Lonza
Small Molecules

Executive Summary

Integrated API Services at Lonza Site in Nansha, China

Rhony Aufdenblatten
Executive Director, Head of Commercial EMEA, Small Molecules

Any pharmaceutical company looking to bring a promising compound to market has important decisions to make about the partners they choose to work with. Selecting a single contract development and manufacturing organisation (CDMO) offers significant advantages over contracting with different companies at the various stages of the development process. A partner that offers integrated services appropriate for all development stages will streamline the entire process. Advantages include cost savings and time savings coming from a holistic planning and project management approach. Furthermore, internal technology transfers needed for process scale up, for example, are simplified. The key to success will be identifying a CDMO that offers all the services required for the successful scale-up and manufacture of your active pharmaceutical ingredient. This is particularly important if specialist niche technologies or processes are required.

Lonza's site network is designed to provide drug substance, particle engineering and drug product services to biopharma companies around the globe. Phase-appropriate assets and capabilities are in place to support early and late phase clinical studies as well as commercial scale manufacturing. This site network operates to consistent global standards and best practices, and spans the key biopharmaceutical markets of Europe, the United States and China.

Lonza is constantly expanding its site in Nansha, China. It is now a premier example of a global manufacturing facility that offers a full range of API services including the handling of highly potent APIs for clinical supply. This summary provides background and information on the site's history, capabilities, and the recent investments that have made Nansha a leading CDMO choice for partners worldwide.

Nansha offering

The Nansha site, leverages expanded capabilities, a broad service offering, convenient location, and world-class expertise in API development and manufacturing. This will facilitate the rapid advancement of molecules across phases, benefiting biopharmaceutical clients from around the world.

Lonza-Nansha's infrastructure and equipment meet world-class standards for API development and production, and build on the company's 125 years of experience in chemical manufacturing. The Nansha facility first opened in 2003, having been planned and constructed by Lonza. Since then, the company has focused on providing state-of-the-art services that allow clients' small molecule compounds to move seamlessly from early-phase manufacturing through to large-scale commercial production, while meeting all necessary global quality and regulatory standards.

Nansha's highly trained professionals design flexible services and business models to meet each client's specific needs, ensuring timely streamlined development programs and cost effective commercial manufacturing. Global infrastructure and management expertise ensure supply chain security to customers throughout the world.

Nansha has a growing client base. Most are based in North America and Europe, and serve global markets. The strong alliances that have been built, allied to the success of the programs, has led to many repeat customers. Nansha's workforce continues to expand to meet the growing customer demand for API services, and there are currently more than 344 dedicated workers supporting all aspects of pharmaceutical API development and manufacturing. About 50 are involved in process development, with a further 109 in analytical development and quality control (AD/QC) and quality assurance (QA). Nearly half of the pharma staff have at least a bachelor's degree, and more than 5% hold a doctoral degree. More than half of the pharma staff have been working for Lonza for at least five years, and half of this group have been with the company for at least a decade.

Services span the development lifecycle

The Nansha site serves customers worldwide, and is fully integrated within Lonza's global development and manufacturing network. The services offered at Nansha span the entire API development lifecycle, from early stage feasibility studies through to product launch and commercial support.

This includes regulatory and process optimisation functions. All services are grounded in Lonza's core development principles: phase-appropriate processing, fit-for-purpose technology selection, manufacturability, scalability, process intensification, and reproducibility.

The site has multiple production lines of different sizes and containment levels, a variety of materials of construction to support a range of syntheses, and a broad chemical toolbox. This maximises flexibility. Nansha personnel work with customers to ensure they have access to the full scope of services required for a project to succeed. Some specific capabilities are described on the next page.

Preclinical and early-phase support
Nansha's flexible manufacturing operations and dedicated development laboratories and personnel enables an extensive range of chemistry, manufacturing, and controls (CMC) services to be offered. These include:

- Route scouting and feasibility studies
- Rapid, phase-appropriate manufacture of APIs for preclinical and clinical programs, in the gram to double-digit-kilogram ranges, incl. OEB 4 compounds
- Data generation and collection for use in future scaleup activities
- Impurity profile studies

To ensure the rapid progression of molecules, the site has kilogram-scale process trains with capacities of up to 50 L, multiple lines, and flexible setups that support both non-GMP and GMP processing.

Manufacturing can then be scaled up to the 250-L to 1000-L scale process trains in Nansha's small-scale plant which, again, can support non-GMP and GMP processing with multiple lines. The plant also has isolation equipment and a range of construction materials, as well as offering specialized technologies, such as reactions using carbon monoxide or hydrogen.

Recent investments
Lonza recently invested more than 20 million Swiss francs to expand mid-scale manufacturing capabilities at Nansha. This will ensure a smooth transition from small-scale to large-scale manufacture, enabling the rapid scale-up and accelerated development of customer compounds. Additions at the site include:

- Three 1,000-L GMP process trains with total reactor volumes of 12m^3
  (ten additional reactors with volumes ranging from 1,000-L to 1,500-L)
- Associated process equipment, including centrifuges, tray dryers, and filter dryers
- New development allowing operations in high containment and GMP HPAPI laboratories

In addition to bridging the gap between small-scale and large-scale manufacturing, these new mid-scale manufacturing assets increase the overall capacity of the site, and provide fit-for-purpose scale for customer programs. They also enable GMP processing of small-scale batches of HPAPIs to OEL > 100 ng/m^3. These molecules represent a growing proportion of the development pipeline.

Late-phase development
At the larger end of the scale, Nansha's manufacturing capabilities include three 10,000-L capacity lines to manufacture APIs for launch and commercial supply. Again, flexibility is maximized with multiple lines of different sizes, different materials of construction, and a broad chemical toolbox. Operations are fully embedded in state-of-the-art infrastructure addressing safety, health, and environmental issues, including the full integration of logistics and waste management. These GMP process trains are designed for all stages of the drug substance's commercial lifecycle, with batch sizes in the hundreds of kilograms.

Analytical/regulatory support
Lonza-Nansha personnel offer a suite of support services across the development lifecycle, including route scouting, process development and optimization, full analytical method development and evaluation, and process validation. Regulatory services are in place to support drug registration, dossier preparation, submission, and maintenance throughout the product's lifecycle.

Lonza-Nansha has an exemplary compliance record and inspection history with regulatory authorities, including the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), Japan's Pharmaceuticals and Medical Device Agency (PMDA), China's Center of Food and Drug Inspection (CFDI), and the Guandong Food and Drug Administration (GDFDA). This gives customers confidence that all products made on the site will meet global regulatory standards.

Customer support

Since the site was opened in 2003, Lonza-Nansha has established strong ties with its customers, resulting in numerous follow-on programs. Clients — whether large companies or smaller biotech firms — know that development programs will be tailored to their API and their specific program needs, and that partnering with Nansha will result in efficient development, project success, and cost savings. These example quotes from customers show why Lonza, and the Nansha team, has become a preferred partner.

"Very dedicated and efficient, goes the extra mile every time and delivers upon all requests."

"Excellent approach and laboratory experimentalists. Open to suggestions and willing to discuss the process in detail. The chemists thought deeply about problems and how to solve them."

"Display great understanding and ability to troubleshoot."

"On-site visits were welcomed and productive."

"We ... appreciated how efficiently development and validation were conducted, especially at the start of the pandemic ... we felt activities were maintained and results delivered in these tough times.

"Program Manager is always responsive and well informed of current project status. He does a fantastic job of organizing and prioritizing resources as needed for the program."

"The Program Manager for this project was excellent. She was definitely very competent, proactive, flexible, approachable, and available. Meetings were organized and efficient. She was a good communicator, had excellent follow up, and worked well with all team members."

"The project meeting was always well organized and prepared for, with appropriate functions represented. The actions were well documented and followed up."

"... Managed the process through three very different time zones with effectiveness and grace."

"Lonza is one of the few CMOs that provided a QA representative during weekly meeting. Our QA rep was approachable and responsive to requests. With this direct communication, many QA related items were quickly addressed and resolved. This was very much appreciated. Documentation was clear and accurate."

Summary

Lonza provides integrated drug substance and drug product development and manufacturing services to the biopharmaceutical industry through its global site network. Lonza-Nansha plays a critical role within this network, providing a full range of drug substance development and manufacturing services across early and late phase clinical studies through to commercial manufacturing. The site operates to world class standards with state-of-the-art infrastructure and capabilities designed for flexibility in meeting client needs on a program specific basis.

Multiple production lines and reactor sizes ensure phase-appropriate and optimized manufacturing for clinical and commercial supply. Recent investments in mid-scale capacity further expands Lonza-Nansha's capabilities to ensure that accelerated timelines can be met, while providing fit-for-purpose production capacity for customer molecules. Contained processing has also been added to support HPAPI development and manufacturing to OEL > 100 ng/m^3.

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