Lonza
Pharma & Biotech

Lonza's Continuing Investment in High Potency API: An Interview with Christian Dowdeswell

Question #1

What are the market drivers for highly potent drug substances?

Highly potent compounds are growing at double the rate of other small molecule active ingredients due to the industry's investment in increasingly targeted and more effective therapies. The increasing demand for highly potent compounds is concentrated among three therapeutic areas – chief among these is oncology, along with diabetes and autoimmune diseases. We track more than 1000 highly potent compounds in the pipeline today.

Question #2

What are Lonza's capabilities in developing and manufacturing HPAPI?

Custom development and manufacture of drug substances is core to Lonza, with highly potent drug substances being a key focus area. With more than 20 years' experience, we have a strong portfolio of HPAPI products across all development phases, scales and modalities, inclusive of commercial manufacturing. A large percentage of these programs are in the Oncology area.

Our capabilities at our HPAPI Center of Excellence (COE) in Visp, Switzerland are extensive and phase-appropriate across early development, clinical manufature and launch, and commercial-scale. Lonza HPAPI commercial process trains are amongst the largest in the world, and we support commercial programs from 1L to 10,000L scale, with OEL capabilities to 0.1 microgram per cubic meter. Our ability to support commercial programs at small scale increasingly comes into play given the market trend towards specialty meds with lower volume requirements.

In order to provide customers with the option of integrated solutions, we also provide particle engineering under containment at our sites in Monteggio, Switzerland (jet milling) and Bend (Oregon), US (spray drying). Additionally, we provide drug product development and manufacturing for HPAPI applications inclusive of sterile fill / finish and liquid / semi-solid formulations using either soft gel or liquid-filled hard capsule formats.

Question #3

What are the critical components for the safe and efficient manufacture of HPAPI?

It takes a lot more than having contained assets for safe, fast and robust HPAPI development and manufacture.

Lonza has developed extensive protocols and best practices in developing, scaling and manufacturing HPAPI products over the last two decades. The containment strategy is a critical element that must be integrated into the risk analysis process, as well as the technology transfer processes, both from external sources into our facilities as well as among internal assets. Unit operations must be well aligned with pre-defined primary and secondary containment strategies, achieved by performing gap analyses for each project.

The most sensitive unit operations are solid-charging containment, sampling, product unloading , cleaning, and waste management (liquids, solids and gases). Proven systems must be available for supporting containment throughout the manufacturing process as well as the QC laboratories. Process automation technology continues to advance and facilitate safe handling for HPAPI material.

You cannot depend on primary containment and infrastructure alone to provide safe handling of HPAPI. Our skilled team is the most critical factor in the operational performance of our HPAPI COE in Visp. Performance indicators for safety, quality and job performance – and ongoing job training – are critical for driving behaviors necessary to ensure safe and efficient operations.

Question #4

What are Lonza's capabilities in antibody drug conjugates?

ADC development and manufacture is another core focus for the company, and we offer integrated services at our Visp COE across the HPAPI small molecule payload, biologic targeting agent and their linkers. This relatively new class of compounds represents a major advance in the cancer treatment, inclusive of oral dosing, with nine commercial ADC products currently on the market, several ofwhich are produced by Lonza. We provide end-to-end

development for the engineered antibody inclusive of large molecule handling, purification and formulation, process optimization and scale-up, and GMP drug substance and drug product manufacture.

Our experience and capabilities in HPAPI are critical to this service offering. Lonza is a proven partner in the safe and efficient manufacture of ADC payloads, which require very strict containment regimes due to the different toxin platforms that exist, e.g. maytansines and auristatins, with new ones continually being developed. The challenge is to safely handle these compounds, which have different properties and toxicity levels, down to single nanogram containment. Demonstrating that processing equipment is clean to nano levels can dicate that platform-dedicated processing is utilized.

Question #5

Tell us about recent investments in HPAPI at Lonza

We have a continuum of investments in the HPAPI space over recent years, and I expect this aggressive expansion to continue going forward.

In 2018, we opened a dedicated production train for Clovis Oncology and their ovarian cancer drug Rubraca® (rucaparib). This new, state-of-the-art "monoplant" utilizes leading edge technologies including extensive automation and on-line analytical monitoring to enable real-time release testing. This approach facilitates process monitoring and consistency, giving the customer faster and more agile delivery, with optimized cost of goods.

Last year, we opened two new manufacturing suites capable of handling HPAPI with OEL down to 1ng/cubic meter. One of these HPAPI suites specifically supports a global biopharmaceutical partner by securing the long-term supply of required ADC payloads. The second suite is now utilized for similar HPAPI and payload development and manufacturing programs. The expansion also increased our capabilities to provide fully scalable HPAPI and ADC solutions from lab to commercialization, and help us meet the accelerated timelines that many drug programs in this category require.

Lonza has also completed another major expansion of HPAPI manufacturing capacity at Visp consisting of two new 4 cubic meter-scale, multi-purpose production lines. These new lines will support the long-term manufacturing agreement with AstraZeneca to deliver a number of drug products from across their portfolio, with additional capacity utilized to support other customers' HPAPI requirement.

Christian Dowdeswell is the Head of Commercial Development for Lonza Small Molecules, which encompasses Lonza's service offering to the pharmaceutical industry across drug substance, particle engineering and drug product. Christian has 25 years of experience in the CDMO business across a breadth of functions, both operational and commercial and is motivated by a desire to bring the next step change in service offering.

For more information on Lonza's high potency API capabilities, please visit our website.