Global Sterile Manufacturing and Lyophilization Capabilities of Large and Small Molecule Biologics – PCI Shows the Way

PCI's global manufacturing capabilities are in complex formulations, high potency, and lyophilization and your capabilities cover a broad range of injectables including nanoparticles, mRNA, mAbs, proteins, oligonucleotides, and other biologics across multiple delivery formats.

Q: Can you please share any specifics about PCI's sterile fill-finish achievements so far?

A: At the end of 2021, PCI Pharma Services acquired Lyophilization Services of New England, Inc. (LSNE), expanding PCI's breadth of services as a global CDMO, building on our expertise in specialty drug product manufacturing and packaging at both clinical and commercial scale. Already perceived as a pioneer in the packaging of biologics, the addition of LSNE cements PCI's reputation as a leading global CDMO, providing an integrated solution to clients across the entire drug product lifecycle from sterile development to commercialisation, meeting the demands of the ever-growing biologics market and bringing life-changing therapies to patients faster.

Our company culture, employees and processes are fully aligned to our strategy of focusing on our customers and the patients that they serve. Providing an all-encompassing streamlined sterile supply chain, many of our clients are leveraging the benefits of mitigating distribution and handling risks of their valuable biologic therapies as our sterile fill-finish manufacturing facilities are located within close proximity to our biotech packaging centres of excellence. Both of which, continue to grow with significant resource investments in terms of manufacturing and packaging processing technologies, in-house analytical laboratories and temperature-controlled storage and distribution capabilities.

Most recently, our sterile fill-finish and lyophilization facility in Madison, WI received its first commercial approval from the FDA. This now makes five commercially approved manufacturing facilities in our global network, with another four manufacturing sites coming online in the next year extending our global reach and capabilities further.

Q: How do you differentiate PCI Pharma Services from other CDMOs in the biologic market?

A: PCI continues to grow and evolve and as a fully integrated global CDMO, we are truly spanning the drug product lifecycle, connecting development and commercialisation, de-risking the supply chain and delivering true speed to market on behalf of our clients. We are a strategic partner and an integral part of the supply chain as the bridge between life-changing therapies and patients. Our expertise combined with innovative technologies means we deliver more than just a service, we are a trusted partner sharing an industry-leading depth and breadth of knowledge.

As part of the ongoing evolution of PCI and by listening to our clients, we are proud to introduce *speed***solutions**™ to the market. Providing the ultimate in solution flexibility and complete customer-centricity, speed-solutions combine value-added services and expertise, delivering an integrated approach to every client project, de-risking their supply chain by eliminating the need to transfer services such as packaging design and artwork to alternative suppliers as well as providing expert regulatory and clinical support services. Irrespective of where our clients enter the PCI world, they are supported with the option of an end-to-end solution both within specific phases of the product's lifecycle and across their development to commercialisation journey.

Differentiating what we do, PCI Pharma Services is commitment to and invests in digital transformation utilising innovative technology. One such platform is pci | bridge™ which complements our project management capabilities by creating efficient and uncomplicated ways of working together.

This industry-leading digital customer platform provides our client partners with real-time insights into their portfolio of work at our sites around the globe, unlocking productivity with access to real-time supply chain information and digital workflows.

Q: PCI's journey into sterile fill-finish and lyophilization is very prominent. What led to the decision to enter this field?

A: PCI Pharma Services has been an industry leader in providing specialist biologic packaging solutions from our global centres of excellence for many years. As a company driven by innovation and a wish to meet the needs of our client's, investing in sterile fill-finish manufacturing capacity and capabilities to complement our existing packaging expertise was a natural progression in our journey to deliver an integrated end-to-end solution. Our sterile development and manufacturing capabilities have been built upon the foundations of the recently acquired Lyophilization Services of New England, Inc. (LSNE) with significant further investments planned. As the name suggests, LSNE was an industry pioneer in the service provision of expert sterile fill-finish and lyophilization solutions, especially on the larger scale.

We continue to see a growing demand for lyophilization manufacturing technology in support of parenteral products. The boom of biologics versus small molecule pharmaceuticals has also impacted the traditional approach for sterile fill-finish services. Due to the stability challenges seen with many biologics, lyophilization is essential to improve product stability and reduce the complexity associated with cold chain logistics. Large molecule products such as monoclonal antibodies and fusion proteins are perfect examples of the challenges involved in liquid presentations that lack stability and require specialist cold chain packaging, storage and distribution solutions.

With over 25 years' experience in lyophilization and sterile fill-finish manufacturing and the specialised packaging of

biologics, PCI has developed industry leading technical expertise in the end-to-end processing of these often challenging and complex molecules. We truly support full product lifecycle management from formulation and lyophilization cycle development through clinical to commercial packaging, labelling, and distribution with phase appropriate processing and analytical/ microbiology testing.

Q: How will PCI respond to the increasing market demand for sterile fill-finish?

A: As part of our global strategy to increase our sterile fill-finish capabilities and capacities, and to address the ongoing global capacity shortage, PCI is continuing to build on its current capabilities to assist both existing and new clients in drug development and manufacturing.

With recent successful FDA inspections and larger scale manufacturing investments, both our Madison and Bedford facilities can provide flexible commercial solutions for our clients. At Madison, Wisconsin, we recently added an additional large-scale lyophilizer, now doubling our initial capacity and we are expanding our presence in New England with a $100m investment in a high-throughput commercial facility on our Bedford, New Hampshire campus. This investment supports the construction of a new 57,000ft^2 facility expansion, enhanced capabilities and increased capacity all using state-of-the-art isolator technology including high speed, large volume sterile fill-finish lines with the capacity to fill 400 vials per minute and auto-loading twin 40 square meter lyophilizers.

We have also further invested in industry leading robotic technology to complement our existing global sterile fill-finish capabilities. This investment comprises two robotic Cytiva Microcell Vial Filler units supporting clinical scale manufacture, one located in San Diego, California and one in Melbourne, Australia. In addition, a large-scale Cytiva SA25 Aseptic Filling Workstation, also located at our San Diego facility, allows us to deliver a seamless, end-to-end, sterile fill-finish solution across multiple dosage forms including vials, prefilled syringes and cartridges, with flexible small to large-scale production capabilities meeting the bespoke needs of our customers.

These advanced robotic technologies provide advanced methodologies of improving efficiency, reducing cost and increasing sterility assurance, and are gaining huge popularity for the primary filling of Ready to Use (RTU) containers such as vials, syringes and cartridges. They have successfully completed final stages of validation and are fully operational.

Q: What do you foresee for oligonucleotide and mRNA therapeutics?

A: Oligonucleotides and mRNAs have been the fastest growing market segment in the last 5 years. PCI has seen a tremendous rise in the number of our clients developing RNAi or siRNA products. With the clinical and commercial API of these drug types, as well as Oligonucleotide API, often extremely valuable and in very short supply, our clients benefit from our continuous drive for efficiency and focus on reducing line-loss, one of the major benefits of our robotic aseptic filling platforms.

We also work with a large number of lipid nanoparticle (LNP) formulations, a common formulation technology used in mRNA based therapeutics and vaccines. The processing and lyophilization of LNPs involves great expertise, as lipids in the LNP may be difficult to reconstitute without the experience of a lyophilization development specialist.

The development of new Covid-19 vaccines and the emergence of mRNA therapeutics has created a market constraint on access to critical raw materials and technical expertise. At PCI, we have over ten years' experience in the development and manufacture of mRNA therapies, and together with our biotech packaging centres of excellence, our end-to-end solutions enable our clients to move their mRNA therapeutic from development to commercialisation and beyond.

Q: What capabilities are needed for today's complex therapeutics?

A: Today's drug products are increasingly varied with new break-through technologies being developed across a wide range of therapeutic classes. CDMOs must therefore meet the challenge by providing clients with a high level of expertise, such as the ability to formulate and fill a variety of complex processes, with scalable development and manufacturing solutions delivered in a quality-driven, cost- and time-efficient manner.

At PCI, we have noticed an increased demand for the formulation of Lipid Nanoparticles (LNPs), aseptic ball milling, self-assembling polymer particles for controlled release products, and APIs that require organic solvent lyophilization. The technical transfer to GMP manufacture of these complex processes can often require multiple engineering runs and process-specific media fill validation programs.

Where possible, CDMOs should use disposable product contact manufacturing materials, firstly to reduce the risk of any potential cross contamination, and secondly to eliminate the need for time-consuming and expensive cleaning procedures and validations. The product lifecycle stage should also be considered to ensure that any processes or analytical methods are developed to the appropriate validation requirements. The engineering team should ensure the aseptic process is scalable and will maintain compliance through the development stage to commercial manufacture of the product, as these complex products require strong process engineering capabilities.

To meet the demands of a dynamic marketplace, CDMOs need to be collaborative and creative, with the ability to provide their clients with a tailored service. Whether it be for complex formulation process development, scale up, technology transfer or bespoke packaging of biologic drug products, this approach allows CDMOs to deliver flexible, agile and timely solutions to help bring life-changing therapies to patients.

Q: Can you share some innovation used for your Sterile Manufacturing Programmes?

A; Utilising the latest advancements of the robotic Microcell and SA25 technologies, PCI delivers flexible aseptic fill-finish solutions for both small and large-scale production across a variety of dosage forms including vials, prefilled syringes and cartridges for use

in auto-injectors, helping to meet our clients' scalable aseptic manufacturing needs, delivering products to patients safely and efficiently.

The addition of these innovative robotic aseptic fill-finish platforms at our San Diego, US and Australian facilities enhances our renowned global sterile and lyophilization capabilities. These advanced technologies not only expedite the filling process with automation, but enable us to pivot between filling multiple dosage formats, bringing even broader sterile fill-finish solutions to PCI clients across the entire drug product lifecycle allowing therapies to be brought market with increased speed and safety.

A key advantage of working with PCI is our high level of technical expertise. Current innovation in the vaccine space has placed tremendous strain on the manufacture of sterile filters and their supply chain, resulting in lead times of 50 weeks or longer in some geographies. A prime example of our client and innovative focus is when faced with filter procurement challenges, our in-house expert engineering team found the same membrane could be used in different filter housings – and then designed the interfacing gamma irradiated tubing sets to allow us to use the new filter within the customer's process following validation. In short, we think outside the box to keep supply chains moving to ensure we meet client and patient needs. We are proud to say that time and time again, as in this example, our creative teams turn problems on their heads and find solutions!

Q: PCI has the capability to support any stage of a "Sterile fill-finish project" Can you briefly explain to our readers, what process you follow when working with challenging formulation processes?

A: At PCI, we employee formulation subject matter experts across our global manufacturing network and ensure relevant expertise is assigned to every client project. We also boast the necessary state-of–the-art equipment and in-house analytical capabilities to support these more challenging formulation processes. Applying Quality by Design principles, we have the ability to establish critical product temperature attributes using tools such as scanning, DSCs and freeze dry microscopy to ensure project success. These in-house capabilities allow us to reduce suspensions, time release formulations, etc. to practice.

If there is a particularly challenging formulation, our network of scientists work together to develop the required solutions. From the handling of liposomes to designing 100% aseptic formulations, we have the experience and expertise to deliver life-changing therapies to patients.

Q: PCI are experts in packaging capabilities relating to biologically derived products. Can you explain what the current market demand in this area is, and how you are meeting industry needs?

A: With the pharmaceutical industry's growing pipeline of biologics, the need for technically advanced manufacturing and specialised packaging support has grown considerably. Committed to being a market leader in the packaging of biologic products for our global clients, our goal is to help our customers safely and efficiently bring their novel medications to patients. With more than five decades in the healthcare services business, 20 plus years of which have been in biologics, and delivering over 90 successful product launches each year, PCI has developed industry leading technical expertise in the end-to-end processing of these often challenging and complex molecules. Our industry insights and expertise enable us to provide biologic packaging solutions that truly differentiate products.

Driven by innovation and the trend towards self-administration and patient-centricity, we offer advanced, flexible packaging solutions for a diverse portfolio of conventional and specialty injectable drug delivery devices. We have the flexible scalability to handle the dynamic volumes of biopharmaceutical therapies, whether large or small, from niche personalised medicines to large-volume treatments.

Complementing our sterile manufacturing investments, we continue to expand our European, North American and UK biotech Centers of Excellence for clinical and commercial packaging. These state of the art facilities are equipped with advanced packaging technologies for the labelling and assembly of vials, cartridges, standard prefilled syringes, advanced safety syringes, autoinjector and pen devices complete with integrated top-load Dividella cartoning and in-line serialisation.

Partnerships with leading suppliers such as Dividella, Groninger, Marchesini Group and Syntegon (formerly Bosch Packaging Technology) and investments in the latest high-speed automatic packaging technologies allows for greater flexibility in serving our customers across their clinical and commercial supply-chain requirements for global clinical trials, product launches, global ramp-up, or ongoing market supply.

Meeting the dynamic demands of the marketplace whether it be for sterile process development, scale up, technology transfer or bespoke packaging of biologic drug products, at PCI we provide a collaborative, creative and tailored approach to deliver upon our mission of being the bridge between life-changing therapies and patients. By combining our expertise in sterile fill-finish manufacturing with specialist biologic packaging, labelling and cold chain distribution provides a valuable end-to-end solution, simplifying the supply chain while delivering time and cost efficiencies.

Shawn Cain

Shawn Cain is currently the SVP at PCI Pharma Services, a pharmaceutical full service CDMO. Mr. Cain has over thirty years of experience in combining process engineering and project management to direct the development and manufacture of sterile pharmaceuticals, cell-based biologics, and medical devices. Most recently he was the COO of LSNE, which was acquired by PCI. Mr. Cain also worked at Organogenesis and was the Director of Operations for another pharmaceutical CDMO, Formatech, Inc. Prior to that, he was Interim President and Chief Executive Officer of Arbios Systems, Inc. Previously, Mr. Cain was employed at Becton Dickinson's Biologics Business. Mr. Cain was also the Vice President of Operations for Circe Biomedical, Inc., where he led the development of the bioartificial liver technology. Mr. Cain holds six patents, received his M.S. degree in Biological Sciences from the University of Massachusetts and a B.S. in Biological Sciences from Northeastern University.