INDUSTRY LEADER INSIGHT

PHARMACEUTICS KNOW-HOW AND SERVICE EXCELLENCE **TO RE-ENERGIZE A CDMO**

→ BY **KURT R. NIELSEN, Ph.D.,** PHARMACEUTICS INTERNATIONAL, INC. (PII)

Pharmaceutics International, Inc., otherwise known as Pii, is reemerging as a customer-focused market-leading contract development and manufacturing organization (CDMO). The company is undergoing a transformation, returning to our deep and established roots as a provider of contract development and manufacturing services and leveraging our unparalleled scientific insight and deep product knowledge — as well as the legacy of our proactive commitment to quality — to provide flexible, customized solutions to partners looking to accelerate projects through development and on to the sustainable supply of commercially approved high-quality dosage forms for the patients we ultimately serve. We are dedicated to serving our People, Products, and Patients.

ROOTS IN CONTRACT DEVELOPMENT SERVICE WITH A FOUNDATION IN PRODUCT DEVELOPMENT AND PHARMACEUTICS KNOW-HOW™

Pharmaceutics International, Inc. (Pii) was initially founded in 1994 as a services organization, helping customers solve formulation, analytical development, and manufacturing process challenges. Gradually, the company adopted a dual strategy of services and proprietary products, relentlessly utilizing and leveraging our deep understanding of pharmaceutical sciences and regulatory approval pathways across a range of industry segments and ultimately delivering new affordable treatments to patients, providers, and physicians. The first product we codeveloped was for an orphan disease for which we provided clinical trial material (CTM) supply under a physician's investigational new drug (IND) and commercial supply following U.S. FDA approval, and we have focused on such scale and types of products ever since.

WITH MORE THAN 400 DEVELOPMENT PROGRAMS COMPLETED, **PII IS A LEADER IN PHARMACEUTICAL PRODUCT DEVELOPMENT, TECHNOLOGY TRANSFER, AND PRODUCT SUPPLY.**

During our history, we ventured into complex specialty generics and branded products by developing our own products and securing marketing partners to sell our products through retail and hospital channels. We learned to move quickly and reliably through product selection, R&D, and commercial supply, and recognized the need to diversify our portfolio to include both partnered and self-funded R&D programs. We learned the importance of routinely combining innovation, speed, and entrepreneurship, while at the same time deepening our appreciation for the ever increasing need to bring affordable, effective, and safe medicines to patients. We are now able to utilize this unique experience, enabling us to be a best-in-class CDMO and partner. We have "walked in the shoes" of our partners and are a uniquely qualified CDMO that understands product success. Our ultimate goal is for our partners to view Pii as a natural extension of their development operations and commercial supply chain – to sustainably function as a trusted and reliable strategic partner.

Backed by our unique experiences and our belief in the fundamental purpose of the pharmaceutical industry – to enhance the lives of patients worldwide – we determined that we could have the most significant impact by returning solely to our CDMO foundation, helping partners navigate the product development, approval, and commercialization continuum. Joining the company at the beginning of 2019 – Pii's 25th year – we began our journey to accelerate our transformation, reset our strategy and vision, and ensure a successful transformation into an industry-leading CDMO for our next 25 years.

PHARMACEUTICS KNOW-HOW™

The bricks of Pii's foundation are made from our expertise in pharmaceutics. We are an entrepreneurial science-driven CDMO providing dosage form development, technology transfer, and cGMP manufacturing services to small, medium, and large pharmaceutical companies. For over 25 years, we have provided scientific insight and depth of product development knowledge, including regulatory affairs strategy, while continually supplying high-quality products for the benefit of the patients we ultimately serve.

With more than 400 development programs completed, Pii is a leader in pharmaceutical product development, technology transfer, and product supply. Our scientific team has extensive experience working with drug substances representing a range of physicochemical characteristics and overcoming their associated challenges. Our specialized capabilities, multiproduct facilities, and knowledge base allow us to work with DEA-controlled substances, cytotoxic and potent compounds, and hormones, to develop complex dosage forms, and to support a wide array of manufacturing processes for aseptic and non-aseptic products.

With our unique synthesis of pharmaceutics experience, service excellence, and entrepreneurial adaptability, we are able to say "yes" to customers who have heard "no" too many times (for too many reasons) from other, often larger CDMOs. We bring our wide spectrum of core competencies together in a unique offering that enables us to provide solutions tailored to each of our valued customers. No matter what the program or its inherent challenges, we never say "no" – we say, "let's find a solution together."

FOCUS ON SERVICE EXCELLENCE

One key change we have made over the last year was intensifying our focus on quality and service excellence. It is essential to understand the needs, aspirations, and stakeholder demands of our partners, which are not always obvious, to ascertain the best use of our expansive core offerings and deliver the optimum solutions, which are also not always straightforward. Quality is embedded at every level of Pii, and we have not only established a quality organization, but continually nurture a proactive quality culture in which everyone strives to anticipate the ever-emerging *current* in cGMP while exceeding cGMP guidelines at every stage. While we pride ourselves on our science-based approach to product, formulation, and analytical development, we also realize that we need to go beyond the science to understand the challenges that our customers face.

We are working every day and with every partner to deliver platinum CDMO service by seeking to truly understand "What are our partners' stated and underlying expectations for service excellence, and what can we do to exceed both sets of expectations?" while at the same time asking ourselves, "Are we truly understanding what our customers really need in each step and stage of an R&D project or commercial product launch and supply?" As we work together with our partners to answer these questions with balanced scorecards and soliciting frequent feedback, we also know from our own experiences in specialty and branded products that predictable supply and on-time delivery is critical, yet uncertainty and risk are often quite common in technology transfer and development. As such, attributes like flexibility, adaptability, agility, and good communication are fundamental to delivering platinum CDMO service.

As one example, whenever we hear from a partner, we respond in some way within two hours. In some cases, it may only be to say that we received the message and will provide a detailed response the next day. As a service provider, one of the most essential tasks is to make sure customers know that you hear their requests and are working on their issues.

Our quality systems – driven by process performance and product quality monitoring, corrective action and preventative action (CAPA), change management, and internal, customer, and regulatory inspections – are designed to provide our customers with consistent product quality through thoughtful quality planning, control, and measurement. Every project begins with

the establishment of mutually agreed key performance indicators (KPIs) in consultation with the partner, and the performance data are analyzed and reviewed monthly by our Quality Council to ensure that we exceed cGMP requirements and our partners' expectations at every step in the program's life cycle. While no provider can guarantee that no challenges will arise, Pii makes sure – using KPIs, scorecards, and open and transparent lines of communication – that we proactively address potential program and delivery issues before they become problematic.

Our service excellence never requires a commitment from our partners that a given program will mature into commercial production with us. Companies can partner with Pii to develop a robust formula and process, but if the commercial demand does not ultimately align, we support our partner's technology transfer strategy from our facility.

EXPANDING CAPABILITIES

Since 1994, Pharmaceutics International has grown from 12 employees to over 275 highly skilled staff members across all functions, with over 360,000 square feet of state-of-the-art manufacturing, warehouse, and laboratory space conveniently located near Baltimore in Hunt Valley, Maryland. Recently, in response to a growing need we observed among our partners, we expanded our aseptic capabilities to provide lyophilization cycle development services, as well as CTM fill/finish supply, with an innovative robotic automated filling line.

Using our integrated preformulation and lyophilization cycle development capabilities, we can support partners in the early-phase development of this technically challenging pharmaceutical manufacturing process, providing them with a solution that can be readily transferred and scaled up for CTM or commercial manufacturing.

We expanded our already substantial aseptic fill/finish capacities and capabilities with the addition of the innovative, fully integrated and robotic GENiSYS® R filling line from AST (Automated Systems of Tacoma, LLC) that can support small to medium-scale production of syringes, vials, and cartridges. Pre-sterilized components are fed into the system, and final products – including small molecule parenterals and biologics – are thus produced. The highly efficient, flexible, and adaptable filling line with electronic batch records can be used to produce anywhere from a few hundred to 50,000 vials per day of finished products with extremely high yields. We recognize the value of our partners' precious early-phase development materials and can minimize the amount required for a given program to make the most of their resources.

ONGOING INVESTMENT

Pii continuously adds offerings at the small to medium scales for clinical trial and commercial manufacturing for both oral and parenteral drug delivery technologies. In some cases, investments are made to directly support a partner with a specific problem – including issues with developing a unique drug delivery technology, potency, toxicity, solubility, or bioavailability of their molecules. Pii will also in-license a delivery technology that is impractical for a single partner to invest in, but is strategic for multiple partners with products in different therapeutic categories. Lastly, to share risk and maximize return on invested capital (ROIC) for our partners, we coinvest for dedicated filling lines, suites, and facilities (e.g., "plant-in-a-plant").

As we find ways to look farther into the future to anticipate the needs of our partners, we are always monitoring developments in the industry to identify opportunities for proactive investment in new technologies. We not only look at new molecules in clinical development, but also what trends are developing in the patent literature regarding new chemical entities (NCEs), and what issues are receiving regular coverage in the scientific literature and trade journals. It would not be practical to try to build new capabilities or capacity at the point when the demand already exists – to ensure that we have the capabilities and capacity online when they are needed, it is critical that we examine trends as close to their origin as possible to see what is coming over the horizon, not only in three years but also in 10. Ideally, we look for trends involving the unique confluence of different Pii capabilities, such as potent compounds that require lyophilization (e.g., oncolytics and antibody–drug conjugates (ADCs)), reduced dosing frequencies through the use

Meet Pii

With more than 400 development programs, Pii's highly trained scientific team has extensive experience working with a variety of drug substances with a range of physicochemical characteristics. We offer:

- preformulation testing,
- dosage form development,
- analytical development and testing,
- clinical trial material manufacturing,
- commercial manufacturing, and
- clinical packaging and distribution.

Pii's cGMP facilities are state-of-the-art and contain over 70 manufacturing rooms, as well as containment suites for handling high potency compounds and hormones, dedicated manufacturing suites for soft gels and injectables, a formulation development center, and analytical laboratories. Pii's facilities have been inspected by the FDA, EMA, and MHRA and are registered with the DEA (schedules I–V).

We understand that designing an efficient drug delivery system cannot be successful with a "one size fits all" approach. It is critical to tailor the development process to the characteristics of the API and the development goals of the client. Pii strives to be a reliable and flexible partner by responding and adapting to the individual needs of each client. From project kick-off through close-out, our focus is to exceed client expectations by providing a high level of customer service.

All of our efforts are supported by our extensive pharmaceutics know-how, which includes formulation, process and manufacturing, commercial quality, process management, and regulatory expertise.

of depot or long-acting injectables, monoclonal antibodies (mAbs), RNA and protein therapeutics, or increasing the rate and extent of oral drug delivery via a softgel or liquid-filled gelatin capsule. The challenge is to determine how best to integrate our core capabilities to provide optimum solutions as fast as possible for the ever-expanding universe of drugs and biologics.

Part of our success will be achieved by moving up the technology adoption curve. Indeed, 10 years from now, we project that Pii will be an early adopter of technology and an investor in leading-edge solutions, making it possible for us to contribute to the pharmaceutical ecosystem at a higher level.

WORKING *FAST* ON SMALL TO MEDIUM SCALE

While many CDMOs appropriately focus on larger-scale projects, small- to medium-scale processes have been in our DNA for over 25 years. By focusing on the small to medium scale for drugs and biologics, we can provide a unique combination of agility, flexibility, and responsiveness; for example, Pii can complete the production of partner early clinical batches within 90 days of receiving all of the components and materials.

For R&D and technology transfer projects, our agility and responsiveness make us an ideal fit for smaller companies that have limitations on internal staff. Often, they have small, energetic, highly motivated, and agile scientific teams that really engage in the collaboration process and are empowered to evaluate the data and drive the decision-making process. These firms are clear about where they are going and the goals they need to achieve. When problems or hurdles inevitably arise, only a select few are involved in making decisions about how to move forward.

Pii is, ultimately, that same type of agile entrepreneurial company. As the President and CEO, I am directly involved in partner meetings, weekly R&D reviews, and daily stand-ups and make it a point to be readily accessible. We respond rapidly to unexpected events, whether it is a change in the manufacturing plan or an unanticipated increase in demand for a new product. While we can serve any kind of partner organization, those that can benefit the most from a relationship with Pii are typically structured the same way and have the same type of focus on agility and entrepreneurial action.

On the commercial side, we align best with partners that have one – or just a few – products and are looking to enter the market in the most efficient manner possible. Pii can help them figure out how to expedite approvals. We also provide guidance on developmental and regulatory strategies that will ensure that approval applications are sufficiently flexible for a range of commercialization scenarios. This approach is particularly beneficial for companies with little available working capital that need to start slow and be able to respond quickly, from a regulatory and supply chain standpoint, if demand takes off faster than expected.

PHARMA REGULATORY AFFAIRS EXPERTISE

Our Regulatory Affairs (RA) staff has the experience often associated with much larger integrated pharmaceutical companies. From the moment a project comes to us, our world-class RA department advises our partners on enabling strategies, approval cycle time reductions, and where common and uncommon issues and risks might occur, not just with respect to manufacturing and supply, but also with FDA approval of their applications.

As Pii works through the product development stages, we are consistently building in characteristics that will increase the likelihood of first cycle approval and reduce timelines for post-approval regulatory moves. This approach leads to a better overall strategy and the delivery of products on time, and with the flexibility to quickly adapt the scale of manufacturing to meet changes in market demand.

IN THE SHOES OF OUR PARTNERS

As a CDMO that has had experience developing and manufacturing our own products, we have stood in our partners' shoes. This additional perspective adds significant value to the services Pii provides. This "been there and done that" experience of Pii is particularly important when it comes to development scale-up and technology transfer. We seek to learn as much as possible about our partners' timing constraints, including why these constraints exist. We also investigate our partners' working capital strengths and challenges and determine how we might be able to provide solutions. This empathy, supported by over 25 years of extensive experience tackling issues related to tech transfer and scale-up, enables us to rapidly provide solutions so that our partners can bring their life-changing and life-saving medicines to the market more rapidly than they otherwise could.

Perhaps most importantly, we continue to be engaged in and inspired by the work that we do. We know there is so much more at stake than any one particular activity we are pursuing at the moment. Our work isn't about just one method or one formulation. The products we help to produce – provided that they meet regulatory requirements and fill an unmet medical need – will make a real difference for people. That is an important part of the Pii legacy – Products, Partners, and Patients. P

ABOUT THE AUTHOR

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Dr. Kurt Nielsen joined Pii in 2019 as President and CEO. He is a seasoned pharmaceutical executive with over 20 years of diverse experience, most recently as the President of Lupin Somerset, responsible for all their generic and branded products. Prior to Lupin, he held the post of Vice President, U.S. Development, Portfolio and Launch Management at Sandoz Inc., where he was accountable for the U.S. development of generic, OTC, and specialty brand products. Dr. Nielsen has also held positions at Catalent, where he was Senior Vice President of R&D and Chief Technology Officer, and URL Pharma where he was the Executive Vice President, Pharmaceuticals.

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