertise, quality systems, and regulatory experience have enabled these organizations to support not only development programs but also regulated late-stage and commercial supply for U.S., European, and global markets. When combined with competitive cost structures and deep technical capabilities, CDMOs like Kingchem with strong cGMP US footprint and with established Asian operations are valuable strategic partners of modern pharmaceutical supply teams.

Taken together, these trends underscore a clear reality: **small-molecule supply is no longer defined solely by early development support**, but by the ability to deliver scalable, compliant, and resilient manufacturing solutions across the full product lifecycle—from clinical development through commercial launch and beyond.

[1] *Source: U.S. Food and Drug Administration (2025), novel drug approvals data; analysis via Our World in Data.*

3. Clinical-to-Commercial Continuity: Why It Matters

As pharmaceutical programs advance from mid-stage development toward commercialization, **manufacturing continuity becomes a critical risk factor**. While changing suppliers in early development is often manageable, transitions at **Phase II or Phase III** significantly increase technical, regulatory, and operational complexity.

One of the primary risks of switching CDMOs late in development is the **loss of accumulated process knowledge**. Critical insights—such as route rationale, impurity controls, and scale-sensitive parameters—are often only partially captured in formal documentation. When this knowledge does not transfer cleanly, programs may experience extended redevelopment timelines, unexpected impurities, or reduced process robustness during scale-up.

Technology transfer itself frequently introduces disruption. Differences in equipment, raw material sourcing, and operational practices can lead to process drift, particularly for complex or tightly controlled chemistries. In late-stage programs, even minor deviations can delay pivotal trials or commercial launch.

Regulatory friction further compounds these risks. **DMF updates, comparability assessments, and additional audits** are commonly required when manufacturing responsibility changes, increasing the likelihood of regulatory questions and timeline delays. For products nearing commercialization, these activities can materially impact launch readiness.

Finally, late-stage supplier changes often drive **cost escalation rather than savings**. While unit pricing may appear favorable, indirect costs associated with redevelopment, revalidation, regulatory work, and internal resource diversion are frequently underestimated.

For these reasons, pharmaceutical companies increasingly prioritize CDMO partners capable of **seamless continuity from late-stage clinical supply through commercial manufacture**, reducing risk and supporting more predictable regulatory and commercial outcomes.

Hidden Costs of Changing CDMOs After Phase II

Commonly overlooked impacts of late-stage CDMO changes include:

- Re-optimization of synthetic routes and impurity controls
- Yield loss or batch failures during re-scale
- Delays from tech transfer and equipment mismatch
- additional DMF updates, audits, and regulatory questions
- Comparability studies or supplemental filings
- Internal resource drain across CMC, QA, and regulatory teams

What appears to be a supplier change often becomes a program reset.

4. Kingchem's Small-Molecule Capabilities at Scale

Kingchem supports the development and manufacturing of **small molecules across the full lifecycle**, from early route evaluation through validated commercial production. Kingchem's capabilities and capacities are designed to address the phase-appropriate technical and operational demands of clinical and commercial programs, where robustness, reproducibility, and regulatory readiness are essential.

Capabilities and Molecule Types Supported

Kingchem's experience spans a wide range of diverse small molecules, including:

- **Heterocyclic compounds**, multiple ring systems and functional group densities
- **Fluorinated molecules**, precise control of conditions and impurity profiles are critical
- **Liquid products or intermediate** high theoretical plate distillation to achieve purity
- **Cryogenic chemistries** multiple liquid nitrogen cooled reactors for broad capabilities
- **Chiral molecules**, defined stereochemical control and consistent product quality

These capabilities among others at Kingchem enable support for a broad range of complex synthetic routes commonly encountered in modern pharmaceutical pipelines.

Scale Range

Kingchem provides a scalable manufacturing platform supporting gram-scale for early development, kilogram-scale for clinical supply, to over 1,000 MT scales for commercial requirements. This flexibility in capacity strengthens business continuity.

Manufacturing Modes

Kingchem supports manufacturing modes tailored to program stage & technical needs:

- **Route scouting and optimization** to identify efficient, scalable synthetic pathways
- **Process development and scale-up**, with a focus on robustness and reproducibility
- **Late-stage process validation** to support regulatory filings & commercial readiness
- **Commercial campaign manufacturing**, consistent quality and long-term supply

Program strategies balance technical risk, cost efficiency, and regulatory expectations.

Analytical & Quality Infrastructure

Analytical and quality systems are integrated throughout Kingchem's development and manufacturing activities to support both clinical and commercial requirements including:

- **Analytical method development** and **optimization**
- **Impurity profiling** and **structure elucidation**
- **Method verification, validation** and **GMP release testing**

These capabilities support comprehensive process understanding, consistent product quality, and alignment with global regulatory standards.

5. Regulatory & Quality Infrastructure

Kingchem routinely supports products destined for regulated global markets, most often in the US and EU. Kingchem's regulatory and quality infrastructure is designed to support **late-stage clinical and commercial drug substance programs**, where compliance, inspection readiness, and data integrity are critical to successful regulatory outcomes.

Regulatory Experience & Inspections

- Successful audit experience with the FDA (Nov 2024, no 483's), PMDA (November 2024), & many large and small pharmaceutical companies
- Continued support for products supplied to regulated global markets
- Audit-ready facilities, systems, & documentation aligned with GMP expectations
- Experience supporting both clinical-stage & commercial drug substance supply

DMF Support & Regulatory Documentation

- Provision of all necessary technical, quality, & manufacturing information to enable customers to prepare successful Type II Drug Master Files (DMFs)
- Ongoing support for DMF maintenance, amendments, and lifecycle updates, in coordination with customer regulatory teams
- Cooperation to support regulatory inquiries, supplements, & change notifications
- Aligning process, analytical, & quality documents with customer regulatory strategies

Commercial Inspection Readiness

- Quality systems designed to support routine and for-cause inspections
- Reliable process validation, change management, & deviation handling procedures
- Experience supporting commercial manufacturing campaigns requiring consistency, reproducibility, and regulatory oversight

Data Integrity & Change Control

- Robust data integrity controls aligned with global GMP expectations
- Formal change control systems to evaluate and document process, raw material, and analytical changes
- Risk-based evaluation of change to support regulatory compliance & supply stability

Together, these regulatory and quality systems enable Kingchem to support customers through late-stage development and commercial manufacture with confidence. By maintaining inspection-ready operations, strong documentation practices, and disciplined change control, Kingchem helps reduce regulatory risk while supporting reliable drug substance supply for regulated markets.

6. Clinical-Stage Supply (Phase I–III)

Kingchem supports pharmaceutical programs across **Phase I through Phase III**, providing drug substance supply designed to meet the evolving technical, regulatory, and timeline demands of clinical development. These capabilities are structured to ensure continuity as programs advance toward late-stage development and commercialization.

Rapid Timelines for Toxicology and First-in-Human Supply

Kingchem supports accelerated timelines for **toxicology and first-in-human (FIH)** material through efficient route evaluation, rapid scale-up, and flexible manufacturing execution. This enables sponsors to meet critical early clinical milestones while maintaining alignment with downstream scalability and quality expectations.

Phase II/III Scale-Up and Comparability

As programs progress into Phase II and Phase III, Kingchem supports **process scale-up and refinement** with a focus on reproducibility, impurity control, and comparability. These activities are designed to preserve process understanding and minimize disruption as material demand increases and regulatory scrutiny intensifies.

Trusted Supplier of RSMs and Raw Materials to the Industry

In addition to supplying drug substance directly to sponsors, Kingchem routinely provides **regulated starting materials (RSMs) and raw materials (RMs)** to other CDMOs supporting late-stage clinical and commercial programs. Customers consistently cite Kingchem's **reliability, technical execution, and supply consistency** as key reasons for long-term partnerships. As a result, Kingchem is frequently designated as a **preferred supplier** within broader CDMO and pharmaceutical supply networks, supporting programs where continuity and commercial readiness are critical.

Why Late-Stage Programs Choose to Stay with Kingchem

- Proven ability to support scale-up from early clinical through late-stage supply
- Reduced risk from supplier changes during Phase II–III
- Established reliability for both drug substance and critical RSM supply
- Alignment with commercial manufacturing and regulatory expectations

7. Commercial Supply Case Snapshots

Case Snapshot A

- **Indication**: Antihistamine
- **Stage**: Commercial, Generic Drug
- **Scale**: 400-800 kg / year
- **Regions**: US, EU, etc
- **Client Challenge/ Background**: Multiple customers were interested in bringing back an older API for use in both human health and animal health as an antihistamine.
- **Kingchem role**: Updated 20-year-old ASMF, DMF, and VMF to current standards including performing: gap assessment; intermediate process validation; additional characterization testing added: FTIR, LC-MS, NMR, elemental analysis, TGA, DSC; forced degradation study; related study method verification; fate and purge study; additional impurity identification and standard synthesis; related substance method verification. Kingchem updated, filed, and holds the ASMF, DMF, and VMF. Kingchem now manufactures as the primary supplier of this API worldwide.

Case Snapshot B

- **Indication**: a kinase inhibitor approved to treat adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) as well as mantle cell lymphoma (MCL).
- **Stage**: Commercial, Innovator Branded Drug
- **Scale**: >10 MT
- **Regions**: Approved in over 50 countries globally (US, EU, etc)
- **Client Challenge/ Background**: Customer came to Kingchem for initial route development / optimization of their lead asset which was moving very quickly into and through early clinical trials. Kingchem served as the supplier of 2 key RSMs throughout clinical trials and commercial launch and remains a commercial supplier to this day.
- **Kingchem role:** Kingchem was involved in the initial route development / optimization early on while working with a smaller privately held biopharmaceutical company. That company was acquired by a large pharmaceutical company and Kingchem continued to serve as the main RSM supplier of the 2 key intermediates in the API synthesis. Kingchem has worked directly with the large pharmaceutical company to supply multiple downstream CDMOs tasked with manufacturing the API for different regions globally.

Case Snapshot C

- **Indication**: SARS-COV-2
- **Stage**: Commercial
- **Scale**: 3 MT/year
- **Region**: US, EU, China, Japan
- **Client Challenge/Background**: When Covid was active in 2020-21, our client quickly gained approval for the only API to treat the virus. Because of the magnitude of people to be treated, they needed metric tons of API quickly.
- **Kingchem role**: Another CMO was originally awarded PO but could not deliver RSM. Kingchem leveraged its global manufacturing capabilities to quickly back-integrate the RSM to ensure its timely delivery for the downstream intermediate to be made at our Wisconsin site. Kingchem leveraged our cryogenic capability in Wisconsin to make the downstream product at -15°C. Kingchem delivered the initial quantity ahead of schedule.

Case Snapshot D

- **Indication**: Oncology
- **Stage**: Phase 1/2
- **Scale**: Scaling RSM up to 200kg (currently)
- **Region**: US
- **Client Challenge/Background**: The client's program was at risk after a scale-up campaign of a Regulated Starting Material (RSM) at another CDMO failed. The existing route relied on a trifluoromethylation reagent that 1) Demonstrated poor compatibility with standard reactor materials of construction, resulting in significant equipment damage, 2) Generated problematic impurity profiles that complicated purification and regulatory positioning. With no viable manufacturing path forward and escalating technical risk, the program faced potential termination.
- **Kingchem's role**: Kingchem proposed a strategic route redesign centered on introducing the CF_3 functionality earlier in the synthesis using reliable SF_4-based fluorination chemistry. This approach offered: Improved materials compatibility, Greater control over impurity formation, A more robust and scalable synthetic pathway. An initial R&D program successfully demonstrated proof of concept. Following validation of technical feasibility, Kingchem executed a process development campaign and achieved initial scale-up to 3 kg then a 50 kg manufacturing campaign was successfully completed. Scale-up to 200 kg is ongoing to support Phase II clinical trials. Kingchem Established a scalable, reproducible, and regulatory-aligned manufacturing route. Kingchem is now developing a superior route from the RSM to the API in parallel.

Case Snapshot E

- **Indication**: Congestive Heart Failure in Chronic Kidney Disease
- **Stage**: Phase 3, Commercial
- **Scale**: >10MT (25, 30MT campaigns completed)
- **Region**: Worldwide
- **Client Challenge/Background**: An established EU-based pharma company has an API in phase 3 that was showing marked success. Given that 15% of the industrialized world has chronic kidney disease, the client was going to need tens of metric tons of API and corresponding RSM to service the global market. The client had one supplier that used a route for the RSM that used cyanide, posing an acute environmental risk.
- **Kingchem's role**: Kingchem was asked to make an analytical sample of the desired RSM. Kingchem does not use alkali cyanides at our plant for environmental and safety reasons; as such, Kingchem devised a 5-step process starting from a very common, readily available raw material to provide the desired RSM. Our route does not use cyanide, and is significantly less expensive than the client's other supplier, allowing us to offer a much more competitive price. Upon completion client verification of a 2g sample, Kingchem was asked to make 1100kg, which we did in a few months. The following year, we were asked to make 8.1MT. Kingchem invested workshops containing larger reactors to more easily accommodate multi-ton scale. In 2022, we completed 30MT, and in 2023 we completed 23MT. We will complete another 25MT campaign in 2027

Case Snapshot F

- **Indication**: Oncology
- **Stage**: Phase 1
- **Scale**: 10-20kg/year
- **Region**: West Coast, US
- **Client Challenge/Background**: Client had assured investors that they would file an IND on their kinase inhibitor in 12 months before any process R&D or CMC work had been completed. A new CMC director was hired to select a GMP CDMO to either push through material from an existing second-generation medicinal chemistry or devise a new route. Of 6 CDMOs evaluated, Kingchem was selected for our creativity in devising a new route, which was the client's only likely chance at being able to obtain GMP API in time for their proposed filing date
- **Kingchem role**: The existing route was 14 steps. This route included three Pd-mediated reactions, one that used stoichiometric organotin, and one potentially explosive step. It also needed 60kg of a raw material that cost $1800/kg to produce 1kg API. Furthermore, all steps required column chromatography purification. Kingchem devised a new and innovative route within 3 months which required only 7

steps and no chromatographic purification. We needed only 15kg of raw material that cost $250/kg per kg of API. The process hinged upon a very novel selective reaction that was unlikely to be devised by others. Furthermore, we were able to identify a proper RSM for the client. Due to the tight timelines, we were forced to begin production as soon as possible. We were able to produce 1.5kg cGMP API in 5 ½ months. The client was able to file their IND by the self-imposed deadline with the investment community. This allowed the client to raise $200,000,000 via capital markets and venture capital. Kingchem was subsequently awarded a second campaign the following year in which we improved the overall yield markedly, delivering over 4kg API from the same amount (15kg) of starting material.

8. Partnering Model

Kingchem's partnering approach is designed to support collaborations at any point in the development or product lifecycle while maintaining clarity, transparency, & predictability. Kingchem strives to align with needs & long-term supply objectives.

Flexible Engagement Model

Kingchem supports a range of engagement structures, from **single-project development support** to **long-term clinical and commercial supply partnerships**. Programs may begin with limited-scope development or manufacturing activities and expand as requirements evolve, without forcing unnecessary contractual complexity.

Transparency & Communication

Successful development programs depend on clarity, alignment, and proactive communication. Kingchem maintains defined technical and project leadership points of contact throughout each engagement, ensuring clear expectations around timelines, deliverables, risk mitigation, and change management. Our highly technical global business development team—most members holding PhDs in chemistry—enable direct & technically fluent dialogue from initial scoping through development and scale-up and minimizes surprises as programs advance from early phase to clinical & commercial.

Technology Transfer Philosophy

Kingchem approaches technology transfer as a **structured, collaborative process** focused on preserving process knowledge and ensuring reproducibility across scale. Transfers are supported by detailed documentation, cross-functional technical review, and early identification of scale- or site-dependent variables to reduce downstream risk.

Freedom-to-Operate–Respecting IP Model

Kingchem operates under a **freedom-to-operate–intellectual property model**, where:

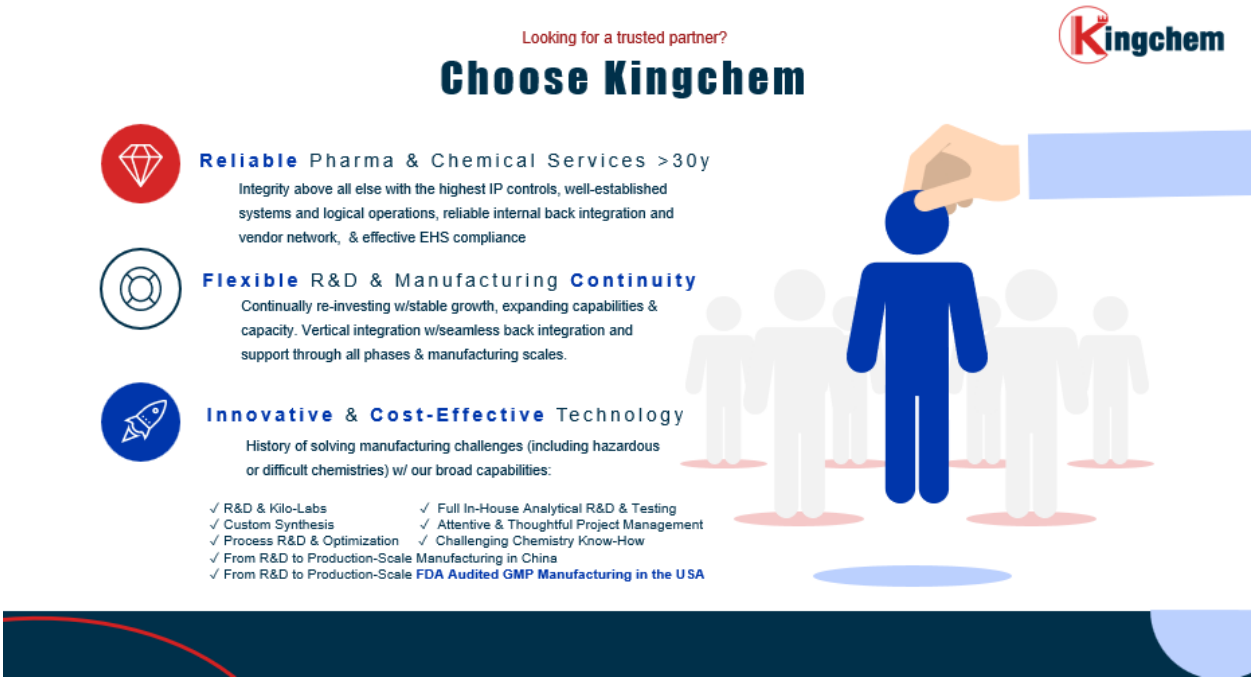
- **Customer-owned intellectual property is fully respected and protected**

- Process execution, optimization, and manufacturing are conducted **within the scope of customer-provided rights**
- Kingchem does not assert ownership over customer molecules or project related IP
- Confidentiality, data segregation, & contractual clarity are maintained in all programs

This model enables sponsors to advance programs with confidence that **IP ownership and regulatory control remain clearly defined**, while benefiting from Kingchem's technical expertise and manufacturing execution.

Cost Predictability

Cost structures are designed to support predictability across development and commercial stages. Early alignment on scope, scale assumptions, and change control reduces unplanned cost escalation and supports long-term planning for both clinical and commercial supply.



9. Looking Forward: Supporting the Next Wave of Small-Molecule Drugs

As pharmaceutical pipelines continue to evolve, the next generation of small-molecule drugs is increasingly characterized by **greater structural complexity, tighter impurity controls, and more demanding manufacturing requirements**. These trends reinforce

the importance of CDMO partners that not only support today's programs but also invest ahead of demand to enable future clinical and commercial success.

Kingchem has **invested over $30 million to date in the USA** and is actively expanding its infrastructure to support this next wave of small-molecule development and commercialization. At its GMP facility in **St. Francis (Milwaukee), Wisconsin**, Kingchem has acquired a neighboring property and is currently renovating the building to serve as a **dedicated Analytical R&D (AD) and Quality (QA/QC) facility**. This investment is designed to strengthen analytical development, quality oversight, and cross-functional integration in support of both clinical and commercial drug substance programs.

In parallel, Kingchem is planning the construction of a **future manufacturing facility on the newly acquired property**, with **millions allocated** toward this expansion. This planned build-out reflects a long-term commitment to increased manufacturing capacity, operational flexibility, and sustained support for regulated markets.

Kingchem is also actively expanding its **existing manufacturing footprint** through targeted equipment and utility upgrades. Planned investments include additional **large-capacity Hastelloy reactors** to support complex and corrosive chemistries, as well as a **second liquid nitrogen tank and heat exchanger with dedicated transfer lines** to expand cryogenic processing capabilities. Together, these enhancements are intended to support increasingly demanding reactions, improve scheduling flexibility, and relieve potential bottlenecks for late-stage and commercial programs.

Looking ahead, these investments position Kingchem to continue supporting:

- **Complex small molecules**, including chiral, heterocyclic compounds, and those requiring advanced capabilities (e.g., high temp. distillation or cryogenic conditions)
- **Diverse volume requirements**, spanning IND-enabling material through Phase I–III clinical supply and long-term commercial manufacture
- **Full lifecycle management**, from R&D and process development through validated commercial production and sustained supply

By aligning infrastructure investment with evolving scientific and regulatory demands, Kingchem is focused on remaining a **reliable, technically capable partner** for small-molecule programs as they progress from development into sustained commercial manufacture.

10. Conclusion

Kingchem's role in the pharmaceutical supply chain extends well beyond early development. With decades of experience supporting **late-stage clinical and commercial small-molecule programs**, Kingchem has demonstrated the technical

depth, operational reliability, and regulatory readiness required to support products as they advance toward—and remain in—commercial manufacture.

Across a wide range of molecule types, scales, and regulatory pathways, Kingchem has established a **proven track record of execution**. Its ability to support complex chemistries, scale efficiently from development through commercial campaigns, and maintain continuity of supply has made Kingchem a trusted partner for biopharmaceutical companies and global CDMOs alike.

Underpinning this track record is a **robust quality infrastructure, scalable manufacturing platform, and long-term commitment to continuity and investment**. Together, these capabilities position Kingchem to support current and future small-molecule programs with the consistency, compliance, and technical excellence required for success in regulated global markets.

Taken together, Kingchem's capabilities, infrastructure, and operating model enable **true continuity across the full small-molecule lifecycle**—from early development through commercial manufacture—without the disruption, risk, or loss of knowledge.