Drug Development & Delivery

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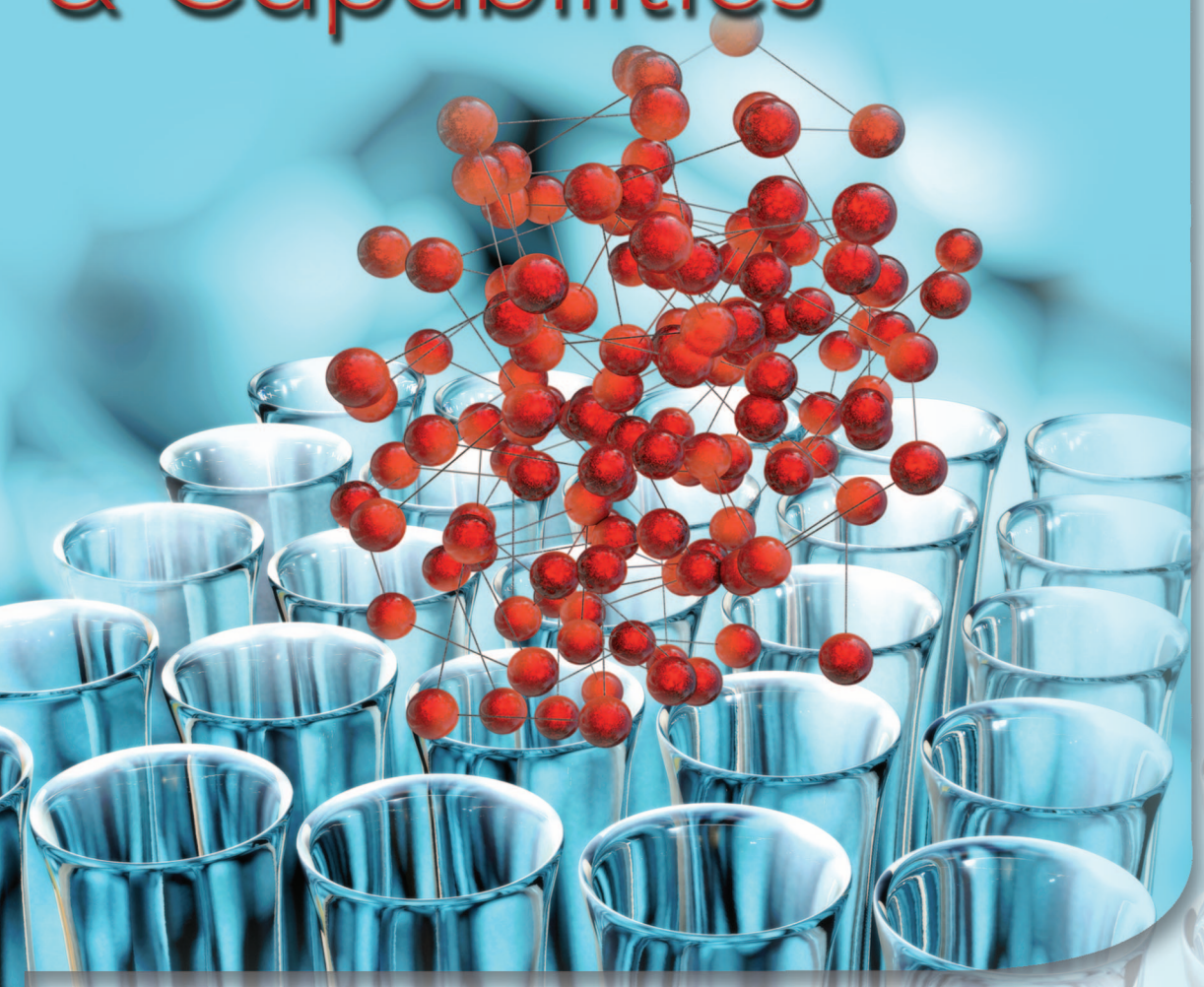
Company Profiles & Capabilities



The Science & Business of Pharmaceutical and Biological Drug Development

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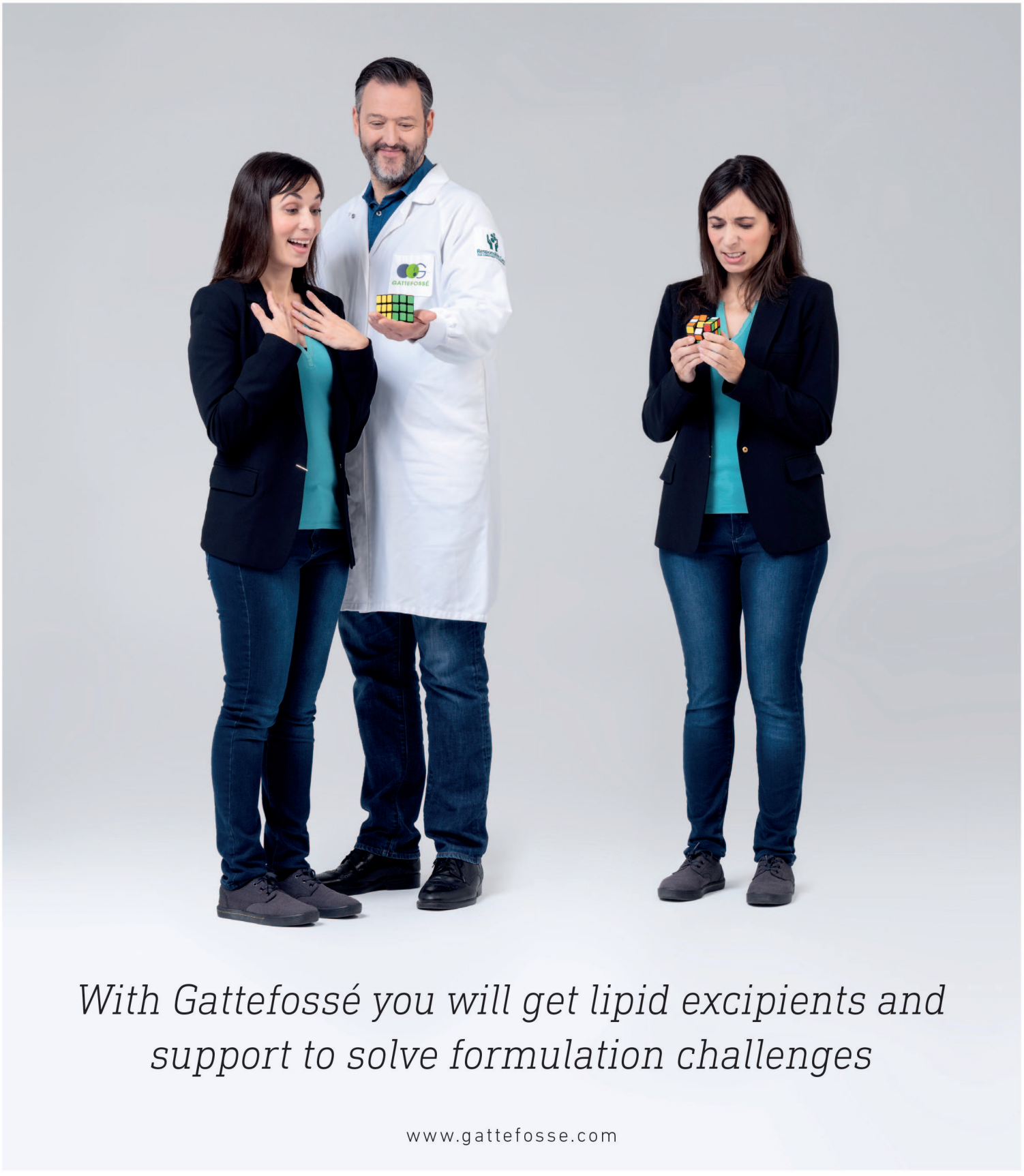
INTERVIEW WITH YOURWAY'S SENIOR VP MARKETING & BD

LEANDRO MOREIRA



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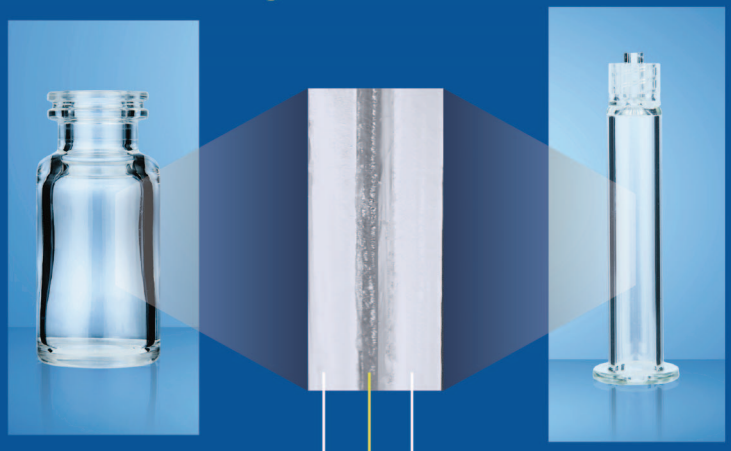

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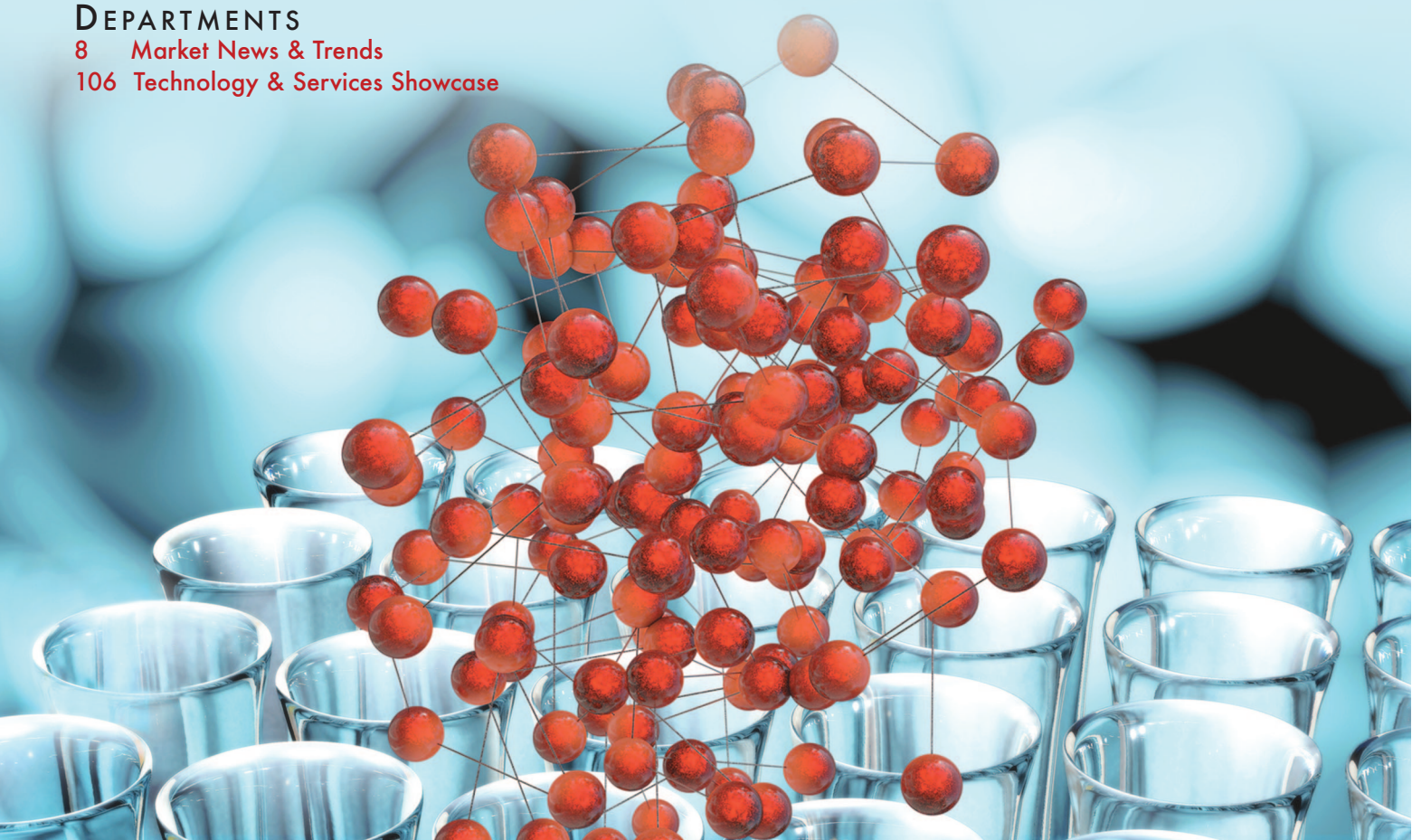

Real World Challenges
in *Drug Delivery and Formulation*

The Objective

Need to understand the changing dynamics of clinical-stage pipelines by indication, molecule type and most advanced phase to present to senior management

The Challenge

How do I obtain this information in a format that will allow me to quickly evaluate overall trends in pharmaceutical development?

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Croda Enters Contract With Pfizer for Innovative Delivery System for COVID-19 Vaccine

Croda International Plc, the speciality chemical company that uses smart science to create high-performance ingredients and technologies that improve lives, recently announced it has entered into an agreement with Pfizer Inc. to supply novel excipients used in the manufacture of a COVID-19 vaccine candidate. The contract with Pfizer runs for 5 years and awards Croda an initial supply contract for four component excipients used in the production of the vaccine candidate for the first 3 years of the contract. Demand remains subject to relevant approvals.

Croda's recently acquired subsidiary, Avanti Polar Lipids, Inc. (Avanti), specializes in the development and production of high-purity lipids, to produce research and clinical trial quantities of excipients in order to stabilize formulations and enable delivery into the body by parenteral mechanism (injection) for drug and vaccine applications. Croda's existing health care business has a 20-year track record in developing IP-rich, innovative technologies for drug delivery systems for the pharmaceutical industry and has been working with Avanti, prior to and since its acquisition by Croda, to refine the complex processes involved in achieving the volumes of high-purity excipients required by its pharmaceutical customers. Croda has reprioritized investment, resources, and other projects across the Group over the past few months to focus on the delivery of this project.

Commenting on the new contract, Steve Foots, Chief Executive Officer, said "I'm very proud of Croda's involvement in the battle to fight the most significant pandemic that we have seen in a generation. The application of our innovative capabilities is testament to the strong progress we have made to create industry-leading drug delivery systems, focused on developing speciality excipients and adjuvants to improve the effectiveness and stability of complex drug actives and vaccines. It is another example of why our Purpose – Smart Science to Improve Lives – sits at the heart of our strategy and will continue to drive our priorities and ambitions in the years ahead."

Part of the Life Sciences business, Croda Health Care is a long-established supplier of choice to the pharmaceutical, vaccine adjuvant, nutritional, consumer and animal health markets. With a wide and constantly growing range of products, including high performance excipients, vaccine adjuvants and solubilisers, the Health Care portfolio is unsurpassed in excellence. This offering, along with our in-house formulation expertise, helps Croda Health Care meet the most stringent customer demands and future health and wellbeing needs.

Established in 1925, Croda is the name behind sustainable, high performance ingredients and technologies in some of the world's most successful brands: creating, making, and selling speciality chemicals that are relied on by industries and consumers everywhere. For more information, visit www.croda.com.

Axovant Gene Therapies Announces FDA Clearance of IND for Gene Therapy

Axovant Gene Therapies Ltd. recently announced the US FDA has lifted its clinical hold and cleared the Investigational New Drug (IND) Application to initiate a registrational study of AXO-AAV-GM2 gene therapy to treat patients with Tay-Sachs disease and Sandhoff disease. AXO-AAV-GM2 is the first investigational gene therapy to achieve IND clearance for Tay-Sachs and Sandhoff diseases. The company received a letter from the FDA indicating that it has satisfactorily addressed all issues related to the clinical hold.

Axovant aims to advance the program through strategic partnerships with leading research organizations. The Company recently announced a partnership with Viralgen, an AskBio subsidiary, to support AAV-based vector manufacturing of clinical trial material for the registrational study. Additionally, through an existing genetic testing collaboration with Invitae, ongoing partnership with GM2 gangliosidosis patient groups, and collaboration with leading academic researchers at the University of Massachusetts Medical School and Massachusetts General Hospital, Axovant expects to begin patient identification and site startup activities in preparation for dosing children in the planned clinical study.

AXO-AAV-GM2 is an investigational gene therapy for Tay-Sachs and Sandhoff diseases, which are rare, monogenic neurodegenerative lysosomal storage disorders caused by mutations in the genes that encode β-Hexosaminidase A, HEXA and HEXB. Children affected by Tay-Sachs and Sandhoff diseases suffer from a progressively debilitating disease course and reduced life expectancy. AXO-AAV-GM2 delivers two vectors encoding the HEXA and HEXB genes directly to the central nervous system to produce a fully functional β-Hexosaminidase A enzyme. In 2019, clinical evidence from two patients under an investigator-initiated study found that treatment with AXO-AAV-GM2 was generally well-tolerated and associated with improved bioactivity outcomes. In addition, the data demonstrated the attainment of normal neurodevelopmental milestones and improvement in myelination. AXO-AAV-GM2 has been granted Orphan Drug and Rare Pediatric Disease Designation by the FDA.

The study will enroll both infantile and juvenile subjects with GM2 gangliosidosis in the U.S. The two-part trial, sponsored by Axovant, will consist of (1) a dose ranging cohort evaluating the safe and efficacious dose of the gene therapy, followed by (2) an efficacy cohort, both of which form the basis of the registrational program. Terence R. Flotte, MD, Professor of Pediatrics and Dean at the University of Massachusetts Medical School, will serve as principal investigator on the clinical trial.

AXO-AAV-GM2 is an investigational gene therapy for GM2 gangliosidosis (also known as Tay-Sachs and Sandhoff diseases), a set of rare and fatal pediatric neurodegenerative genetic disorders caused by defects in the HEXA (leading to Tay-Sachs disease) or HEXB (leading to Sandhoff disease) genes that encode the two subunits of the β-hexosaminidase A (HexA) enzyme. These genetic defects lead to progressive neurodegeneration and shortened life expectancy. AXO-AAV-GM2 aims to restore HexA function by introducing a functional copy of the HEXA and HEXB genes via delivery of two co-administered AAVrh8 vectors.

Mateon Therapeutics & Windlas Biotech Enter Commercialization Agreement for Covid-19 Drug

Mateon Therapeutics recently announced an agreement with Windlas Biotech Pvt. Ltd. of India (Windlas) to commercialize ARTIVeda, Mateon's lead ethnobiology drug against COVID-19.

With clinical data supporting anti-viral activity in-vitro and in-vivo, and with its high safety index, the commercial path has been accelerated both as an Ayurvedic therapy and Nutraceutical in India that can be prescribed by physicians. We, with and through our commercialization partners Windlas, are in active discussion with large distributors, marketers, and manufacturers to establish a consortium for distribution of this drug product in an equitable manner across all territories.

Early data from ARTI-19 suggests efficacy trend and safety, which is further supported by an independent recently completed study published in Int J Antimicrob Agents. 2020 Nov 2. In this study, time to undetectable SARS-CoV-2 RNA in the treatment group was significantly less than the control group (Treatment: 10.6±1.1 days), Control: 19.3±2.1 days) and Length of hospital stay for Treatment group was 13.3±4.8 days, and Control was 21.3±9.1 days.

Windlas is a leading CDMO since last 20 years. It promotes more than 120 chronic and acute care branded products (allopathic, nutraceutical and Ayush formulations) through its "affordable generics platform" spanning over 950 wholesalers across India. Windlas branded medicines and wellness products are sold in several markets across the globe like Sri Lanka, Vietnam, Thailand, Myanmar etc.

In order to maximize the accessibility and the reach of "ARTIVeda", Mateon and Windlas intend to launch it through its distribution network as well as through strong co-marketing partners who are existing clients of Windlas.

"We are very excited by the early data of our Phase 4 Clinical trial in Indian COVID-19 patients, and confirmatory data of other global researchers. Given the well-established safety profile of this product, with hundreds of years of usage against viral fever and associated symptoms, ARTIVeda has the potential for use even beyond the pandemic as a safe and effective anti-viral therapy," said Hitesh Windlass, Managing Director of Windlas. "Windlas has the capability to manufacture and supply several hundred million doses of ARTIVeda a month to address the dire patient needs."

Saran Saund, Chief Business Officer and GM of AI division of Mateon, commented "Signing the definitive agreement with Windlas is a significant milestone for the companies to come together to address this epidemic in India and rest of world. We look forward to this partnership having an impact that can make slow down or even stopping this pandemic. Windlas, with its world-class manufacturing and commercialization operations and Mateon's innovative science team

Dolomite Microfluidics & MilliporeSigma Collaborate to Release Off-the-Shelf Microfluidic Device Kits for the Fabrication of PLGA Particles

Dolomite Microfluidics and MilliporeSigma have partnered to create a range of off-the-shelf NanoFabTx microfluidic device kits for the production of PLGA nano- and microparticles for drug development and controlled drug-release applications. The kits, which will be available exclusively from MilliporeSigma, are also ideal for the encapsulation of drugs and other therapeutics in liposomes, such as the SARS-CoV-2 (COVID-19) vaccines currently under investigation.

The increasing use of biodegradable PLGA polymers for drug encapsulation and formulation of controlled-release preparations has created a market for easy-to-use, ready-to-go microfluidic solutions that simplify the workflow for researchers. The new NanoFabTx kits include a microfluidic chip, holders, and accessories, along with application data for the production of a variety of particle types and sizes; simply connect the kit to the pumps and start your application. This user-friendly microfluidic approach offers better encapsulation efficiency and higher monodispersity than traditional methods. Particles of the correct dimensions can be isolated without wasteful filtering, ensuring the tight control of size and shape that is essential to regulate the speed of drug delivery and release. The new kits are intended for use with MilliporeSigma's NanoFabTx PLGA-Nano and NanoFabTx PLGA-Micro Reagent kits, and are perfectly optimized for microfluidic pumps and software from Dolomite to give high accuracy and consistency. The kits can also be combined with Dolomite's high throughput Telos technology for scaled up experiments.

Richard Gray, Commercial Director at Dolomite Microfluidics, said "MilliporeSigma chose Dolomite Microfluidics because of our reputation and many years' expertise in providing excellent microfluidic solutions that deliver consistent and reliable production of particles. The controllability and reproducibility that microfluidics offers means the process is really finding its place in drug and vaccine development, making it the method of choice. We are looking forward to continuing our work with scientists to keep getting particles out there at the forefront of this area."

Established in 2005, Dolomite Microfluidics has grown to be the world leader in the design and manufacture of high quality innovative microfluidic products. The company offers a range of microfluidic systems, components and specialist chemicals – including pumps, chips, connectors, temperature controllers, sensors, accessories, and custom-made components – as well as software for analysis or automation.

The Life Science business of Merck KGaA, Darmstadt, Germany, which operates as MilliporeSigma in the U.S. and Canada, has some 22,000 employees and 59 manufacturing sites worldwide, with a portfolio of more than 300,000 products focused on scientific discovery, biomanufacturing and testing services. Merck KGaA, Darmstadt, Germany completed its $17 billion acquisition of Sigma-Aldrich in November 2015, creating a leader in the $125 billion global life science industry. Merck KGaA, Darmstadt, Germany, a leading science and technology company, operates across healthcare, life science and performance materials.

eGenesis Announces Research Collaboration With Leading Academic Medical Center

eGenesis recently announced the initiation of a research collaboration with Duke University School of Medicine. The collaboration will encompass evaluation of gene-edited pancreatic islet cells in non-human primate recipients as a prerequisite to advancing to human clinical trials. This collaboration is in addition to an existing eGenesis partnership with Massachusetts General Hospital, initiated in 2017.

The research on gene-edited pancreatic islet cells will be conducted in the laboratory of Allan Douglas Kirk, MD, PhD, David C. Sabiston, Jr. Distinguished Professor of Surgery Chair, Department of Surgery, Professor of Surgery, Professor in Pediatrics and Professor in the Department of Immunology at Duke University School of Medicine.

"There are 1.6 million Americans who live with type 1 diabetes and whose quality of life is greatly impacted by the monitoring of their glucose levels and the need for multiple insulin injections on a daily basis," said Dr. Kirk. "With advancements in gene editing technology, there is now the potential of developing and safely transplanting human-compatible xeno-islet cells, which could allow these patients to reduce or eliminate their need for glucose monitoring and insulin injections. The research we will conduct at Duke will help determine whether a minimally-invasive approach into human clinical studies might be possible."

Michael Curtis, PhD, President of Research & Development of eGenesis, added "eGenesis' mission is to develop human-compatible organs, tissues and cells to alleviate the organ shortage crisis and to improve the health and quality of life of all patients who could benefit from transplant. This collaboration with Duke, a leading transplant center with deep expertise in immunology and diabetes, will accelerate our research and provide validation of our xeno-islet cell program, leading to the evaluation in human clinical trials in patients with type 1 diabetes. We look forward to working with our new colleagues to advance the field of organ, tissue, and cell transplantation."

The demand for lifesaving organs far outnumbers available supply. In the US today, 20 people die every day due to lack of available organs for transplant and every 10 minutes an additional name is added to the national transplant waitlist. There are more than 110,000 people in need of a lifesaving organ transplant in the US alone.

The concept of xenotransplantation, or the transplantation of organs, tissue and cells from one species to another, has been explored for several decades, with the pig considered the most suitable donor species for humans. However, challenges related to molecular incompatibilities between species as well as virologic concerns have stymied the advancement of the field.

eGenesis' goal is to advance the field of transplantation and make available safe and reliable xeno organs, tissues, and cells to patients in need. eGenesis uses gene editing technology such as CRISPR to directly address the key virology and immunology hurdles that have impeded xenotransplantation to date.

Novartis Acquires Vedere Bio, a Novel Optogenetics AAV Gene Therapy Company

Vedere Bio, Inc. recently announced it has been acquired by Novartis. Shareholders in Vedere Bio received $150 million upfront and will be eligible for up to $130 million in milestone payments, for a total of $280 million. Based on technology from the laboratories of Drs. Ehud Isacoff and John G. Flannery of UC Berkeley, and technology directed at enhanced ocular gene therapy delivery arising jointly between UC Berkeley and the School of Veterinary Medicine at the University of Pennsylvania, Vedere Bio was formed in the Atlas Venture incubator in June 2019. The company was launched with a $21 million Series A financing and began lab operations at LabCentral in Cambridge, MA where it advanced its lead programs from concept to development candidate within one year. Immediately prior to the acquisition, certain earlier-stage vision restoration and vision preservation assets leveraging the company's ocular gene therapy toolbox were spun out into a newly formed entity – Vedere Bio II, Inc.

"The medical need for new therapies to treat blindness is unambiguous," said Jay Bradner, President of the Novartis Institutes for BioMedical Research. "Vedere Bio's innovative technologies expand the potential for gene therapy to improve the lives of patients facing vision loss due to photoreceptor death attributable to a number of prevalent eye diseases."

"Vedere Bio's photoreceptor-protein-based optogenetics program has important advantages over competing approaches and brings us one step closer to delivering functional vision to patients in need. Our proprietary intravitreal capsids enable not only Vedere Bio's optogenetics products but also other ocular gene therapies," said Cyrus Mozayeni, M.D., Chief Executive Officer, President of Vedere Bio and Atlas Venture Entrepreneur in Residence. "Our sale to Novartis is an important milestone in advancing Vedere Bio's most advanced programs to patients around the world. At the same time, I look forward to working with our experienced team to advance our highly innovative, earlier stage assets as part of the newly established Vedere Bio II."

The newly formed Vedere Bio II, Inc. will operate as a wholly independent entity from Novartis and Vedere Bio. Vedere Bio II aims to develop a pipeline of novel vision restoration and vision preservation medicines by targeting underserved indications. Backed by the full Vedere Bio investor syndicate of Atlas Venture, Mission BioCapital and Foundation Fighting Blindness (RD Fund), the Vedere Bio II team will launch with Vedere Bio's founders, team and facilities to advance its pipeline.

"The acquisition of Vedere Bio by Novartis speaks to the strength of the underlying science from our founders and to the incredible job the team has done in advancing these programs over the past year. We are very excited by the potential of this technology and the opportunity to deliver true restoration of sight for patients who have been living in darkness for so long," said Kevin Bitterman, PhD, Partner at Atlas Venture and Chairman of the Vedere Bio Board of Directors.

Nemera to Acquire Copernicus to Boost Parenteral Product Portfolio & Small Series Capabilities

Nemera recently announced it has entered into an agreement to acquire Copernicus. Copernicus, based in Szczecin Poland, specializes in the development and manufacturing of injection devices. Their range of reusable and disposable pen injectors are tailored for the treatment of several chronic pathologies.

Founded in 2004, Copernicus is regarded as one of the most valued innovative companies in the Polish health sector. They provide a comprehensive range of services in the introduction of modern and intuitive parenteral drug delivery devices.

This acquisition reinforces Nemera's vision of becoming the most patient-centric drug device combination solutions company. It bolsters its small series production capabilities, R&D expertise, and parenteral product offering. Most importantly it expands its overall proprietary product portfolio. Copernicus' fast and agile clinical manufacturing, adapted for small series, complements Nemera's historical large-scale manufacturing capabilities. Furthermore, Copernicus' marketed reusable pen injectors are of great value from a sustainability standpoint.

With this acquisition Nemera establishes an operations footprint in Eastern Europe. In order to accompany Copernicus' solid forecasted growth, Nemera will work together to build a new state-of-the-art manufacturing facility in Szczecin, Poland.

Marc Hämel, CEO of Nemera, said "This acquisition is a great strategic and cultural fit for us. Copernicus' strong focus on patient needs aligns perfectly with our purpose of always putting the patient at the center of everything we do. We're about to write a new chapter of Nemera's growth story, and I'm really excited about our bright future.

"Nemera's unaltered focus on patient needs and passion to develop combination product solutions of the future convinced us that this was the right next step. We're thrilled to join Nemera and together make products that truly improve patients' lives," added Alberto Lozano, CEO of Copernicus.

Nemera is a world leader in the design, development, and manufacturing of drug delivery devices for the pharmaceutical, biotechnology, and generics industries. Nemera offers a comprehensive portfolio of products and services across ophthalmology, nasal, inhalation, dermal, transdermal, and parenteral delivery. Nemera's vision is to be the most patient-centric drug delivery device company. Nemera always puts patients first, providing high-quality solutions that have a demonstrable impact on patients' health. Nemera's Insight Innovation Center, with offices in North America and Europe, provides consultative services to support your overall device strategy. Providing user research, Human Factors, User Experience design, and Design for manufacturing, our Insight Innovation Center helps customers navigate their device strategy for both novel and platform solutions. Users are at the center of everything that we do in our effort to always put patients first. For more information, visit www.nemera.net.

Calithera Biosciences Announces Expansion of Ongoing Clinical Trial

Calithera Biosciences, Inc. recently announced the expansion of the company's ongoing clinical trial evaluating telaglenastat in combination with Pfizer's CDK 4/6 inhibitor palbociclib (IBRANCE). This Phase 1/2 study, which is being conducted by Calithera, will be expanded to include an additional cohort of patients with pancreatic ductal adenocarcinoma (PDAC) whose tumors harbor mutations in both KRAS and CDKN2A.

"There is a strong rationale to target KRAS and CDKN2A mutated tumors with the combination of palbociclib and telaglenastat," said Susan Molineaux, PhD, President and Chief Executive Officer of Calithera. "Mutations in CDKN2A lead to upregulation of both CDK4/6 activity and glutamine utilization in cancer cells. By inhibiting these activities simultaneously with the telaglenastat-palbociclib combination, we hope to have a measurable impact on pancreatic cancer, which still has very few viable treatment options."

Telaglenastat blocks glutamine consumption in tumor cells, which, due to specific genetic alterations such as mutations in KRAS and CDKN2A, often become dependent on increased metabolism of glutamine. Approximately 50 percent of PDAC patients harbor mutations in both KRAS and CDKN2A. In preclinical studies with KRAS-mutated cancer models, telaglenastat showed synergistic antitumor effects when used in combination with CDK4/6 inhibitors, such as palbociclib, enhancing cell cycle arrest and blocking cancer cell proliferation. In the ongoing Phase 1/2 clinical trial (NCT03965845), encouraging efficacy and safety of the combination was observed in PDAC patients treated in the dose escalation phase of the trial.

The new cohort of the Phase 1/2 clinical trial will be evaluating the safety and anti-tumor activity of telaglenastat in combination with palbociclib in patients with advanced, metastatic PDAC whose tumors harbor mutations in both KRAS and CDKN2A. The ongoing Phase 1/2 trial is currently enrolling patients with colorectal cancer and non-small cell lung cancer whose tumors harbor mutations in KRAS.

Calithera Biosciences is a clinical-stage biopharmaceutical company pioneering the discovery and development of targeted therapies that disrupt cellular metabolic pathways to preferentially block tumor cells and enhance immune-cell activity. Driven by a commitment to rigorous science and a passion for improving the lives of people impacted by cancer and other life-threatening diseases, Calithera is advancing a pipeline of first-in-clinic, oral therapeutics to meaningfully expand treatment options available to patients. Calithera is headquartered in South San Francisco, CA. For more information, visit www.calithera.com.

Lonza Significantly Expands Its Capsule Manufacturing Capacity

Lonza recently announced a $93-million investment in its Capsules and Health Ingredients (CHI) Division, a dosage form delivery partner to the biopharma and health nutrition industry. The investment will enable the company to expand its overall production capacity of capsules within CHI's Capsugel portfolio by 30 billion capsules annually while maintaining the high-quality standards with Lonza's Sigma Series. Production capacity will be increased across Lonza's global manufacturing and supply chain network to help further strengthen the company's position as a leading global supplier of capsules. The investment will allow a 15% increase in CHI's current capsule production capacity.

"We continue to see strong demand for our products across all markets, as consumers and patients alike take a more active interest in their health. Therefore, we felt it is critical that we make this commitment to expand the manufacturing capacity of our network, not only addressing supply needs in the near term but also supply availability over the long term," said Claude Dartiguelongue, President Capsules & Health Ingredients, Lonza.

This latest commitment follows on from an initial investment initiated in 2019 to increase CHI's capacity by 10 billion capsules. The addition of manufacturing capacity for a further 30 billion capsules will address the high growth across CHI's gelatin, vegetarian, and specialty polymers portfolio as well as the liquid-filled hard capsules sold under the Licaps brand. This investment will be made over two fiscal years, 2020 and 2021, across eight global Lonza manufacturing sites, including Bornem (BE), Colmar (FR), Greenwood (USA), Haryana (IN), Jakarta (ID), Puebla (MX), Sagamihara (JP), and Suzhou, (CN).

The current industry trends are leading to an increased demand for capsules both in the pharmaceutical and nutritional supplements markets. Patients are seeking preventative treatments, while consumers want to support healthier lifestyles. Expanding the manufacturing capacity of Lonza's entire network will allow ample supply both in the near- and long-term. Additionally, the expansion underlines the strategic position of capsules within the broader nutrition industry and will also support production as CHI also introduces new dosage technologies such as Lipid Multi Particulates (LMP) technologies and several new time-release functional capsule solutions. For more information, visit www.capsugel.com.

At Lonza, we combine technological innovation with world-class manufacturing and process excellence. Together, these enable our customers to deliver their discoveries in the healthcare, preservation, and protection sectors. We are a preferred global partner to the pharmaceutical, biotech and specialty ingredients markets. We work to prevent illness and promote a healthier world by enabling our customers to deliver innovative medicines that help treat or even cure a wide range of diseases. We also offer a broad range of microbial control solutions, which help to create and maintain a healthy environment.

Quantum Genomics Enters Exclusive Licensing & Collaboration Agreement With Qilu Pharmaceutical

Quantum Genomics recently announced it has entered into an exclusive licensing and collaboration agreement with Qilu Pharmaceutical to develop and commercialize firibastat in Greater China region, Hong Kong, and Macao. After its first partnership in Asia, this new agreement is the second step of Quantum Genomics' partnering strategy in Asia.

Under the terms of the agreement, Qilu Pharmaceutical will receive exclusive commercialization rights to firibastat for the treatment of difficult to treat/resistant hypertension in Geater China region, including Hong Kong and Macao. Additionally, Qilu Pharmaceutical plans to join the global study of difficult to treat/resistant hypertension in China. Quantum Genomics will receive upfront and milestone payments amounting up to $50 million, plus double-digit royalties on sales. The population suffering from difficult to treat and resistant hypertension in the above territories is estimated to be between 25 and 30 million.

"Qilu Pharmaceutical is one of the leading pharmaceutical companies in China with 5 R&D centers across US and China and 10 domestic manufacturing sites. Qilu Pharmaceutical has launched over 200 products in China, is a leading player in the cardiovascular field and has established long-term cooperative relationships with international companies. With a comprehensive sales network and multiple professional in marketing, Qilu Pharmaceutical is a partner of choice and we look forward to working with them," said Jean-Philippe Milon, Chief Executive Officer of Quantum Genomics.

"Quantum Genomics is the leading biopharmaceutical company specializing in the development of a new drug class based on the central action mechanism of Aminopeptidase A inhibition," added Dr. Binhui (Ben) Ni, Chief Business & Investment Officer, Corporate Vice President of Qilu Pharmaceutical. "Development of Firibastat, first-in-class for the treatment of high blood pressure and/or in combination with others anti-hypertensive drugs offers alternative treatments to address the significant unmet needs in China. We are confident that the unique mechanism of action with strong clinical data position Firibastat to make a meaningful impact on patients' lives."

Qilu Pharmaceutical is one of the leading pharmaceutical companies in China, with mission of caring through Science and Technology. The company develops, manufactures and commercializes novel pharmaceuticals, biologics, as well as generics and biosimilars. Qilu has 12 subsidiaries, and 10 manufacturing sites with over 23000 employees worldwide and launched over 200 products in China with revenue of over 3.3 bn USD in 2019. Qilu Pharmaceutical is among the top GMP manufacturers in the world, fully complied with major global regulatory agencies and exports the products including active pharmaceutical ingredients (APIs) & finished formulations over 70 countries.

With commitment to develop innovative medicines for solutions that improve people's lives and meet the unmet medical need in multiple therapeutic areas, Qilu has 2000+ dedicated scientists and comprehensive clinical team that work in its R&D centers across US and China. The company is actively looking for partnership with global players via in-/out-licensing and/or co-development strategy.

Formulation Forum

Age-Appropriate Pediatric Formulation Development

By: Jim Huang, PhD, Founder & CEO, Ascendia Pharmaceuticals

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BACKGROUND

Pediatric patients are defined as patients aged from birth to less than 16 or 18 years, depending on the country. The EU guideline on clinical investigation of medicinal products in the pediatric population (CPMP/ICH/2711/99) uses the following age groups in relation to developmental stages.

- Preterm newborn infants
- Term newborn infants (0-27 days)
- Infants and toddlers (1 month to 23 months)
- Children (2-11 years)
- Adolescents (12-16 or 18 years)

It has been recognized that the requirements of drug formulation for children are different from those of adults. The lack of appropriate pediatric formulations is the main obstacle for use of many drugs in children. Historically, children have been treated with off-label used medications by means of extemporaneous compounding, which, however, is not ideal due to potential safety/efficacy concerns. As a result of the US Best Pharmaceuticals for Children Act (BPCA) and Pediatric Research Equity Act (PREA) of 2007 and European Union medicinal products for pediatric use in 2006, more and more companies are encouraged to develop and generate clinical data for the pediatric population in order to gain accelerated drug approval and extended market exclusivity.

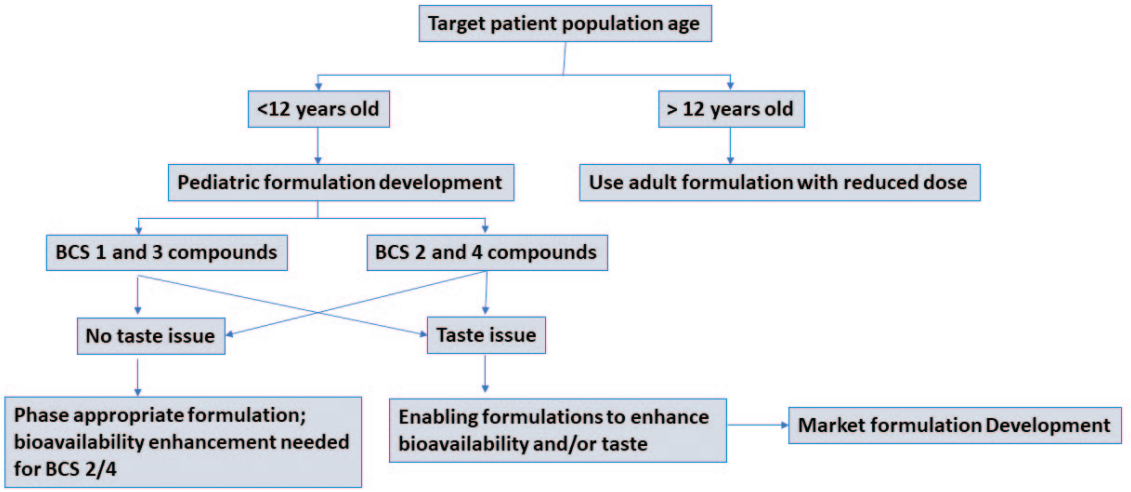
The development of pediatric formulations can be challenging due to specific requirements of the patient population. A pediatric formulation should consider the following factors: difference in physiological and pharmacokinetic of patient populations, dosage form selection, route of administration, dose accuracy, dose flexibility, drug and excipient tolerability (safety and toxicity), patient compliance (palatability/swallowability), stability, and drug accessibility.

BIOPHARMACEUTICAL CONSIDERATIONS & CLINICAL DEVELOPMENT STRATEGY

One of the most important issues in the development of medicinal products for pediatric patients is selection of the most appropriate formulation in relation to patient age. Due to substantial changes in the absorption, distribution, metabolism, and excretion (ADME) profile in pediatric populations, particularly during the first years of life, there is a significant variability in the pharmacokinetics of the same drug and dosage form between the pediatric and adult populations. For example, due to the immaturity of the pediatric population, the intestinal mucosa of infants and young children is more permeable than that of adults; as a result, there is significant increased absorption for the pediatric population than that in the adults. In addition, the factors impacting drug bioavailability, such as the gastrointestinal pH, gastrointestinal motility, gastric emptying time, and intestinal transport systems, is different in children from those in adults.

A decision tree in clinical formulation strategy, based on drug BCS classification, age, and drug palatability, is illustrated in Figure 1 as a guide for pediatric formulation development. A phase-appropriate enabling formulation strategy can be adapted if the compound is BCS class 1 or 3 and does not present issues in palatability. However, for a BCS 2 and 4 compound with palatability issues, development of a market image/commercial formulation is desired to avoid biopharmaceutical risk in BA/BE between clinical and market formulations. Typically, initial studies of a pediatric formulation is done in an adult population to demonstrate acceptable BABE; once the safety and efficacy of the formulation in adults is demonstrated, clinical trials in children can then be conducted using the pediatric formulations.

FIGURE 1



Clinical Development Strategy for Pediatric Formulation

DOSAGE FORM SELECTION

One of the most important issues in the development of medicinal products for pediatric patients is its appropriateness for the target patient age without presenting problems in palatability and swallowability. According to the EU guideline on the clinical investigation of medicinal products in the pediatric population (CHMP/ICH/2711/99), a matrix combining different age groups, routes of administration, and dosage forms has been developed to assist in dosage form selection (Table 1). The age classification has been further divided into pre-school children (2-5 years) and school children (6-12 years) because of the significant changes in ability to handle some dosage forms between 2-12 years of age.

EXCIPIENT SAFETY CONSIDERATIONS

In addition to the incompatibility of excipients with API that generate toxic impurity, the interactions of certain excipients under intracellular environments may also produce toxic metabolites that may interfere with children's development processes. It is critical that the daily update amount of excipients in a pediatric formulation be within the allowable daily Intake of the excipients and be within the limit of previously approved pediatric products in the major pharma markets, such as the US and EU.

Although excipients are generally considered to be inert, there are cases that excipients may play a role in enhancing solubility and bioavailability and thus impact on drug safety and efficacy. Particularly for neonates and infants, because they have immature metabolic systems, the drug itself or toxic metabolites may accumulate inside the body that cause side effects. The excipients associated with potential toxicity in pediatric oral, topical, and intravenous formulations are: propylene glycol used as solvent, which may cause central nervous system (CNS) effects, especially in neonates and children under 4 years; ethanol as solvent may introduce intoxication due to its ease to cross the BBB; benzyl alcohol as solvent and preservative have "Gasping syndrome" in neonates; benzoic acid as preservative may cause jaundice in neonates; parabens used as preservative might generate oestrogenic and potential reproductive effects; sorbitol as a sweetener causes GI discomfort as a result of osmotic diarrhoea; saccharin as sweetener and dyes as coloring agents may induce hypersensitivity and photosensitivity reactions, etc. Those excipients should be used with caution in very young patients.

Overall, the following aspects are to be considered when selecting excipients for use in pediatric formulations: 1) the function of the excipient; 2) the safety profile of the excipient for children in the target age group(s) on the basis of single and daily exposure; 3) the expected duration of the treatment (short term or long term); 4) the severity of the condition to be treated (risk/benefit ratio); 5) the patient acceptability (palatability/swallowability), etc.

FORMULATION CONSIDERATIONS

Ideally, a pediatric formulation should be a flexible, good-tasting, sub-divisible dosage form that is an oral dispersible, oral liquid form, or granules that can be sprinkled to children's foods or drinks. It is desired that pediatric medicines allow for flexible and precise dosing for children at different developmental stages with swallowing difficulties. Pediatric formulations should also be developed with taste, color, and texture that are acceptable to children of different ages and different cultures. Taste-masking is one of the biggest challenges in pediatric formulation development, which can be achieved by

TABLE 1

Route / Dosage Form	*Preterm newborn infants*	*Term newborn infants (0d-28d)*	*Infants and Toddlers (1m-2y)*	*Children (pre school) (2-5y)*	*Children (school) (6-11y)*	*Adolescents (12-16/18y)*
Peroral						
Solution/ Drops	2	4	5	5	4	4
Emulsion/ Suspension	2	3	4	5	4	4
Effervescent DF*	2	4	5	5	4	4
Powders/ Multiparticulates	1	2	2	4	4	5
Tablets	1	1	1	3	4	5
Capsules	1	1	1	2	4	5
Orodispersable DF	1	2	3	4	5	5
Chewable tablets	1	1	1	3	5	5
Nasal						
Solution	3	4	4	4	4	4
Semisolid DF	2	3	3	4	4	4
Rectal						
Suppositories	4	5	5	4	3	2
Rectal Enema	5	4	4	3	3	2
Rectal capsules	2	3	4	4	4	3
Topical/ transdermal						
Ointment, Cream, Gel	4	4	4	5	5	5
Liquid DF	4	4	4	5	4	4
Transdermal Patch	1	2	2	4	4	5
Parenteral						
i.v. Solution	5	4	4	4	4	3
i.m.	3	3	3	4	4	3
s.c.	4	4	4	4	4	3
Pump system	5	4	4	4	4	3
Pulmonary						
Nebuliser	2	3	4	5	4	3
MDI / Spacer	1	3	4	5	4	4
DPI	1	1	3	4	5	5
Ocular						
Eye drops	3	4	4	4	5	5
Semisolid DF	2	3	4	4	4	4

*DF: Dosage Forms

Guide in Selection of Dosage Form Per Age Population
(1 = not applicable, 2 = applicable with problems, 3 = probably applicable, but not preferred, 4 = good applicability, and 5 = best and preferred applicability)
Reference: EMEA/CHMP/PEG/194810/2005: Reflection Paper: Formulations of Choice for the Pediatric Population.

coating the API, complexing the API with excipients, eg, polymers, and by adding sweeteners and flavors to the formulation. Prior to a human taste panel for evaluation of formulation palatability, an e-tone machine can be explored to screen taste-masking formulations.

Most pediatric formulations are liquid dosage forms, including solutions, micron or nano-suspensions, emulsions, syrups, and less frequently, elixirs with a targeted dosing volume of </=5-10 ml for children. Pediatric formulations should ensure palatability and dose accuracy for administration. Liquid solution and suspension formulations are preferred due to advantage in ease of dose adjustments and accurate dose uniformity for infants and younger children. However, the production of liquid formulations may be limited by the solubility and stability of drugs, and the requirements of taste-masking agents, preservatives, and solubility of excipients. The API may need to be micronized or nanosized before incorporated to suspension to increase drug loading and solubility. Furthermore, salt formation or solubilization technologies, such as Ascendia's nano-technology platforms in nanoparticle engineering, amorphous nano, and nano-emulsions may be explored to improve drug solubility and bioavailability. The recent advances in nanotechnology delivery systems have resulted in the development of nanomedicines for the treatment of various disease conditions. Nanomedicine has advantages over traditional formulations in terms of enhancement of safety and efficacy by increasing solubility and bioavailability of insoluble drugs, optimizing drug loading and stability, enabling taste-masking, reducing local irritation in GI and injection site, and enabling targeted delivery of drugs to specific targets tissues, etc.

From a product quality perspective, residual solvents, heavy metals, potentially genotoxic impurities, degradants from drug/excipient incompatibilities and impurities from excipients should be controlled for pediatric products. In addition, it should be made aware that in some parts of the world, particularly in tropical areas, refrigeration may not be available, and the climates there have high temperatures and humidity levels that may impact on the product's chemical and physical stability. Child-resistant packaging is required, and dosing devices (droppers, measuring cups, graduated pipettes) should be evaluated as a part of the pediatric product development.

SUMMARY

The lack of appropriate pediatric formulations is the main obstacle for use of many drugs in children. Pediatric formulations make precision, personalized medication for children possible, which could also benefit the drug manufacturers with accelerated drug approval and extended market exclusivity. The development of pediatric formulations can be challenging due to specific requirements of the patient population. A pediatric formulation should consider the following factors: difference in physiological and pharmacokinetic of patient populations, dosage form selection, route of administration, dose accuracy, dose flexibility, drug and excipient tolerability (safety and toxicity), patient compliance (palatability/ swallowability), stability, and drug accessibility. ◆

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PLATFORM TECHNOLOGY

Overcoming the Challenges of Drug Brain Delivery With a Novel Brain Delivery Vector

By: Mei Mei Tian, PhD

INTRODUCTION

Central nervous system (CNS) disorders affect as many as 1.5 billion people worldwide and account for an economic burden of more than $2 trillion in the EU and US combined and significant areas of unmet need in global health.[1,2] In recent years, many life sciences companies have pursued clinical development of CNS drugs, but these development programs statistically often have considerably lower clinical success rates compared to drugs in non-CNS indications.[3] One critical factor affecting the success of development programs targeting treatments for CNS disorders is challenges with drug brain delivery.[4]

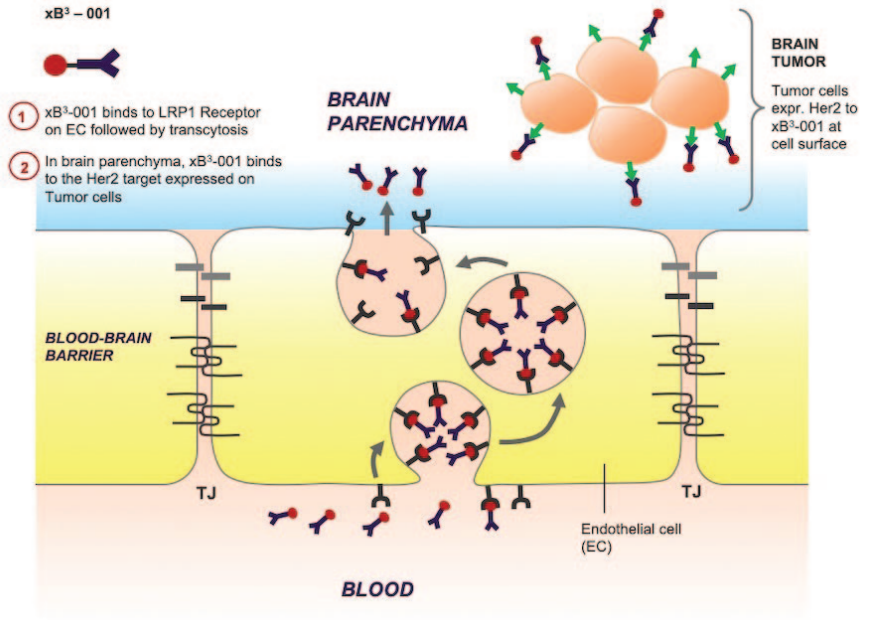
The largest obstacle to effective drug brain delivery is the blood brain barrier (BBB), a network of specialized capillary endothelial cells that protect the brain from harmful substances while facilitating access to the essential nutrients to support proper function.[5] While peripheral capillaries in the body allow relatively free exchange of substances between cells and tissues, the endothelial cells that form the BBB strictly regulate the transport of substances into the brain using both physical and metabolic barriers.[6] These barriers regulate brain homeostasis (the balance of electrolytes, glucose, nucleosides, and amino acids) through multiple efflux and uptake transporters, metabolic enzymes, low pinocytotic activity, and low paracellular permeability.

In biomedical research to date, many potentially effective drugs have been unable to target and transport across the BBB safely and effectively. To design drugs able to reach the CNS at therapeutic concentrations, developers can consider three different approaches: invasive, pharmacological, and physiological. Invasive approaches often have limited applications and may not be a viable option for many needs, including treatment of older patients requiring chronic medications. Pharmacological methods use factors including molecular size (< 500 Dalton), charge (low hydrogen bonding capabilities), and lipophilicity (the ability of a chemical to dissolve in fats, oils, lipids and non-polar solvents) to exploit the natural properties of the BBB. Drugs designed based on this approach are generally limited in their ability to deliver diverse chemical or biological entities across the intrinsically impermeable structure of the BBB.

As recent scientific advances have helped researchers gain a better understanding of the cellular biology at the blood-brain interface, more drug developers are pursuing a physiological approach to deliver therapeutic agents across the BBB, which can help minimize or avoid the limitations of invasive or pharmacological approaches. With this approach, drugs can be modified to take advantage of native BBB nutrient transport systems or be joined with conjugates able to target receptors expressed at the BBB, allowing a drug to "piggy-back" across the BBB through the process of receptor-mediated transcytosis.[7] Despite recent advances in research, most drugs, including small molecules, proteins, and peptides based on a physiological delivery approach, are unable to efficiently cross the BBB.

When developing therapies for CNS diseases, drug delivery must be targeted to the appropriate brain cells and intracellular compartment associated with a disease. This precision helps to ensure that a drug is delivered to affected cells while reducing the risk of toxicity. Given the many limitations of traditional drug delivery mechanisms, research efforts have recently focused on development of new strategies to more effectively deliver drugs to the CNS through the BBB.

FIGURE 1



Schematic representation of the transport of xB³-001 across the BBB. xB³ fusion molecules such as xB³-001, introduced into the blood circulation via intravenous injection, bind to LRP1 receptors expressed on the luminal surface (blood side) of the brain capillary endothelium through interaction with the xB³ peptide portion of the molecule for transcytosis across the BBB. Upon reaching the abluminal surface (brain side) of the BBB, xB³-001 is released from the receptor. Subsequently, the high affinity between Herceptin (trastuzumab) and Her2 targets facilitates the binding of xB³-001 to Her2 targets expressed on the surface of tumor cells in the brain, thereby suppressing cancer cell growth, proliferation and survival.
(Photo credit: Dr. Reinhard Gabathuler, Dr. Siti Yusof, and Bioasis Technologies Inc.)

THE MECHANISM OF ACTION OF THE XB³ PLATFORM

Research led by Bioasis has led to development of a platform technology called xB³ that can transport molecules across the BBB via receptor-mediated transcytosis. In this process, molecules attach to receptors on the surface of endothelial cells forming the BBB. The receptors pull the molecules by vesicular transport through the cells, gaining access to the brain.

Formerly called the transcend-peptide, xB³ is a small 12 amino-acid peptide that works with a wide variety of payload types, including antibodies, enzymes, small interfering RNA (siRNA) and small molecules.[8-10] The peptide was derived from xB³ full-length (also known as melanotransferrin, MTf), an endogenous protein that is found at very low concentrations in the blood and has been shown to actively transcytose across the BBB at a transport rate 10 to 15 times higher than that of the proteins transferrin and lactoferrin.11 The xB³ platform technology traverses the BBB via a process that involves the low-density lipoprotein-related protein 1 (LRP1), which offers significant advantages as a transport system given its broad expression throughout the CNS, ability to recognize a wide range of structurally and functionally diverse ligands, and rapid endocytosis rate. High affinity receptor binding does not necessarily translate into high transport efficiency, as seen with transferrin-transferrin receptor (Tf-TfR) binding where most of the cargo remains associated to the vasculature and cannot detach from the TfR and remain associated with the BBB. By contrast, lower TfR-ligand binding affinity has resulted in about 50% higher ligand release from the BBB into the brain.[12] The lower affinity, high-capacity LRP1 receptor binding with xB³ thus could present a valuable alternative in targeting drugs to the brain.

Clinically, LRP1 has been associated with neurodegenerative diseases through its role in importing cholesterol into neurons to maintain proper cell function. It has also been implicated in local catabolism of amyloid beta protein through endocytosis in neurons, and LRP1 in astrocytes plays a critical role in clearance of amyloid beta protein from the brain. Overexpression of LRP1 has been reported in several types of brain tumors, including brain metastasis and glioblastoma. Given the distribution of LRP1 on the BBB's endothelial cell surfaces, neuronal LRP1 localization within the CNS, and the upregulation of LRP1 in key target tissues in many neurodegenerative diseases, LRP1 is likely involved in promoting dual targeting of both delivery across the BBB and target engagement of specific diseased areas, such as tumors and metastases. Moreover, with the endogenous origin of xB³, immune hypersensitivity and elimination by neutralizing antibodies are likely to be minimized after repeated treatment.

VALIDATION OF XB³ IN EFFECTIVELY PENETRATING THE BRAIN

In a range of preclinical studies, the xB³ peptide has been shown to help therapeutics effectively penetrate the BBB and reach target areas within the brain. Intra-

venous administration can also provide a relatively non-invasive route for efficacious delivery of xB^3-modified therapeutics. In one example, preclinical disease models showed that intravenous treatment of HER2$^+$ breast cancer-related brain metastases with an xB^3 version of herceptin (xB^3-001) led to a 68% reduction in the number of brain metastases. The data also showed that the remaining tumors were 46% smaller compared to the control groups, while treatment with herceptin alone had minimal to no effect on either the number or size of the brain metastases.[8] In addition, xB^3-001 showed significantly higher brain tissue penetration with brain/blood concentration ratios that were 10 to 225 times higher than corresponding ratios for the group treated only with herceptin. Preferential uptake into brain metastases compared to normal brain tissue distal to metastatic lesions were also observed.

An independent study conducted by MedImmune research group has also demonstrated that xB^3 greatly increased the transport of an antibody payload to the brain with a systemic profile similar to the antibody itself and prolonged brain exposure, with peak exposure of more than 4 to 6% (compared to a peak of <1% following treatment with the antibody alone).[9]

In a separate neuropathic pain mouse model, systemic administration of xB^3-IL1RA (interleukin-1 receptor antagonist) fusion protein reversed induced mechanical hyperalgesia (enhanced sensitivity to pain), which was only previously achieved via intrathecal administration of IL-1RA.[9] In another example, in a preclinical model of Hunter syndrome (MPS II, a lysosomal storage disease) where xB^3 was fused with the enzyme iduronate-2-sulfatase (IDS), the compound appeared fully active and effective in the periphery areas of the brain at levels equivalent to treatment with recombinant IDS (Elaprase®, idursulfase). The xB^3-IDS fusion protein was able to reduce hallmarks of Hunter syndrome in the brain, including cellular vacuolation (the formation of vacuoles) in brain cells and buildup of lysosomes and heparan sulfate in the brain.

The xB^3 platform technology has also been shown preclinically to deliver small molecules (eg, Adriamycine®, doxorubicin) to the brain, thereby resulting in an increase in survival in mice with intracranial glioma.[10] Preclinical data have also shown that in a mouse ischemic stroke model pre-treatment with a combination of xB^3-siRNA led to a significant reduction in brain infarct volume and an improvement in neurological deficit.

Preclinical research highlights several potential advantages in this approach, including:

- Improvements in the pharmacokinetic parameters of the payload with xB^3 peptide vectors compared to the full-length MTf vectors, including faster time to maximum therapeutic concentration and extended half-life of the payload construct. Therapeutic agents linked to xB^3 peptide vectors should have higher and more extended brain exposure than constructs with the full-length MTf protein.

- Therapeutic efficacy corresponding to the payload and no signs of toxicity, as demonstrated in various types of rodent models.

- Versatility in design, homogeneity, stability, and reproducibility from batch to batch (by fusing an xB^3 peptide vector and therapeutic payload).

- Higher levels of convenience in manufacturing and chemical manipulation with the potential to lower production costs compared to the full-length MTf protein.

POTENTIAL APPLICATIONS OF XB^3

Through continued research and refinement, the xB^3 platform technology has transitioned from a large naturally occurring human protein to its core functional 12 amino-acid peptide. Preclinical studies have demonstrated that this advanced technology outperforms TfR-based transport in both efficiency and versatility with respect to the types and sizes of payloads that can be delivered to the CNS. Development of the xB^3 peptide as the proprietary vector for brain transport has been focused on three primary disease areas: brain metastases, glioblastomas, and neurodegenerative diseases.

The xB^3 platform has the potential to support a broad range of development programs targeting effective transport of therapeutic agents through the BBB. Recently, Bioasis announced partnerships with Prothena Biosciences and Chiesi Global Rare Diseases to support their clinical research efforts. The xB^3 peptide has also been shown to penetrate the lymphatic system, demonstrating its potential applications in non-CNS indications.

Bioasis is also advancing its own internal development programs focused on orphan drug indications, including brain cancers and rare genetic neurodegenerative diseases, such as lysosomal storage disorders (LSDs) where proof-of-concept for approved medications exists and where

there is potential for more rapid development and (fast track) approval using the xB^3 peptide. Our most advanced program, xB^3-001, targets brain metastases, with the potential for rapid human proof-of-concept regarding payload brain penetration, target engagement and efficacy. Following a positive response from the FDA to pre-IND submission, Bioasis is focused on advancing the pre-clinical development of xB^3-001 toward IND filing and has initiated pilot scale manufacturing.

SUMMARY

In addition to the significant unmet needs in the rare disease sector, more patients will develop brain cancer or various neurodegenerative diseases as the population ages. Demand for new and more advanced CNS therapies will continue to expand, but the ability to meet this demand with new and proven safe and effective therapies will be limited if therapies are not able to penetrate the BBB effectively, and if they cannot be produced cost effectively. As a brain delivery vector, the xB^3 platform technology represents a promising alternative for treating CNS diseases. By transforming existing or novel non-brain penetrating therapeutics into new, more efficacious agents that can cross the BBB, this platform has the potential to support development of treatments for CNS diseases that can treat thousands of patients in the years ahead. ◆

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BIOGRAPHY

Dr. Mei Mei Tian is a Vice President and the Head of External Research at Bioasis Technologies, Inc. Dr. Tian has more than 15 years of experience working on melanotransferrin-related research in both academia and biotech. At the University of British Columbia, she investigated the role of melanotransferrin in melanoma malignancy, as well as mechanisms involved in melanotransferrin uptake in cells. Since joining the Bioasis team in 2012, she has been a significant contributor in the early development and continued expansion of our proprietary blood-brain barrier technology, xB^3. With her oncology and neurology background, she is a committed and driven individual with a passion for the success of our platform. Dr. Tian earned her PhD in Microbiology and Immunology from the University of British Columbia.

POLYMERIC DELIVERY SYSTEM

Next Generation Long-Acting Implantables Using Surface-Eroding Elastomers

By: Stephanie Reed, PhD, Carissa Smoot, and Dennis Shull

ABSTRACT

Poly(glycerol sebacate) (PGS) (Regenerez®, Secant Group) is a synthetic polyol resin that can be cross-linked using urethane chemistry to create poly(glycerol sebacate) urethane (PGSU). PGSU is a highly flexible, water-impermeable, shelf-life stable, and biocompatible elastomer that biodegrades via surface erosion. Unlike bulk-degrading polymers or non-degradable polymers that rely on diffusion, the hydrolytic surface erosion properties of PGSU confer near zero-order release kinetics, even at high-drug loadings, and maintains a near-constant release rate across drug loadings. PGSU is an attractive delivery system for very hydrophobic drugs, which otherwise may not be able to diffuse out of the matrix, and for very hydrophilic drugs, which otherwise may have an uncontrolled burst release. PGSU can be loaded with both hydrophilic and hydrophobic drugs up to 80% w/w, demonstrating minimal burst release *in vitro* and *in vivo* and sustaining release for greater than 6 months' duration. The cross-linking density of PGSU is critical to reducing fluid percolation in and API permeation out of the matrix, especially at high-drug loadings, in order to limit burst release and diffusion. PGSU ultimately offers many advantages over other polymers for long-acting implantables (LAIs), particularly for high-loading, long-duration implants that are gaining interest in the pharmaceutical industry.

THE NEED FOR AN IMPLANTABLE DRUG DELIVERY SYSTEM

Long-acting implant technology is taking center stage in pharmaceutical development. This technology is gaining traction because it allows a sustained delivery of a therapeutic drug over the course of many months and even years, improving patient compliance and comfort. Long-acting implants can also deliver drugs systemically or to a targeted site, avoid the inefficiencies of first-pass metabolism, and reduce side effects.

FIGURE 1

Drug-loaded PGSU elastomeric implant.

One of the biggest advantages of implantable drug delivery systems, whether manufactured as rods, tubes, sheets, fibers, microspheres, or coatings, is that they can be made of bioresorbable polymers. Over time, the body breaks down and metabolizes these polymers until there is no implant left to remove at the end of drug therapy.

LIMITATIONS OF CURRENT POLYMERS ON THE MARKET

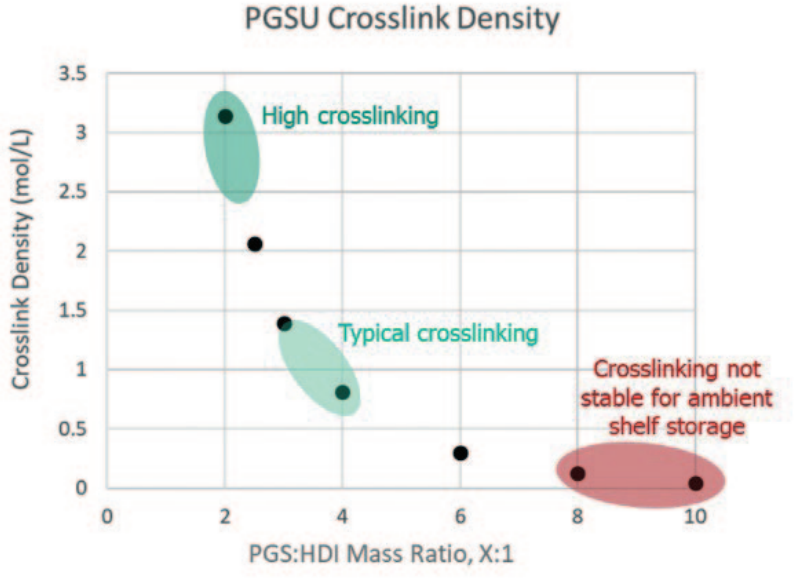
Commercially available bulk-degrading polymers, such as poly(lactic-co-glycolic acid) (PLGA), polyglycolic acid (PGA), polylactic acid (PLA), polycaprolactone (PCL), and non-degradable polymers, such as poly(ethylene-co-vinyl acetate) (EVA), polyurethane (PU), and silicone, demonstrate many limitations as drug delivery systems. Most notably, these types of polymers rely on diffusion for drug delivery; therefore, achieving high-drug loading with sustained release is challenging due to the steep concentration gradient that drives fast diffusion. With such polymers, this dose-dependent release rate is sometimes sufficient for achieving a few months of controlled release when the loading is about 40% w/w or less. Higher loadings exhibit significantly faster release rates and often only provide 1 month of controlled-release therapy.[1] These polymers can also exhibit a severe increase in stiffness at higher drug loadings, impacting patient comfort and leading to brittle fracture. Moreover, while degradation of the delivery vehicle is generally considered a market preference, bulk-degrading polymers exhibit inconsistent mass-loss behavior and, consequently, uncontrolled release. In contrast, surface-eroding polymers display a controlled and predictable volume loss over time, occurring from the outside edge slowly inward, allowing zero-order release kinetics and a dose-independent release rate.

Highly soluble active pharmaceutical ingredients (APIs) pose a challenge to non-degradable and bulk-degradable polymers because they are likely to rapidly diffuse away from the polymer matrix, causing a large burst release and fast release rate. On the other hand, poorly soluble APIs pose a challenge to non-degradable and bulk-degradable polymers because these APIs have a difficult time diffusing away from the polymer matrix, causing insufficient release following implantation. A polymeric delivery system that does not rely on diffusion and releases both highly soluble and poorly soluble APIs agnostically through surface erosion addresses an unmet market need.

CHEMISTRY OF POLY(GLYCEROL SEBACATE) URETHANE (PGSU)

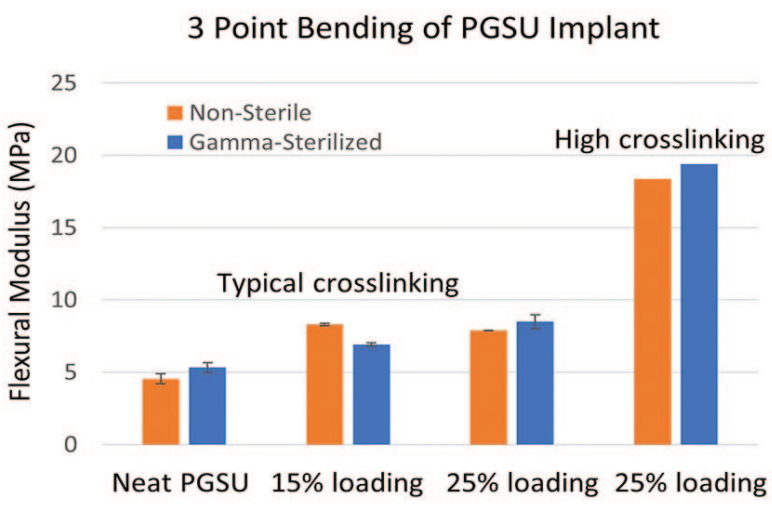
Poly(glycerol sebacate) (PGS) (Regenerez, Secant Group) is a polyester prepolymer resin synthesized by reacting glycerol and sebacic acid together in a polycondensation reaction. Secant Group's water-mediated reaction process to synthesize PGS conveys many product and manufacturing benefits.[2] PGS resin can be further cross-linked into a solid elastomer thermoset, poly(glycerol sebacate) urethane (PGSU), which is formed using urethane chemistry by reacting the PGS resin polyol with an isocyanate cross-linker and a tin-based catalyst. API is incorporated by blending the neat powder with PGS resin prior to urethane reaction. This PGSU reaction occurs within minutes at room temperature, allowing inclusion of thermolabile and form-sensitive APIs in the formulation; the process may be accelerated using mild heat. The total amount of tin catalyst used is well below the human permitted daily exposure limit, and no

FIGURE 2



How PGSU cross-linking density, as determined by an empirical swell test, relates to PGS:HDI mass ratio.

FIGURE 3



Mechanical testing results from 3-point bending applied to PGSU rod products with and without 10% to 30% w/w API loading at different cross-linking densities, before and after gamma sterilization at 18-29 kGy.

residual isocyanate is leftover after reaction completion. The end result is a drug-loaded, elastomeric PGSU implant (Figure 1).

PGS resin may be formulated solvent-free, or it can be solvated to reduce viscosity using USP class 3 solvents, such as acetone and propyl acetate. If solvents are used, residual solvent can be driven off using vacuum and mild heat at 40°C. Solvent-free and room-temperature manufacturing reduces post-processing steps and avoids detrimental changes to the API.

The mass ratio of PGS:hexamethylene diisocyanate (HDI), which can be converted to isocyanate:hydroxyl stoichiometric ratio if the polyol's hydroxyl value is known, dictates the cross-linking density obtained with PGSU (Figure 2).

Selection of an appropriate PGSU cross-linking provides a shelf-stable product that can be stored at room temperature and humidity for up to 3 years, per ICH Q1A(R2) long-term and accelerated studies. By tuning the cross-linking density, PGSU matrix permeability, elasticity, degradation, and drug release can be manipulated to desired specifications that meet the target product profile.[3]

The two-component PGSU reaction is thoroughly mixed within its pot life to achieve API content uniformity and cross-linking uniformity. High-shear mixing, achieved using speed mixers, static mixers, dynamic mixers, twin-screw compounders, or similar equipment, evenly distributes and fully incorporates both API and isocyanate into the PGS resin. One solution for fabricating PGSU implantable rods uses a dual-feed system, providing consistent and scalable manufacture. Dual-feed techniques can be scaled up and translated to a reaction injection molding manufacturing process to support global supply needs. Ultimately, PGSU and API-loaded PGSU can be manufactured into rods, tubes, sheets, fibers, microspheres, coatings, and other geometries by a variety of processing techniques, such as reaction injection molding, extrusion, casting, drawing, emulsion, spray coating, dip coating, and additive manufacturing. PGSU can be gamma irradiated as a method of sterilization without any detrimental effects to product performance.

Once implanted, PGSU is biodegradable via surface erosion, making it an excellent candidate for controlled drug release. The mechanism of surface erosion in vivo for PGSU is hydrolysis, enzymatic degradation by esterase and lipase, and oxidative degradation. By altering the cross-linking density of PGSU and stoichiometry of the starting reagent PGS resin, the elastomer's degradation rate can be tailored to match the desired duration of drug treatment. Degradation rates of 2 to 12 months are easily achievable with PGSU, spurring opportunities for many long-acting therapies.

THE ELASTICITY ADVANTAGE

As a bioresorbable urethane with tunable degradation rates, PGSU is designed to deliver API in a controlled, surface-eroding mechanism. It also provides elastomeric compliance that can be tailored to mimic the elastic properties of tissue. These properties of PGSU present a stark contrast to rigid, thermoplastic lactides and glycolides that bulk degrade and lack sufficient elasticity. For example, when PLGA and PCL are formulated with high-drug loadings, they become embrittled and prone to fracture. Under the same loadings, PGSU remains flexible and compliant.

PGSU exhibits stretchable, compressible, and bendable mechanical properties that can be tuned by changing the cross-linking density of the polymer (Figure 3). At a typical cross-linking density and up to 60% w/w API loading, PGSU demonstrates significant flexibility and resilience, where the implant can be folded in half and spring back with full elastic recovery. For-

mulating PGSU with different cross-linkings can augment the stiffness somewhat, but its flexibility remains intact. At a typical cross-linking, the bend radius of PGSU and API-loaded PGSU remains unchanged across a variety of model drugs and loadings, demonstrating mechanical compliance that is key for patient comfort when implanted subcutaneously.

BIOCOMPATIBILITY & PATIENT SAFETY INDICATIONS, INCLUDING RETRIEVABILITY

Implants often suffer from a persistent inflammatory response that leads to increased incidence of fibrosis and fibrous encapsulation, which hinders drug release rates, drug permeation into target tissues, drug distribution within target tissues, patient comfort, patient mobility, implant retrieval, and implant location identification.

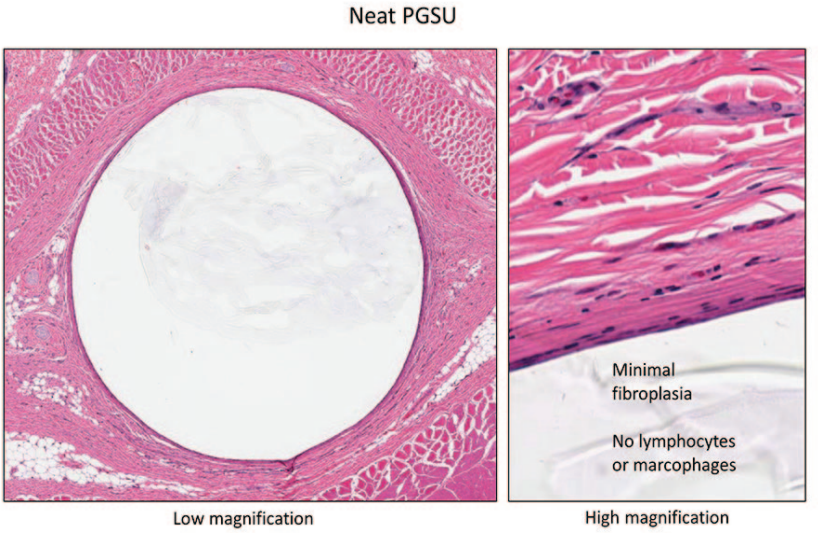
Compared to less cross-linked PGSU and even other biodegradable polymers, Secant Group's range of cross-linked PGSU results in an implantable polymer with reduced inflammatory response, complement activation, cellular attachment, and fibrous encapsulation. This may be due to fewer free functional groups present on the surface that are known to aggravate inflammatory cells, circulating cells, and local cells, and activate complement response. Another reason could be due to slower oxidative degradation, generating fewer free radicals that are known to be pro-inflammatory.[4,5] As PGSU surface erodes, the implant material remains biocompatible and non-inflammatory throughout its lifespan, leaving behind minimal changes to the underlying tissue when the implant is 100% degraded.

Unlike other PGSU processes that target lower cross-linking, the reduced cellular attachment to Secant Group's PGSU creates an implant that has minimal biological interaction with surrounding tissues and more efficient drug release unhindered by cellular adhesion and growth.[6]

PGSU demonstrates a zero-to-minimal inflammatory cell presence as indicated by the absence of lymphocytes and macrophages, minimal fibroplasia, and no fibrous encapsulation after 12 weeks of implantation (Figure 4). Additionally, PGSU demonstrates zero cytotoxicity, zero acute systemic toxicity, zero irritation, zero subcutaneous implantation side effects, and zero intramuscular implantation side effects, per ISO 10993 and USP Class VI test methods.

The surface erosion behavior of PGSU allows the implant to remain intact and retrievable for a much longer proportion of the implant lifetime compared to bulk-degrading polymers, which become soft and diffuse quickly. The retrievability afforded by PGSU is important in the instance when a patient has an adverse reaction to the API, needs to receive oral or intravenous therapy that is contraindicated with the drug delivered by the implant, needs to receive therapy that cannot additively stack with the dose delivered by the implant, or otherwise needs emergency removal of the implant for any reason.

FIGURE 4

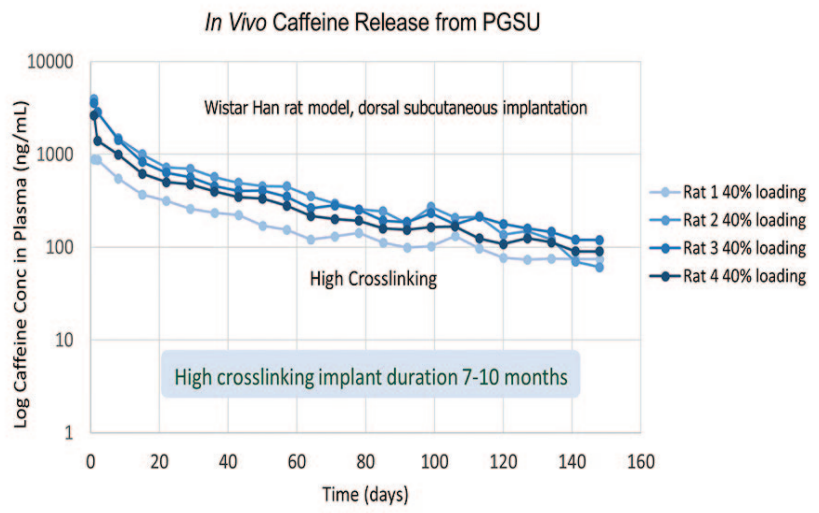


Histology at 3-month timepoint of explanted PGSU rod products with typical cross-linking density (3.5:1 PGS:HDI mass ratio), initially unloaded, and the surrounding subcutaneous tissue and underlying muscle for biocompatibility assessment. Similar results were seen at 15% and 25% loading w/w caffeine loading.

SURFACE EROSION PROVIDES LONGER-LASTING, CONTROLLED DRUG RELEASE

As a surface eroder, PGSU demonstrates the ability to maintain near zero-order release kinetics across 10% w/w to 80% w/w loadings throughout implant erosion to 100% degradation, both *in vitro* and *in vivo* with good correlation (Figure 5). The release rate of API from PGSU is dictated by the rate of surface erosion. Unlike diffusion-driven non-degradable and bulk-degrading polymers, PGSU does not experience a drug concentration gradient between the internal polymer and external environment. Accordingly, PGSU offers a

FIGURE 5



Non-cumulative release curves as plasma concentration of caffeine *in vivo* for implanted solvent-free PGSU rod products with 40% w/w caffeine loading at a high cross-linking density (2:1 PGS:HDI mass ratio).

nearly dose-independent API release rate in which higher drug loading does not significantly impact the rate constant. Cross-linking density instead drives the release rate; PGSU has been shown to maintain a near-constant release rate from 10% w/w to 80% w/w API loadings.

The surface erosion behavior of PGSU allows a therapeutic concentration of a drug to be reached immediately after implantation, in contrast to diffusion-driven non-degradable and bulk-degradable polymers. Specifically, surface erosion reduces the burst release common to hydrophilic APIs and avoids the lag effect common to hydrophobic APIs. Surface erosion allows a rapid onset of degradation at the end of the implant lifetime, reducing the tailing sub-therapeutic concentration that commonly lingers in non-degradable polymers. It also avoids dose dumping that commonly afflicts bulk-degradable polymers. Finally, as mentioned earlier, surface erosion eliminates the need for implant removal, thus improving patient experience.

ACHIEVING SURFACE EROSION AT HIGH DRUG LOADING

PGSU is water impermeable and hydrophobic, as confirmed by water permeability and water vapor transmission rate tests. PGSU is also minimally swelling, and the swelling behavior and sol content change with cross-linking density.

However, when API is loaded into the PGSU matrix, consider how drug particles may impact impermeability of PGSU. Factors such as drug solubility, distribution, particle surface energetics, particle size, loading, wetting by PGS resin, and PGSU cross-linking density all impact water permeation and percolation into and through the PGSU matrix, which in turn affects burst release and release kinetics. Permeability and percolation must be managed to ensure effective controlled drug delivery by surface erosion with minimal diffusion.

Water penetration issues can be mitigated by improving API distribution and reducing agglomerations, which results in well-dispersed API particles that are not initially interconnected so water cannot percolate in. Even with excellent API dispersion, particles can become interconnected above a certain threshold, restricting the maximum drug loading that is still deliverable by surface erosion. This is particularly true for hydrophilic APIs. For hydrophobic APIs, particle distribution and interconnectivity become less crucial due to the drugs' poor solubility and invulnerability to diffusion.

Water penetration can be further mitigated by increasing the cross-linking density, which results in a smaller polymer mesh size that hinders the permeation of water and APIs through the PGSU matrix. Increasing PGSU cross-linking slows the erosion rate of the thin polymer walls separating API particles, delaying the formation of interconnected ingress channels that emerge during degradation.

As long as the API is well-distributed and loaded below the percolation threshold, water cannot penetrate into the minimally swelling, hydrophobic PGSU matrix. Only the outer circumference of PGSU matrix is accessible by water, and thus surface erosion by hydrolysis occurs inward layer by layer.

SUMMARY

Secant Group's PGSU outperforms commercial polymers as the only implant that is simultaneously tunable, flexible, surface-eroding, and capable of sustaining release at high-drug loadings for many months. Taken together with the biocompatibility and shelf-life stability of PGSU, pharmaceutical formulators now have improved and expanded polymer options for long-acting delivery using PGSU to achieve unprecedented therapy durations and deliver challenging APIs. ◆

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BIOGRAPHIES

Dr. Stephanie Reed is the Director of Advanced Biomaterials Development at Secant Group, garnering 13-plus years of experience in biomaterial drug delivery for pharmaceuticals and medical devices. Dr. Reed earned her BS in Mechanical Engineering with a Biomedical Engineering minor at Massachusetts Institute of Technology, and her MS and PhD in Biomedical Engineering at the University of California Los Angeles.

Carissa Smoot is a Scientist II in Advanced Biomaterials Development at Secant Group. Since earning her BS in Chemistry from the University of Delaware, she has spent her time at Secant conducting and scaling polymer syntheses, optimizing polymer formulations, and developing coating technologies. She is now an integrated contributor to Secant's drug delivery platform.

Dennis Shull is an Associate Scientist in Advanced Biomaterials Development at Secant Group. He earned his BS in Biochemistry, Molecular Biology, and Chemistry from Ursinus College, and has 3-plus years of experience characterizing biomaterials and developing analytical methods for drug delivery applications.

VACCINE DEVELOPMENT

COVID-19 Vaccine Focusing on T Cells to Protect the Most Vulnerable

By: Jeffrey Wolf, MBA, JD

INTRODUCTION

As the COVID-19 pandemic persists globally, hundreds of parallel efforts are in place to develop safe and effective vaccines against SARS-CoV-2, the virus responsible for COVID-19. While most vaccines in development are targeted to protect healthy people, few are focusing on those who are most at risk. Two demographics demonstrating especially severe complications and high mortality rates are seniors and those with co-morbidities like heart failure, obesity, or type 2 diabetes.[1] Additionally, most seniors, as well as some people with co-morbidities who are immunocompromised, are less likely to gain full protection from standard vaccines. For seniors, this is because the immune system declines with age.[2] In particular, the immune system loses some of its capacity to maintain immunity to a given virus even after being vaccinated against it or becoming immune to it — as in the case of shingles, the painful condition resulting from reactivated chicken pox virus, in which seniors need a vaccine to avoid developing the disease even after having had chicken pox as a child. Similarly, in the case of COVID-19, even after receiving a traditional vaccine, seniors may risk developing virus symptoms if they encounter SARS-CoV-2 months or years later.

FOCUSING COVID EFFORTS ON SENIORS WILL GO A LONG WAY

With these challenges in mind, Heat Biologics is collaborating with the University of Miami Miller School of Medicine to develop a COVID-19 vaccine designed specifically for seniors and those with co-morbidities, the groups who are both especially vulnerable to COVID-19 and who are less likely to respond to traditional vaccines. Our vaccine is designed to add an extra layer of protection in the form of long-term T cell-mediated immune memory. If the vaccine is ultimately approved, it can be given along with other available vaccines as a second line of defense, or it may be given some time after initial vaccination as a booster shot.

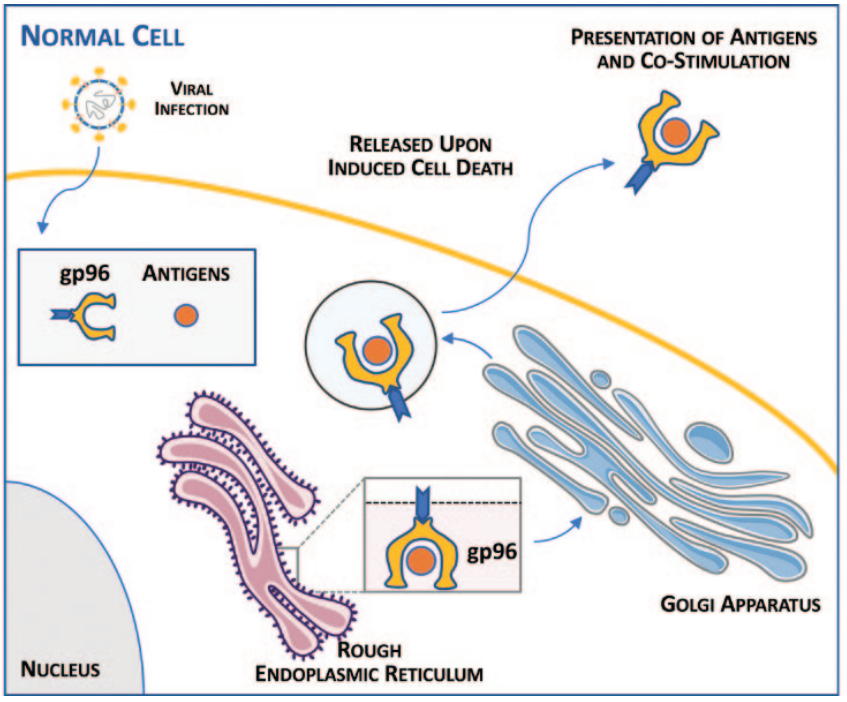
We've built a technology platform for use against cancer and infectious disease based on an immunostimulatory protein called gp96. As the COVID-19 pandemic began escalating in early March, we quickly co-opted our existing gp96 platform to target the SARS-CoV-2 virus in addition to continuing ongoing clinical-stage programs in cancer.

GP96 HARNESSES T CELL-MEDIATED IMMUNE RESPONSES

In the human immune system, gp96 is a chaperone protein — a protein that helps newly made proteins fold into active configurations. It also serves as a potent immune stimulator, or adjuvant, and immune memory inducer. gp96 is normally tethered to the inside of the cells it inhabits and is only released from cells in the event of cell death, or necrosis. Upon necrosis, gp96 molecules display/deliver any proteins or antigens they are carrying to the immune system's dendritic cells. Those dendritic cells stimulate a powerful, specific, and lasting B cell- and T cell-mediated immune response to those antigens.

Necrosis is brought on by adverse conditions, like infection, in the cell, so gp96 acts to "alert" the immune system to agents like tumor markers or viral proteins that may have caused a given cell's death. In this way, gp96 functions as a potent immune warning system that induces immunity against necrosis-causing agents like cancer or pathogens. Importantly, by activating and expanding B and T cell populations, gp96 can upregulate both humoral (antibody) and cell-based immunity, respectively: B cells produce antibodies against a pathogen, while T cells differentiate into both CD8+ T cells that can kill pathogens and CD4+ T cells that "remember" pathogens upon later exposure.

FIGURE 1



GP96 IN CANCER

Our proprietary gp96 vaccine platform comprises whole cells, injected under the skin, that continually secrete a modified version of gp96 that can leave the cell at any time. These cells also continually express antigens of interest, related to a cancer type or infectious disease, which gp96 molecules bind and carry out of the cell. As with gp96's native behavior, gp96 secreted by any of Heat Biologics' vaccines display those bound antigens to the dendritic cells that traffic at high density under the skin, thereby eliciting a powerful immune response.

Heat Biologics' gp96 platform underlies the company's lead cancer immunotherapy programs: its Phase 2 asset (HS-110) is currently being evaluated in non-small cell lung cancer, and its Phase 1 asset, HS-130, is being evaluated in solid tumors. Altogether, the platform has been tested in over 300 patients in clinical trials, with broad T cell activation shown to date.

CO-OPTING PLATFORM TO FIGHT COVID-19 THROUGH T CELLS

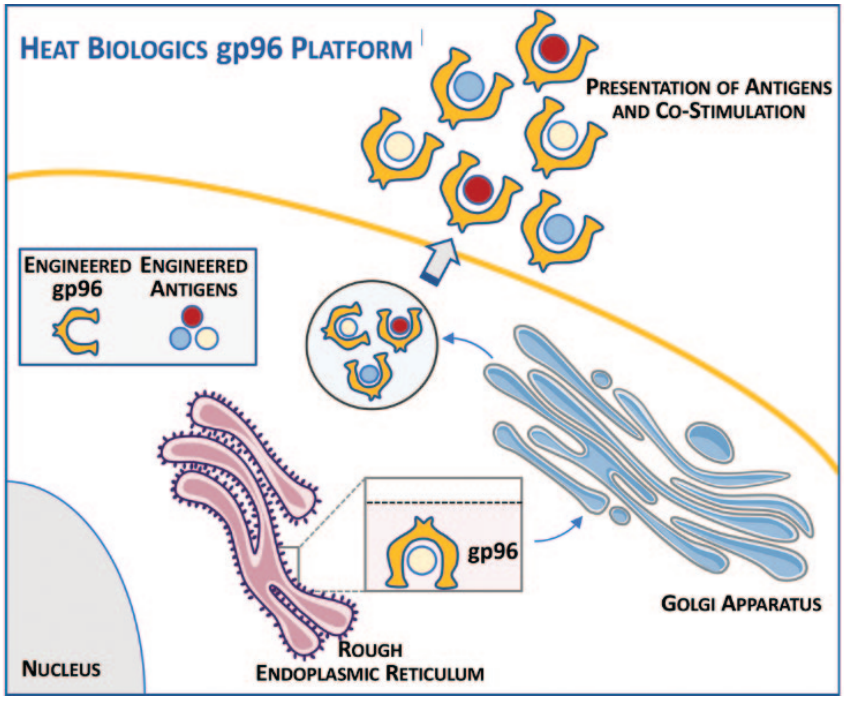
The gp96 platform can be co-opted to target a wide variety of cancers or infectious diseases by transfecting a cell line already expressing Heat's modified gp96 with a carefully chosen set of antigens from each target disease of interest. In the case of Heat Biologics' COVID-19 vaccine program, selected viral antigens from SARS-CoV-2 were transfected into a proprietary human cell line.

This is not the first time that Heat Biologics' technology has been harnessed in infectious disease rather than cancer: it has also been co-opted in National Institutes of Health (NIH)- and Department of Defense (DOD)-funded mouse and non-human primate trials in simian immunodeficiency virus/HIV, Zika virus, and malaria. All studies demonstrated that the gp96-based technology stimulated both B and T cell-mediated immune responses in different target tissues and organs, including the gut, reproductive tract, and liver.

When Heat Biologics began a COVID-19 vaccine collaboration in March of this year, the company joined forces with a team of scientists led by Natasa Strbo, MD, DSc, research assistant professor of microbiology and immunology at the University of Miami Miller School of Medicine. Dr. Strbo has co-developed the gp96 platform and led the aforementioned animal studies in infectious disease.

At the outset, Heat Biologics' COVID-19 vaccine candidate was developed with findings from previous immunological studies in mind in order to help populations like seniors and the immunocompromised to achieve long-lasting immunity they would otherwise be unlikely to attain. While most COVID-19 vaccines in development — and, in fact, most vaccines in

FIGURE 2



general — are designed to generate immunity primarily through activating B cells that produce antibodies against the virus, such immunity tends to be either relatively short-lived or insufficient for full immunity.

In the case of COVID-19, antibody levels in the blood have been shown to wane on the scale of months after infection.[3] Such candidates fail to account for the importance of longer-term adaptive immunity provided by activated T cell populations, which is also the component of immunity that is known to decline with age in the absence of specific boosts from vaccines. T cell responses are critical for directly killing virus-infected cells, producing highly specific antibodies and for long-term immune memory on the scale of years.[4] An ideal vaccine, particularly for seniors and the immunocompromised, would provide long-term immunity by stimulating a coordinated response between both the innate and adaptive arms of the immune system, in which "helper" CD4+ T cells aid B cells in producing highly specific antibodies while activating "killer" CD8+ T cells that kill virus-infected cells.[5] Memory T cells are likely crucial for long-term immunity as well, as suggested by their correlations with patients who recovered from infections with SARS-CoV-1, a related coronavirus outbreak, in 2003.[6]

Heat Biologics' scientists relied on their own experience in developing a product that stimulates such a coordinated response: the company's gp96-based cancer immunotherapy candidate HS-130 activates both CD4+ and CD8+ T cells as well as antibodies that neutralized infection. Similarly, Heat's COVID-19 vaccine candidate is designed to protect against COVID-19 infection if people are exposed to the virus months or even potentially years after vaccination.

Notably, as several developers advance COVID-19 vaccine candidates in parallel, multiple vaccines will likely become available to the public in a staggered fashion, meaning that people may face uncertainty about whether to try the first vaccine available to them or to wait for subsequent options. Heat Biologics' vaccine is designed be administered either in place of or in addition to other vaccines, as a primary or as a booster, thereby complementing or adding to other vaccines' strengths as needed; this particular candidate will not add complexity to a person's choices for themselves or their families.

PRECLINICAL DATA SHOWS T CELL EXPANSION

Since March, Heat Biologics and UM collaborators have already designed and optimized the vaccine and conducted preliminary in vitro and in vivo studies. Recent results from a study in mouse models are highly encouraging, demonstrating robust T cell-mediated immune responses directed against SARS-CoV-2's S glycoprotein, or spike protein.

After a single injection, the vaccine induced the expansion of both "killer" and "memory" CD8+ T cells, as well as "helper" CD4+ T cells, which aid in producing antibodies. Importantly, the memory CD8+ T cells in particular were found to migrate to the lungs and airways - the tissue specific sites of interest for SARS-CoV-2 infection. Such mucosal immunity is critical in mounting an immune response to respiratory viruses like SARS-CoV-2. Taken together, these results meet several requirements for further study, and potentially offer long-lasting T cell-mediated immunity for people who need it most.

MOVING FORWARD

With preclinical data in hand, Heat Biologics has made preparations for man-

ufacturing the vaccine at sufficient scale to conduct clinical trials — a non-trivial matter when it comes to cell-based products, which require especially delicate scale-up and preservation. The company is partnering with Waisman Biomanufacturing, part of the Waisman Center at the University of Wisconsin-Madison, for Phase 1 and 2 clinical trials. Phase 1 trials could begin in early 2021, and UW–Madison may also serve as a trial site. Waisman previously produced therapies for Heat Biologics' clinical trials, so preparations are already in place to quickly begin producing a COVID-19 vaccine.

The company aims to test the vaccine in humans, beginning with standard Phase 1 trials in healthy volunteers. Clinical trial administrators will collect as much data through remote or virtual methods as possible using telemedicine appointments and electronic surveys, in alignment with current FDA guidance. Once safety is established in the healthy volunteers, the company plans to narrow its focus to seniors and high-risk people with co-morbidities by enrolling subjects through veteran affairs hospitals, and large hospital systems in the US to ensure that the vaccine can be evaluated in its target demographics, not just baseline healthy subjects.

CONCLUSION

As COVID-19 continues to spread, it disproportionately harms seniors and those with co-morbidities, who are unlikely to gain protective immunity from many of the vaccines currently in development. We are advancing a COVID-19 vaccine designed to overcome the immune deficits that make those populations vulnerable to the disease. The vaccine is designed to stimulate a coordinated adaptive immune response by focusing on a T cell expansion in addition to immediate antibody production, with the ultimate objective of generating long-term immunity for people who need it most. ◆

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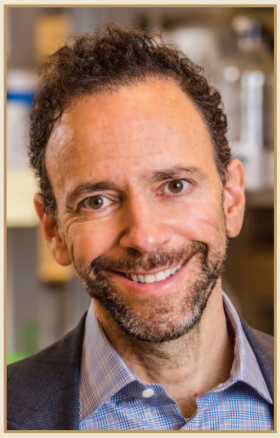
BIOGRAPHY



Jeffrey Wolf is Founder, Chairman, and CEO of Heat Biologics. He also founded Seed-One Ventures, a firm focused on the systematic formation and management of new biomedical companies based upon breakthrough research. Throughout his career, Mr. Wolf has specialized in building new life-science companies from the ground up and has played an active role in supporting the growth of his companies. Mr. Wolf's start-ups include Avigen (Co-founder and Director), a NASDAQ-listed gene therapy company; TyRx Pharma (Co-founder and Chairman), which was focused on the development of novel bio-compatible polymers and recently sold to Medtronic and EluSys Therapeutics (Founder and CEO), focused on the development of novel antibodies against infectious diseases. Mr. Wolf earned his MBA from Stanford Business School, his JD from New York University School of Law, and his BA from the University of Chicago, where he graduated with honors in Economics.

Drug Development
EXECUTIVE

Leandro Moreira

Senior Vice President, Marketing & Business Development

Yourway

YOURWAY
THE BIOPHARMA SERVICES COMPANY

Yourway: Supporting COVID-19 Studies and Vaccine Distribution

The global pharmaceutical cold chain logistics market is poised to grow by $9.48 billion from 2020-2024, driven by the increasing need for transporting temperature-sensitive drug products.[1] This is a need exacerbated by the COVID-19 pandemic and the race to develop and ultimately distribute temperature-sensitive vaccines on a global scale.

Managing complex storage and distribution projects with very strict temperature management and handling requirements has been part of Yourway's core service offering since its founding in 1997. The company provides validated storage to accommodate temperature ranges from -185°C to ambient temperature. In addition to storage capabilities, the Yourway global transportation network facilitates transporting products that require strict temperature-controlled management worldwide, including transportation to and from remote locations.

Drug Development & Delivery magazine recently spoke with Leandro Moreira, senior vice president, Marketing and Business Development, Yourway, to find out what role the company will play in globally transporting COVID-19 vaccine(s), how Yourway is gearing up for this project, and the challenges of this extraordinary task.

Q: How would you describe Yourway's role in the life sciences industry? What need are you filling?

A: Yourway is a single-source packaging and supply chain partner that offers a full range of services, including primary and secondary clinical packaging, temperature-controlled logistics, and storage and distribution services for the global pharmaceutical and biotech industries. Clients enjoy the convenience of having one service provider and one project manager assigned to coordinate the planning and execution of services to assist them in properly solving the operational and regulatory complexities associated with each project. Clients appreciate the fact they can rely on Yourway's unique ability to provide integrated and comprehensive services such as:

- Procurement of comparator drugs and ancillary supplies;
- Primary and secondary packaging;
- Translation services;
- Label and booklet printing;
- Qualified Person (QP) releases;
- Importer of Record (IOR) and customs brokerage services;
- Specialized temperature-controlled transportation and storage for all temperature ranges from -180°C to controlled 15°C to 25°C;
- Temperature-controlled storage at one of our 21 global GMP depots strategically located in all continents; and
- Returns and destruction services with full accountability.

Q: What is Yourway's business model? And what sets Yourway apart from its competitors?

A: Unlike other players in the life sciences logistics space, Yourway offers highly personalized services to drive efficiency through quality and compliance. We provide integrated services such as transportation, clinical packaging, and comparator sourcing. Other companies usually provide one service or the other. We have the bandwidth of a large firm, but remain attentive and responsive to our customers' individual needs. We offer true one-on-one customer service that ensures high-quality, responsive, tailored support from start to finish. As importantly, our people have decades of experience in pharmaceutical logistics and are the key to our rapid growth. They help clients optimize resources and ensure adoption of the most efficient clinical trial logistics strategies. Indeed, many virtual pharma companies turn to Yourway to manage their entire logistics programs.

Time is of the essence in drug development and commercialization. At Yourway, we always operate with the mentality that every project is urgent, whether it is a transportation project, a clinical packing project or any number of services we provide. This approach gives us the necessary agility to excel during normal conditions and during challenging times such as the current pandemic. As a result, Yourway has become a natural choice for clients in need of support for various studies currently in place, including trials focusing on the development of therapies to combat COVID-19.

Being first to the clinic and first to market is essential in the industry today. As such, the greatest benefit Yourway provides to our customers, which range from small virtual biotechs to mid-size and large pharma companies, is shortened turnaround times. We are structured to get materials out the door today – never tomorrow. Our mentality that everything is urgent is well aligned with the need to get vaccines distributed fast and efficiently as soon as they are approved.

Q: What role will Yourway play in COVID-19 vaccine distribution?

A: Yourway's temperature-controlled management services cover storage, pick-up through delivery, and include monitoring and gel pack or dry ice replenishment. Our capabilities, network, and experience are paramount to the efficient distribution of vaccines because they require strict temperature management and speedy deliveries. We have vast experience handling ambient and controlled-ambient, refrigerated (2°C to 8°C), and frozen (-20°C to -80°C) products using both passive and active temperature-controlled systems.

In addition to storage and distribution, our worldwide services also include documentation support and the provision of regulatory advice regarding country-specific requirements. Customs fees are managed proactively and paid by Yourway, regardless of the cost – shipments are never held up waiting for the client to pay fees. Overall, Yourway's proactive management approach helps our clients meet their targets.

Our team of temperature-controlled transportation specialists is highly experienced in supporting client needs for the storage and transportation of Phase 1, 2, 3, and 4 materials, production raw materials, and finished goods, including

vaccines. Throughout the current global pandemic, Yourway has remained fully operational, providing reliable distribution of medicines and clinical trials materials, including COVID-19-related trials. Yourway's capabilities and experience will be extremely valuable when it is time to distribute the vaccines.

Q: How is Yourway preparing for this distribution?

A: We have been expanding our temperature-controlled storage footprint by adding extra storage capacity for products requiring all temperature ranges. In anticipation of increased demand for storage of vaccines requiring -80°C, -30°C, -20°C, and 2°C to 8°C, we have been creating the necessary capacity to fulfill clients' needs. For our transportation services, our staff is properly trained to coordinate shipments of any size destined for anywhere in the world. We have the reputation of performing well under challenging circumstances, including strict timelines and highly complex requirements. That is one of the reasons why we have been chosen by several organizations to ensure their projects remain free of disruption during the pandemic and moving forward. We have been supporting several COVID-19 clinical studies and are well positioned to provide storage and distribution services once vaccines are approved.

Q: What are the challenges of a global vaccine distribution and what have you put in place to overcome these obstacles?

A: Several COVID-19 vaccines being developed will need to be kept at temperatures as low as -80°C from the moment they are bottled until they are administered to patients. Of the three vaccines that have advanced to Phase 3 trials, two need to be kept in a near-constant deep freeze. As an example, Pfizer projects its vaccine will need to be stored in temperatures as low as -80°C, while Moderna's vaccines will need to be kept at -20°C. AstraZeneca and Oxford University expect that their vaccines must be kept cool, but not frozen. These vaccines will need to be transported to patients in all corners of the world.

Q: How will Yourway work with governments and industry stakeholders for quick and efficient transport of COVID vaccines?

A: In addition to having our capabilities, processes, and network properly validated and already in place to fulfill requests for immediate storage and transportation of COVID-19 vaccines, understanding local regulatory requirements and region-specific challenges is key to successfully transport vaccines to various global locations. Overall, Yourway's proactive management approach helps our clients avoid delays of all kinds during the shipment of these critical vaccines. Our worldwide service also includes documentation support and the provision of regulatory advice regarding country-specific requirements. Customs fees are managed proactively and paid by Yourway – regardless of the cost – to ensure shipments are never held up waiting for the client to pay fees.

Q: In addition to time- and temperature-sensitive distribution, what other precautions do you need to consider when transporting a vaccine?

A: In addition to disciplined temperature-controlled management, cGMP- and cGDP-compliant handling are paramount to ensure overall product integrity. Supply chain security will also be a must. Vaccines will be in very high demand, thus a likely target for theft and diversion.

Access to airfreight capacity and reliable storage and transportation networks will play a critical role to support the distribution of vaccines around the world. Complex logistical solutions, understanding of regulatory requirements and how to properly comply with them, stakeholder engagement, and solid experience with temperature-controlled methods will be key to ensure that vaccines are quickly and efficiently transported globally, immediately after they have been approved.

Yourway's cGMP- and cGDP-compliant processes, access to airfreight capacity and transportation networks, disciplined protocols to efficiently manage projects requiring complex temperature-controlled storage and transportation, combined with existing procedures to enforce chain-of-custody and chain-of-identity will be critical to help protect overall product integrity and create barriers to help prevent cargo theft and counterfeiting. ◆

Reference

1. Global Cold Chain Logistics Market for Pharmaceuticals Industry 2020-2024, Technavio Research, Jan. 24, 2020, https://www.businesswire.com/news/home/20200124005130/en/Global-Cold-Chain-Logistics-Market-for-Pharmaceuticals-Industry-2020-2024-Evolving-Opportunities-with-Agility-Public-Warehousing-Co-K.S.C.P-and-Deutsche-Post-AG-Technavio.

COMPANY DESCRIPTION

AbbVie is devoted to the discovery, development, manufacturing, and marketing of products that span the continuum of care in pharmaceutical therapies. Leading-edge science and technologies that hold the potential for improving lives are advanced through AbbVie's dedication to research. Our uniqueness is created by the work we do - producing innovative medicines, continually investing in our pipeline, and giving back to create healthier, more vibrant communities. We have sustained our success by staying true to the key principles on which our company was forged: innovative care and a desire to make a meaningful difference in all that we do.

COMPANY BACKGROUND

AbbVie has a rich heritage of developing and producing pharmaceutical products for more than 130 years. By choosing AbbVie Contract Manufacturing, your team gets so much more than the typical CMO engagement. Alongside our state-of-the-art cGMP manufacturing facilities, AbbVie's partners gain integrated access to deep scientific expertise and processes that have successfully supported many small molecule and biologic medicines through to commercialization.

SERVICES

AbbVie's Contract Manufacturing Business has been serving our partners for more than 40 years. Our contract development and manufacturing capabilities span across 11 production facilities in North America and Europe. Our capabilities are:

- Aseptic Fill Finish (Vial and Prefilled Syringe)
- Custom API & Bulk Manufacturing
- Oral Solid Dose
- Fermentation
- Hot Melt Extrusion
- Potent
- Biologics
- Packaging

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CONTRACT MANUFACTURING

Biologics | Aseptic Fill Finish | Drug Product | Potent
Hot Melt Extrusion | Fermentation | ADCs | APIs

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Experience Unrivaled

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Enable your product to commercial success by leveraging our pharmaceutical and CMO expertise.

CMO LEADERSHIP AWARDS2020 CAPABILITIES

CMO LEADERSHIP AWARDS2020 COMPATIBILITY

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ABITEC CORPORATION
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ABITEC Corporation is dedicated to the advancement of essential **bioavailability enhancement** and formulation development technology. ABITEC develops and manufactures lipid-based excipients to enhance the bioavailability of poorly water-soluble and poorly permeable Active Pharmaceutical Ingredients (APIs) for the pharmaceutical industry.

ABITEC has an expansive portfolio of **CAPMUL**® bioavailability enhancers, which are medium-chain mono- and di-glycerides and propylene glycol esters. These functional lipid excipients act as solubilizers and emulsifiers in oral, topical, transdermal, and parenteral drug delivery systems. CAPMUL excipients are recognized as the ideal starting point when formulating BCS Class II & IV (poorly water soluble) and BCS Class III & IV (poorly permeable) molecules. Lipid-based drug delivery systems may be formulated as liquid or semi-solid formulations for oral dosage forms, as well as creams and ointments for topical and transdermal applications.

Whenever necessary, CAPMUL-based formulations may be customized with the inclusion of **CAPTEX**® medium-chain triglycerides and/or **ACCONON**® non-ionic surfactants, added for enhanced bioavailability.

ABITEC's **INJECTA**™ parenteral-grade lipid excipients to enable improved solubilization and permeation for injectable APIs. The INJECTA-grade portfolio of products include: CAPTEX medium-chain tri-glycerides, CAPMUL mono-and di-glycerides of glycol esters, and ACCONON non-ionic surfactants, fully analyzed and packaged for parenteral application.

ABITEC manufactures high-quality lipid excipients for drug delivery applications in accordance with strict cGMP and applicable IPEC (International Pharmaceutical Excipient Council) guidelines in ISO-certified facilities. ABITEC's customer-preferred portfolio of pharmaceutical excipients are monograph compliant, supported by drug master files (DMFs), and have precedence of use. For more information about all of ABITEC's invaluable solutions please contact us directly or visit our website at www.abiteccorp.com.

Creating Value Through Acquisition

We are excited to announce the recent acquisition of Larodan AB, a manufacturer and international marketer of state of the art, high-purity research grade lipids. This strategic acquisition will expand ABITEC's functional lipid product offerings and scientific capabilities to better serve the pharmaceutical, nutritional, and industrial market sectors.

Dosage Forms Include: Oral, Injectable, Topical & Transdermal, Suppositories, Ophthalmic, and Inhaled

Applications Include: Solubilization, Emulsification, Lubricating Dry Binder, Permeation Enhancement, Encapsulation, Controlled Release, and Self-Emulsifying Drug Delivery Systems

To Request a Sample – visit https://samples.abiteccorp.com/

Social Media Links:

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ABITEC
AN ABF INGREDIENTS COMPANY

FUNCTIONAL LIPID EXCIPIENTS

Breaking the barriers of drug delivery

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Adare Pharma Solutions is a global technology-driven CDMO providing turnkey product development through commercial manufacturing expertise focused on oral dosage forms for the Pharmaceutical, Animal Health, and OTC markets. Adare's specialized technology platforms provide taste masking, ODTs, and customized drug-release solutions. With a proven history in drug delivery, Adare has developed and manufactured more than 40 products sold by customers in more than 100 countries globally.

FACILITIES

Adare Pharma Solutions has four sites located in the US and Europe with over 600 employees worldwide. We have the expertise to take your project from formulation development through commercial-scale manufacturing. Our sites are compliant with cGMP criteria and approved to handle controlled substances and maintain excellent environmental credentials. Our in-house regulatory and quality teams have a proven global track record with the FDA, AIFA in Italy, EMA in Europe, and ANVISA for Brazil

ADARE'S SPECIALIZED TECHNOLOGIES INCLUDE:

The Parvulet™ Technology is a patient-centric dosage solution that enables a solid powder or tablet to convert to a semi-solid in the presence of water within 30 seconds. The final dosage is easily administered as a soft food like texture, which is ideal for pediatric and geriatric populations (including those with dysphagia).

Microcaps® Taste Masking Technology achieves uniform and efficient coating of drug particles by a combination of coacervation (phase separation) and spray coating to build polymeric membranes of varying porosity and thickness. The Microcaps technology can be applied to multiple dosage forms and immediate- and modified-release profiles.

AdvaTab® Orally Disintegrating Tablets (ODTs) incorporates coated or uncoated drug particles that are uniformly dispersed in a low-moisture, rapidly disintegrating matrix. Each ODT is formulated to achieve an acceptable taste and desired release profile. This technology can be combined with Microcaps® and Diffucaps® to create IR or controlled-release ODTs.

Diffucaps® Customized Release Technology has the flexibility to incorporate functional, release-controlling polymers or protective coatings onto drug-layered cores, granules, or crystals. Beads can have different release profiles, different active ingredients, or both — all in one product.

MMTS™ Multi Mini Tablet System Customized Release Technology combines the simplicity of a tablet formulation with the flexibility of multiparticulate dosage forms with high drug-loading capability. Adare has developed Ultra Microtablets — a smaller standard of tablets targeting diameters in the range of 1.2 mm to even 1.0 mm. The small size facilitates the development of products that can offer multiple drugs or varying release profiles within a single capsule.

The DIFFUTAB® Technology is an effective solution for targeted drug delivery through customized and sustained release. The technology assists the development of high-dosage and sustained-release products for once-daily administration. A matrix tablet is coated with functional polymers, followed by a blend of hydrophilic and hydrophobic polymers. Layered erosion and diffusion of the drug matrix tablet result in a controllable release.

Precision Particle Fabrication® Technology produces uniform microspheres and microcapsules with narrow size distribution and precise control over particle structure. The platform technology is flexible and customizable to accommodate a broad range of active ingredients, including small molecules, peptides, and proteins. The technology includes three platforms: Optimμm®, for oral delivery; Stratμm™, for injectable delivery; and Unisun®, for otic delivery.

ADARE PHARMACEUTICALS IS NOW ADARE PHARMA SOLUTIONS

DIFFERENT NAME. SAME CUSTOMER FOCUS.

Adare Pharma Solutions is a global, technology-driven CDMO providing turnkey product development through commercial manufacturing expertise focused on oral dosage forms for the Pharmaceutical, Animal Health and OTC markets. Adare's specialized technology platforms provide taste masking, ODTs, and customized drug release solutions. With a proven history in drug delivery, Adare has developed and manufactured more than 40 products sold by customers in more than 100 countries globally.

Now you can put Adare's formulation technologies and manufacturing expertise to work for you.

EMAIL BUSDEV@ADAREPHARMA.COM TO SPEAK WITH ONE OF OUR EXPERTS AND LEARN MORE ABOUT OUR TECHNOLOGIES AT ADAREPHARMASOLUTIONS.COM

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Company Description

Ajinomoto Bio-Pharma Services is a fully integrated contract development and manufacturing organization, with sites in Belgium, United States, Japan, and India, providing comprehensive process development services, cGMP manufacturing, and drug product fill finish services for small and large molecule APIs and intermediates.

Ajinomoto Bio-Pharma Services offers a broad range of innovative platforms and capabilities for pre-clinical and pilot programs to commercial quantities, including Corynex® protein expression technology, oligonucleotide synthesis, antibody drug conjugations (ADCs), high potency APIs (HPAPIs), continuous flow manufacturing, and more. Ajinomoto Bio-Pharma Services is dedicated to providing a high level of quality and service to meet our client's needs.

Ajinomoto Bio-Pharma Services is your trusted manufacturing partner providing a broad range of capabilities, regulatory excellence, and extensive experience, helping you navigate production challenges, providing solutions to your development process, and delivering your new therapies to patients who need it most.

MARKETS SERVED

Our integrated global network for large and small molecule development and manufacturing has sites in Europe, North America, and Asia, providing the infrastructure and local support to meet your drug process development and manufacturing needs.

SERVICES & CAPABILITES

Phase-Appropriate Services: Our complete range of process and analytical development capabilities offer the tools to address your needs, whether it is producing small quantities for early testing or in developing robust, reliable, and scalable processes that will enable a strong commercial advantage.

Broad Range of Capabilities: Over 40 years of CDMO experience providing a range of manufacturing capabilities enables us to deliver the flexibility and guidance to meet different drug product needs from emerging therapeutics to life cycle management.

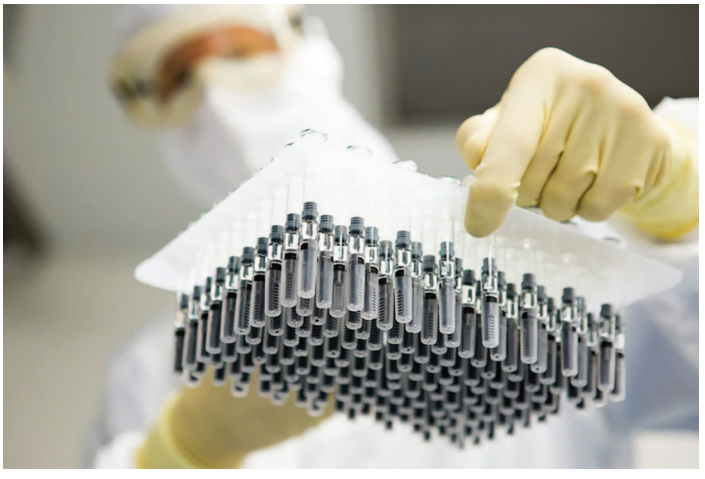
- Drug product aseptic fill finish
- Small molecule manufacturing
- Large molecule manufacturing
- Oligonucleotide and peptide synthesis
- ADC development and manufacturing

Advanced Technologies: Our services are enhanced by a portfolio of innovative and advanced technologies that enable robust, scalable, cost- and time-efficient processes for large and small molecule manufacturing. We are continuously developing new solutions to improve manufacturing processes.

Regulatory Support: With and impressive and successful track record, we are well positioned to advise you on regulatory strategies and navigate hurdles to achieve your program goals. We provide strong, yet flexible quality management to ensure continued program success.

EXPERIENCE THE POWER TO MAKE

We have the capacity and know-how to manage projects from preclinical stage to commercialization successfully, but what truly differentiates us is our dedication to quality and our commitment to fostering trusted partnerships. We're looking forward to hearing from you.



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ABOUT US

Partnering with Alcami connects you to a team of highly intelligent-problem solvers that can advance your product through every stage of the development lifecycle. With over 300,000ft² in the US, our team of 700 professionals across four US scientific campuses serves biologics and pharmaceutical companies of all sizes.

Leveraging over 40 years of experience, Alcami provides customizable and innovative solutions for formulation development, analytical development and testing services, clinical and commercial finished dosage form manufacturing (oral solid dose and parenteral), packaging, and stability services. Whether you are a virtual start-up or a large organization, we can help you deliver breakthrough therapies to patients faster.

ANALYTICAL SERVICES

Our network of cGMP centers offer comprehensive testing services for new drug entities, generic drugs, animal health products, over the counter medications, chemicals, and biopharmaceuticals.

- Analytical development and validation for small and large molecules/biopharmaceuticals
- Environmental monitoring and cleanroom services
- Routine compendial chemistry
- Microbiology testing including rapid sterility and microbial in-use studies
- ICP-MS capabilities including elemental impurities, catalyst control, organometallics, and assays
- Abuse-deterrent studies, pediatric food studies, and additional specialty services
- Stability storage and testing

ORAL SOLID DOSE MANUFACTURING

Alcami can formulate and engineer robust, scalable manufacturing processes to supply your clinical and commercial oral solid dose manufacturing needs.

- Clinical formulation development and commercial dosage form design
- Low shear, high shear, spray granulation, roller compaction, and direct compression
- Powder in capsule/bottle, modified release, minitabs, sprinkle capsules, orally disintegrating, chewable, and other pediatric and specialty dosage forms

PARENTERAL MANUFACTURING

We provide customizable formulation development and sterile fill-finish manufacturing support for small and large molecules from preclinical product development through commercial launch and supply.

- Liquid and lyophilized
- Pre-filled syringes/vials
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- Formulation development of parenteral dosage forms and placebos

PACKAGING & LABELING

Custom packaging services available from stand-alone projects through full development programs.

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- Labeling
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Whether you are a virtual start-up or a large organization, you and your patients deserve subject matter experts who take ownership of your program from clinical trials through commercial supply.

Partnering with Alcami as your contract development and manufacturing organization connects you to a US-based team of dedicated professionals with over 40 years of experience advancing products through every stage of the development lifecycle.




DEVELOPMENT | STERILE FILL-FINISH | ORAL SOLID DOSE | TESTING

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ARL BIO PHARMA

CORPORATE DESCRIPTION

ARL Bio Pharma is a contract laboratory that provides analytical and microbiological testing to pharmaceutical companies and research scientists. Our laboratory is headquartered in Oklahoma City, Oklahoma, and serves over 3,000 clients nationwide. Since 1998, ARL has supported the industry-wide commitment to deliver high-quality therapeutic drug products by providing guidance and test services for all phases of the product lifecycle following USP, FDA, and ICH guidelines.

Whether you are an innovator or pharmaceutical manufacturer, we provide the testing needed to get your protein therapeutics and cell and gene therapies to market. ARL's dedicated team oversees the entire process from understanding your product goals to providing results and helping interpret the data.

ARL is FDA registered and audited, ISO 17025 accredited and DEA licensed for Schedules I through V. Our laboratory maintains programs that support continuous improvement yielding over 20 years of quality service through experience and excellence.

SERVICE HIGHLIGHTS

ARL offers a breadth of testing services on small molecules, biologics, proteins and peptides:

Analytical Testing to verify drug product chemical and physical properties:

- E. Coli and CHO Host Cell Proteins
- E. Coli Residual DNA Quantification
- CHO Residual DNA Quantification
- Human Residual DNA Quantification
- DNA-Protein Binding Detection
- Protein Aggregation
- Protein Size and Charge Variant
- Stability Studies
- Method Development and Validation
- USP Monograph Testing
- Y-Site Compatibility Studies
- Dissolution
- Pre-clinical and Clinical Trial Testing

Microbiology Testing to verify drug product microbiological properties:

- USP <61> Microbial Enumeration
- USP <62> Specified Organisms
- USP <71> Sterility
- Rapid Sterility
- USP <85> Endotoxin
- Bacterial Residual RNA Quantification

For more information about our services, visit www.arlok.com or email info@arlok.com to request a quote.

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Although meeting physically at conferences, trade shows and corporate facilities has been significantly changed, Drug Development & Delivery has remained open and committed to providing digital and print solutions for drug developers around the world.

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ASCENDIA PHARMA

Delivering Sophisticated Formulations

Ascendia Pharmaceuticals is a speciality contract development and manufacturing (CDMO) organization dedicated to developing enhanced formulations of existing drug products, and enabling formulations for pre-clinical and clinical stage drug candidates. We specialize in developing formulation solutions for poorly-water soluble molecules and other challenging pharmaceutical development projects. Combining our extensive knowledge and experience of formulation capabilities with our suite of nano-particle technologies, we can assess the feasibility of a broad array of robust formulation options to improve a drug's bioavailability. Thusly decreasing the amount of drug and the number of injections, as well as, greatly reducing in some cases the daily pill-burden from 20 to 4. Ascendia's expertise spans across (IV, SC, or IM), injection, ophthalmic, transdermal, nasal delivery, along with immediate and controlled-release products for oral administration and complex generics. We execute rapid, comprehensive, and cost-effective programs for our clients and partners that exceed expectations.

Ascendia provides turn-key development services - analytical testing/validation; pre-formulation development and modeling, formulation proof-of-concept, development, and optimization; and cGMP manufacturing/release of clinical trial materials (CTM). Our projects range from discovery-stage molecules (NCEs), to life-cycle-management projects (505b2s).

Our areas of formulation expertise include nano-particle engineering (milled crystals and solid-lipid particles), stable oil-in-water nano-emulsions (using no organic co-solvents), amorphous solid dispersions (both hot melt extrusion and spray drying), oral controlled-release (via fluid-bed coating), liquid-fill, hard capsules and liposome production.

We provide contract cGMP manufacturing services for our clients, quickly transitioning projects from formulation optimization to proof-of-concept for a first-in-man study. We conduct turnkey development of control documentation, and product release requirements as necessary to meet our client's specifications. We can manufacture oral, topical, and sterile dosage forms, using our ISO 5/7/8 cleanrooms and isolator capabilities. We work with controlled-substances and potent compounds, using our isolator capabilities.

Ascendia also has developed and patented a proprietary pipeline of pharmaceutical product candidates for Co-Development and out-licensing, including ASD-005, ASD-002, the first in man injectable formulations that fulfill unmet market needs in the acute-care space of the anti-thrombotic drug clopidogrel, (that may be used in the same acute-care patient) and ASD-004, the next generation improved nano-emulsion cyclosporin for dry-eye syndrome. Ascendia has a state-of-the-art pharmaceutical research, development, and manufacturing center located in North Brunswick, NJ. *Call the number below now to see how we can enhance your product pipeline!*

ASCENDIA PHARMACEUTICALS
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W: www.ascendiapharma.com

CREDENCE MEDSYSTEMS

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Note: This product has not been evaluated by FDA.

Your Premier CMO for Specialized Sterile Injectables

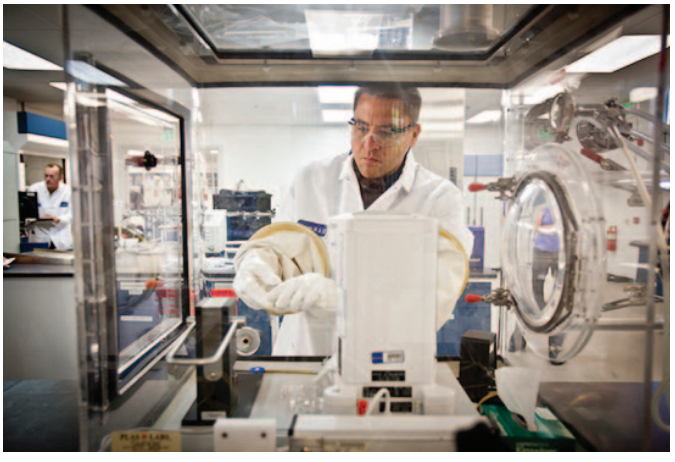
Backed by over 85 years of experience in parenterals, Baxter's BioPharma Solutions (BPS) business collaborates with pharmaceutical companies to support commercialization objectives for their molecules. BPS is a premier CMO with a focus on injectable pharmaceutical manufacturing designed to meet complex and traditional sterile manufacturing challenges with confidence of delivery, service, and integrity. BPS can support your pharmaceutical needs with a broad portfolio of sterile fill/finish production capabilities, and our reputation is built on the high-quality products we manufacture for our clients in a cGMP environment. Our delivery systems include: prefilled syringes, liquid/lyophilized vials, diluents for reconstitution, cartridges, powder-filled vials, and sterile crystallization. Our drug categories include: small molecules, biologics, vaccines, cytotoxics, highly potent compounds, and ADCs (antibody-drug conjugates). From formulation and development, through commercial launch, our extensive, customized support services can guide you through marketplace complexities, helping you achieve the full potential for your drug molecule. Whether you face formulation challenges, clinical supply hurdles, surges in demand due to market fluctuations, risk mitigation concerns, or patent expiry challenges, we offer tailored and versatile solutions to help achieve your commercialization objectives.

FACILITIES

Our state-of-the-art, award-winning facilities specialize in sterile contract manufacturing services and have primary locations in:

Bloomington, Indiana USA - The Bloomington, Indiana facility is a leader in sterile contract manufacturing and offers form/fill/finish services and solutions for injectables designed to meet complex and traditional sterile manufacturing challenges. As a full-service contract manufacturer (CMO), this facility serves client needs with clinical through commercial launch, including: manufacturing, packaging, quality systems, experience with worldwide regulatory agencies, and our Lyophilization Center of Excellence is an industry-leading resource focused on the development of high-quality freeze drying.

Halle/Westfalen, Germany - The Halle/Westfalen, Germany facility has over 60 years of experience and is recognized as a world-class manufacturer of oncology products and other sophisticated compounds. We can navigate complexity - parenteral manufacturing can be a complicated process and present many challenges that require specialized understanding and expertise. Baxter's BioPharma Solutions business brings longevity of experience in handling complex sterile manufacturing challenges. By offering a full complement of services in one location, we are able to meet clients' growing needs for oncology manufacturing in a single location, including early-to-late-stage support to fully engage and service our clients throughout the lifecycle of their products.



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Maximize

Your Molecule's Full Potential

Formulation challenges. Clinical supply hurdles. Limited manufacturing capability or capacity. Market fluctuations and demand surges. Lifecycle management. Risk mitigation. Patent expiry concerns.

At BioPharma Solutions, a business unit of Baxter, we know the high-stakes challenges you face in today's complex parenteral marketplace – and how the work we do is vital to the patients you serve.

That's why we work closely with you at every step to help you achieve your molecule's full potential and your commercialization objectives – building on over 85 years of Baxter innovation, expertise and specialization in parenterals.

Learn more about us at
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Baxter

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BD

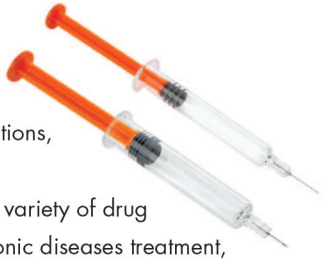
BD Medical - Pharmaceutical Systems

A Partner of Choice for the Pharmaceutical Industry

Founded in 1897, BD is one of the largest global medical technology companies in the world and is advancing the world of health by improving medical discovery, diagnostics, and the delivery of care. BD helps customers enhance outcomes, lower costs, increase efficiencies, improve safety, and expand access to healthcare.

BD Medical - Pharmaceutical Systems Offers Innovative, High-Quality, Clinically Proven & Customized Pre-fillable Parenteral Drug Delivery Systems

BD's drug delivery systems are designed to protect, package, and deliver drug therapies and to maximize healthcare worker and patient safety.



- Pre-fillable Syringes: BD is uniquely positioned to offer pre-fillable syringe systems with expertise in drug container interactions, primary container selection, and container/device integration for a variety of drug therapies, including vaccines, chronic diseases treatment, acute care drugs, anticoagulants, and hyaluronic acid.

- Self-Injection Systems: BD partners with its customers to develop self-injection systems that enable drug administration across a range of volumes and viscosities, leveraging BD primary container technologies and expertise with a focus on reaching the market faster.

- Safety & Shielding Solutions: BD offers a wide range of safety and shielding systems that feature innovative needle shielding system technology for injectable drugs.

BD is a reliable partner that can provide expertise in highly specific fields to support your drug throughout its lifecycle, from development to launch and beyond. The company is committed to building partnerships with pharmaceutical and biotechnology companies and developing product solutions that meet their needs by leveraging our innovative technologies, extensive global manufacturing, and advanced technical, scientific, medical, and regulatory expertise.

BD is Supporting Your Drug Development With a Full Range of services

- Consultative services on drug delivery options
- Regulatory support to optimize time-to-market
- Compatibility testing to mitigate risk
- Global reach and capacity to ensure business continuity
- (Pre)Clinical and Usability assessment Data to support registrations

BD Medical - Pharmaceutical Systems at a Glance

- More than 2.5 million ready-to-administer drug delivery systems manufactured per year
- Products used by more than 500 pharmaceutical and biotechnology companies [1]
- Prefill expertise and consultation at every stage of drug development
- 7 manufacturing plants to meet global production demand
- Worldwide support and regulatory expertise
- Comprehensive cross-functional support and dedicated teams.

[1]SAP Legacy, Tracis, Nodum – January 2018

THE DIFFERENCE OF ONE DRUG DELIVERED

WITH A GLOBAL LEADER IN PREFILLABLE DELIVERY SYSTEMS. BD partners closely with leading pharmaceutical companies to support their success from drug development to launch and beyond. With a broad portfolio of innovative drug delivery systems, a global perspective and regulatory insights, a BD Medical–Pharmaceutical Systems team can partner with you to match the optimal solutions to your product. In addition to prefillable syringes, our technologies include self-injection systems, safety and shielding solutions—which we can customize and develop to meet your precise technical requirements and the demands of your business. You can also count on our depth of regulatory knowledge, product development, medical expertise and responsive support. Discover the confidence of working with the right partner. **Discover the difference of BD.**

Learn more about the Difference of One at drugdeliverysystems.bd.com

BD

Advancing the world of health

CAPTISOL®

A Ligand® TECHNOLOGY

OPTIMIZED DRUG SOLUBILITY AND STABILITY

Captisol is the trade name for Ligand's solvent-free processed modified cyclodextrin preparation. Captisol is a patent-protected mixture of chemically modified cyclodextrins with a modifying structure to optimize drug solubility and stability. Captisol was invented and developed by scientists at the University of Kansas' Higuchi Biosciences Center specifically for drug development and formulation.

Captisol overcomes solubility and stability hurdles faced during each phase of development. Captisol can make a substance more soluble and an agent more stable. Captisol can convert a solid to a liquid or an oil to an aqueous solution. Combinatorial chemistry, high throughput screening (HTS), and molecular genetics have led to an increase in the number of insoluble and unstable molecules, peptides, and proteins being investigated for their therapeutic activity. There are currently more than 50 Captisol-enabled products in clinical development. This unique technology has enabled several FDA-approved products, including Amgen's KYPROLIS®, Baxter International's NEXTERONE®, Gilead's VEKLURY®, Acrotech Biopharma L.L.C.'s and CASI Pharmaceuticals' EVOMELA®, Melinta Therapeutics' BAXDELA™ and Sage Therapeutics' ZULRESSO™. There are many Captisol-enabled products currently in various stages of development.

Captisol, A Ligand Technology

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SEAMLESS TRANSITION TO CLINICAL TRIALS

Captisol may increase systemic exposure for toxicology studies of investigative compounds and has a proven clinical safety record. In early development, Captisol formulation can lead to a seamless transition from nonclinical safety to clinical trials. Captisol-enabled products are approved in more than 60 countries.

MULTIPLE ADMINISTRATION ROUTES ENSURE TARGETED DELIVERY

Captisol's chemical structure was designed to create new products by improving solubility, stability, bioavailability, and dosing of active pharmaceutical ingredients. Routes of administration investigated include parenteral, oral, ophthalmic, nasal, topical, and inhalation products. Once inside the body, Captisol releases the drug agent, which then travels to its target. The interaction between Captisol and the agent is not permanent, and Captisol is safely expressed from the kidneys.

PATENTED AND VALIDATED MANUFACTURING

Of all modified cyclodextrins, Captisol is an ingredient in the most approved products in the U.S. Manufactured under cGMP, at multiple locations, using a patented and validated all-aqueous process, annual manufacturing capacity is being increased to 500 MT. Captisol is supplied in ultra-low endotoxin, ultra-low bioburden, low-chloride forms in 100g, 1kg, 5kg and 20kg packages for R&D use. Commercial pack sizes include 1kg, 5kg, and 20kg, with the ability to fill metric-ton orders.

LIQUID CAPTISOL STANDS ALONE.

Liquid Captisol is a 50% aqueous concentrate of Ligand's Captisol a modified cyclodextrin, developed to improve solubility, stability, bioavailability and dosing of challenging ingredients.

The aseptic-filled 250mL plastic bottles allow you to skip tedious weighing and dispense by volume to reduce time, effort, and cleanup. 50% Captisol inhibits microbe growth and is shelf-stable. It's pumpable and easy to use in large-scale manufacturing. And the all-aqueous solution means no solvents to eliminate or test for in your final product.

When you're ready to move quickly into phase solubility studies, formulation development or safety studies, Liquid Captisol is ready to go!

LIQUID CAPTISOL®

CAPTISOL.com

Catalent®

Corporate Description

Catalent is the leading global provider of advanced delivery technologies, development, and manufacturing solutions for drugs, biologics, cell and gene therapies, and consumer health products. With over 85 years serving the industry, Catalent has the proven expertise, superior technologies and flexible solutions at the right scale to help ensure successful product development, launch, tech transfer and reliable global supply.

Catalent has built this expertise with partners of all sizes, from the smallest innovators to the largest of pharmaceutical leaders, advancing thousands of molecules through development towards commercial supply.

Providing both specific, tailored program support and comprehensive, integrated solutions, Catalent reduces its partners' risks on a variety of programs, including orphan drugs, accelerated and breakthrough treatments, vaccines, next-generation cell and gene therapies, and rare diseases.

Its team of approximately 14,000, at 45+ global sites, manages over 1,100 active development programs and supports more than 180 product launches annually. Every year, Catalent produces more than 72 billion doses of over 7,000 products for more than 1,000 customers, equating to 1 in 20 doses taken by patients globally.

Technology Highlights

With its expert services including analytical, biologics, preformulation, and formulation, Catalent drives faster, more efficient development of differentiated and patient-preferred products, including:

- Catalent Cell & Gene Therapy is a full-service partner for adeno-associated virus (AAV) and lentiviral vectors, and CAR-T immunotherapies, as well as autologous and allogeneic cell therapy development and manufacturing
- GPEx® Boost technology for advanced cell expression, biopharmaceutical development, bioanalytics and biomanufacturing
- Proprietary SMARTag® site-specific bioconjugation technology, affording precision design of next-generation biologic therapies
- OptiForm® Solution Suite for rapid, optimized dose form development
- Bioavailability enhancement including lipid-based systems, spray dry technology, particle-size engineering, and OptiMelt® hot melt extrusion
- Unique delivery technologies: including OptiShell® gelatin-free capsule technology, the Zydis® orally disintegrating tablet platform, OptiGel® DR and other oral controlled release dose design, as well as inhaled and injectable dose forms
- Catalent R P Scherer® Softgel, a global leader in innovative oral and topical softgel technologies. Nearly 90% of NCEs approved by the FDA over the last 25 years have been developed by Catalent

Integrated Solutions

Catalent offers a number of integrated solutions to accelerate clinical and commercial development:

- OneBio® Suite, reduces timelines, risk and complexity for biopharmaceuticals from cell line development through to clinical supply
- OptiForm® Total Supply accelerates drug candidates from development to clinical phase
- OneXpress™ provides the fastest pathway from clinical development to commercial manufacturing

More products. Better treatments. Reliably supplied™

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ENHANCING BIOAVAILABILITY IS SCIENCE. FINDING THE BEST FORMULATION MATCH IS ART.

Optimal formulations are built on the science of understanding your molecule's bioavailability challenge and art of finding the best technology match.

With 5 advanced formulation technologies, from micronization to lipids to amorphous solid dispersions, coupled with our experience optimizing thousands of molecules and track record in scalability and commercial success, Catalent can solve your bioavailability challenges, simple or complex, and turn your science into an optimal formulation fast.

5 BAE TECHNOLOGIES | UNMATCHED EXPERTISE | ACCELERATED FORMULATIONS | PROVEN SCALABILITY | PARALLEL SCREENING

Catalent® | *WHERE SCIENCE MEETS ART.™*

US + 1 888 SOLUTION (765-8846) **EUR** 00800 8855 6178 catalent.com/bioavailability

WHAT WE CAN DO FOR YOU

Celanese works closely with you as a strategic partner to create innovative controlled-release dosage forms for biologics and small molecules to meet the goals of patient-centric therapies, improved medicine and better healthcare economics.

From FEASIBILITY to DEVELOPMENT to COMMERCIALIZATION

Our scientists and engineers are there from concept to commercialization, providing development services, material supply aligned with GMP principles and regulatory support. Our objective is to help our customers reduce time and risk in research and development, so their drug achieves a higher chance of success.

Our VitalDose® Ethylene-Vinyl Acetate (EVA) copolymer drug-delivery platform is an enabling technology for drug-eluting implants, inserts and transdermal films. The platform is flexible and customizable to address a variety of formulation challenges when it comes to tailoring the release rate of your drug.

- Compatible with **biologics** and small molecules
- Provides reliable **local** or **systemic** drug administration
- **High drug loading** capacity (≤ 75%)
- Engineered long-acting dosage profiles (zero-order or nonlinear profiles)
- **Ease of formulation** and configurable into a variety of geometries
- An established regulatory path with **long clinical use history**

VitalDose® EVA has been approved for use in numerous pharmaceutical and medical device applications. We are actively supporting marketed products and development programs in:

- Oncology
- Infectious diseases
- Central nervous system disorders
- Ophthalmic inserts & intraocular implants
- Women's health
- Cardiovascular devices

ABOUT CELANESE

Celanese Corporation is a global technology leader in the production of differentiated chemistry solutions and specialty materials used in most major industries and consumer applications. Our businesses use the full breadth of Celanese's global chemistry, technology and commercial expertise to create value for our customers, employees, shareholders and the corporation. As we partner with our customers to solve their most critical business needs, we strive to make a positive impact on our communities and the world through The Celanese Foundation. Based in Dallas, Celanese employs approximately 7,700 employees worldwide and had 2019 net sales of $6.3 billion.

Celanese has supported key applications and the demanding requirements of the medical market for over 40 years and has developed one of the broadest ranges of special thermoplastics in the world. We are expanding design possibilities as our customers find new ways to improve patient care with cutting-edge medical and pharmaceutical material solutions. Our continuously expanding Medical Technology portfolio includes solutions and technologies for multiple applications in the space of drug delivery, medical devices, orthopedics, advanced surgical instruments and connected devices.

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VITAL Dose®
Controlled Release Excipient

Sustained Drug Delivery

Enabling Technology Platform
Patient-Centric Therapeutics

VitalDose® EVA is a copolymer drug-delivery platform providing controlled release through implant and insert dosage forms. Whether the challenge relates to a new molecular entity and new target, or an opportunity in life cycle management, our scientists and engineers will partner with you to create novel drug-products.

- Biologics and small molecules
- High drug loading capacity
- Variety of geometries
- Local or systemic administration
- Long clinical use history
- Established regulatory path

Collaborate with us:
Email: Healthcare@Celanese.com
Website: Healthcare.Celanese.com

Celanese
The chemistry inside innovation™

CORPORATE DESCRIPTION

Drug Information Association, or DIA, is a global association that mobilizes life science professionals from across all areas of expertise to engage with patients, peers, and thought leaders in a neutral environment on the issues of today and the possibilities for tomorrow. Our goal, and our members' hope is for this collaboration to result in better policies, regulations, science, research and development, and ultimately better patient outcomes worldwide.

Our Events

The world of healthcare is constantly changing. DIA events help you stay on top of those changes. From in-person workshops to conferences, meetings to virtual forums, key stakeholders from multiple disciplines come together to share information and insights. New perspectives are explored, while career-enhancing relationships are formed and nurtured.

DIA Learning Solutions

DIA offers a variety of learning solutions, including on-demand training courses, eLearning programs and certificate opportunities, and customized learning for groups in face-to-face or virtual formats. These offerings are complemented by solution provider webinars, industry-leading whitepapers, podcasts, our monthly digital magazine, peer-reviewed journal and other offerings from our renowned publishing team.

DIA NOW

A comprehensive, personalized resource for the latest trends and up-to-the minute updates within the drug development, regulation, and health policy arenas, DIA NOW features thousands of articles, podcasts, videos and more, in a searchable at-your-service format. Start a free trial today!

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W: https://www.diaglobal.org

Pharmacovigilance and Risk Management Strategies Conference

January 26-28
Virtual

For pharmacovigilance professionals, the complexity of safety and pharmacovigilance efforts is heightened by the rapid development of multiple vaccines and treatments, the emergent nature of knowledge about the etiology of the Coronavirus disease, and pervasive misinformation about prevention and treatment practices.

DIA's *Pharmacovigilance and Risk Management Strategies Conference* provides the foundation for strong strategic planning and practical decision-making in pharmacovigilance programs. Developed by recognized experts from the biopharmaceutical industry and global regulatory agencies, this conference provides the background, context, and opportunities to discuss current challenges and to problem-solve around issues that matter most to professionals working in the field.

REGISTER AND SAVE

Join Us Before the Conference for a Short Course!

January 19 | 10:00AM-1:30PM

- Short Course 1: Reference Safety Information

January 20-22

- Short Course 2: Pharmacovigilance and Risk Management Planning (Three Parts)

  Wednesday, January 20 | 10:00AM-12:00PM

  - Pharmacovigilance and Risk Management Planning Part 1

  Thursday, January 21 | 10:00AM-1:45PM

  - Pharmacovigilance and Risk Management Planning Part 2

  Friday, January 22 | 10:00AM-1:45PM

  - Pharmacovigilance and Risk Management Planning Part 3

January 25 | 10:00AM-1:30PM

- Short Course 3: Introduction to Statistics in Pharmacovigilance

January 25 | 2:00-5:30PM

- Short Course 4: Naming and Labeling Considerations to Prevent Medication Errors

Learn More at DIAglobal.org/PVRMS21

DDL®

Testing experts.
Service specialists.

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For over 30 years, DDL has provided extraordinary service and specialized testing expertise to the medical device and pharmaceutical industries. Our reliable quality, responsive attention, and on-schedule completion for packaging, medical device, and combination products testing secures confidence in performance and safety while achieving regulatory compliance.

Package Testing

DDL's package testing services evaluate the strength and integrity of packaging systems before and after simulating the anticipated distribution and storage conditions that the systems may undergo. Packaging professionals use this combination of simulation and evaluation to validate package compliance with ASTM, ISO, ISTA and other accepted industry standards. DDL offers full service package testing in Eden Prairie, MN and Irvine, CA, and select package testing capabilities in Edison, NJ.

Combination Product Testing

DDL specializes in mechanical and performance testing for pre-filled syringes (ISO 11040) and needle-based injection systems (ISO 11608). In preparing for regulatory submission or verifying your products conform to the required industry standards, DDL provides reliable test data to document the performance and safety of your combination product.

Container Closure Integrity Testing

Package integrity verification requires careful examination of package leakage given the specific product and its life cycle. DDL's CCI services include both the most recent deterministic capabilities, as well as probabilistic methods, as outlined in USP <1207>. We can provide tailored expertise to design and execute a CCI study based on your system, providing the support you need.

Medical Device Testing

DDL specializes in testing medical devices such as luer fittings, syringes, needles, catheters, guidewires, surgical sutures, cannulae and tracheal tubes. DDL tests to ANSI, ASTM, IEC, ISO, JIS, EN and other industry standards. Vibration, physical shock, thermal shock, friction, flow rate, force to operate, leakage and compression testing are among the many tests provided. Custom test development and protocol creation are also available.

Stability Storage

DDL provides stability storage space for products requiring environmental conditions based on ICH Q1A guidelines as well as customizable storage conditions. Our facilities contain over 38,000 cubic feet of validated storage space for long-term and short-term shelf life studies under various temperature and humidity requirements.

DRUG DELIVERY EXPERTS
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DRUG DELIVERY EXPERTS (DDE LABS) is your go-to partner for Contract Drug Product R&D, Simple Solution to Complex Liquid Formulations, and Clinical Trial Materials Manufacturing in a Sterile Suite.

We specialize in parenteral drug products from solutions to particulate systems and long-acting technologies. We are also experienced in oral, nasal, and ocular formulation development.

GMP FACILITIES: TRANSITION FROM FORMULATION TO CLINICAL TRIALS

DDE Labs now has GMP fill finish manufacturing for sterile drug products to serve our client needs. We offer compounding and filling capabilities from simple solution to gel-forming polymer, and micronized suspension. Our lab specializes in therapeutic modalities from small molecules to peptides, proteins, oligonucleotides, and antibodies.

The quality system is designed for aseptic manufacturing under GMP conditions of early phase clinical trial materials and toxicity test article. Vials are filled using disposable containers in a semi-automated operation in ISO 5 laminar flow hoods in an ISO 6 clean suite. GMP release testing is conducted in-house and stability testing is conducted for ICH conditions in 24/7 monitored chambers.

CUSTOM DESIGNED FORMULATIONS FOR TARGETED DELIVERY

DDE Labs can custom design a delivery system for your product by improving stability, bioavailability, solubility, and dosing frequency. We have experience in multiple routes of administration including parenteral (SC, IV, IM, intrathecal, intraarticular), oral, ophthalmic, nasal, topical, and inhalation products.

- Develop methods for formulation, analytical, process, chemistry, and device
- Peptide and small molecule chemistry, conjugation (e.g., PEGylation), salts
- Lead candidate selection, optimizing pharmaceutical properties
- Extended-release injectable delivery technology
- R&D for novel and proprietary delivery technologies (ours and yours)

Our expertise ranges from preclinical formulation to clinical supply and commercial product reformulation with extensive experience in small molecules and biologics.

WE COLLABORATE WITH YOUR SCIENTISTS FOR THE BEST POSSIBLE PROJECT OUTCOME

- Specialists in combination drug product development
- Extensive industry experience in biologics drug development
- Creative formulation solutions drawn from broad experience base
- Highly-qualified Ph.D. scientists from pharma backgrounds
- State-of-the-art R&D lab
- We thrive while working on your most challenging formulations and processes

R&D SUPPORT FROM RESEARCH THROUGH COMMERCIAL PRODUCT LIFE CYCLE SUPPORT

Each of our experts has more than twenty years of experience in pharmaceutical research, development, and commercialization. Our experts work to customize a formulation or drug delivery solution that best meets your product profile.

Your drug product is our work product and we treat it as if it were one of our own.

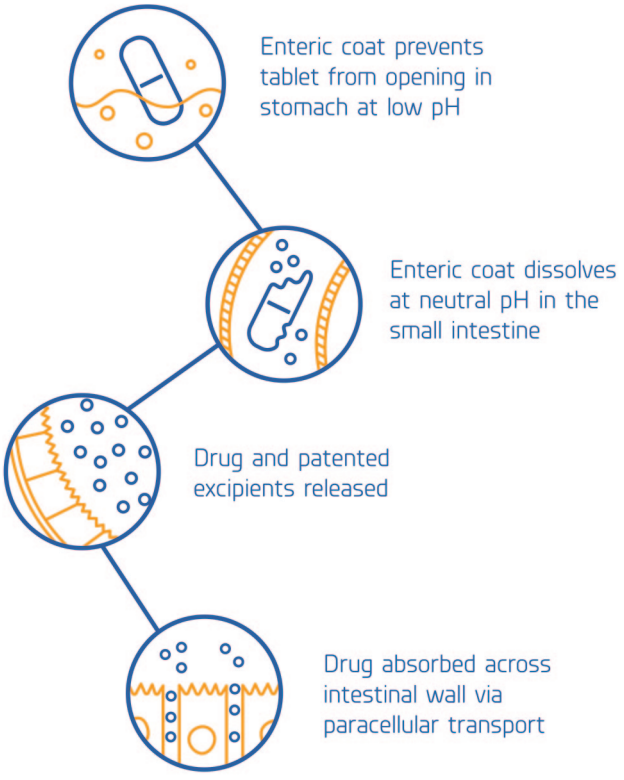
The Preferred Partner in the Oral Delivery of BCS III and BCS IV Compounds.

Enteris BioPharma is a clinical stage biopharmaceutical company offering innovative formulation solutions built around its proprietary oral drug delivery technologies. In addition to its formulation development expertise, Enteris BioPharma has a 32,000 square-foot GMP facility in Boonton, New Jersey, offering an expanding range of manufacturing and development services.

Enteris BioPharma operates as an independent, wholly-owned subsidiary of SWK Holdings Corporation (Nasdaq: SWKH). Since its founding in 2013, Enteris has advanced into the clinic multiple internal and external programs leveraging its Peptelligence® platform. The technology has been developed and proven effective over the last decade to enable the oral delivery of BCS III and IV compounds that suffer from poor solubility and permeation, resulting in low oral bioavailability including peptides, peptidomimetics, and small molecules.

Enteris's formulation technology is made up of two key components, the first is a permeation enhancer, which loosens tight junctions in the intestinal enterocytes and allows paracellular transport. The permeation enhancer, a surfactant, also acts as a great solubilizing agent. The other main excipient, citric acid, also plays an active, multifunctional role in transport by acting as a calcium chelator and membrane permeation enhancer, a pH-lowering agent that increases absorptive flux, and a membrane wetting/charge dispersal agent.

For more information about the Peptelligence® oral formulation technology please download our brochure:
https://enterisbiopharma.com/download-peptelligence-brochure/



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ILC DOVER

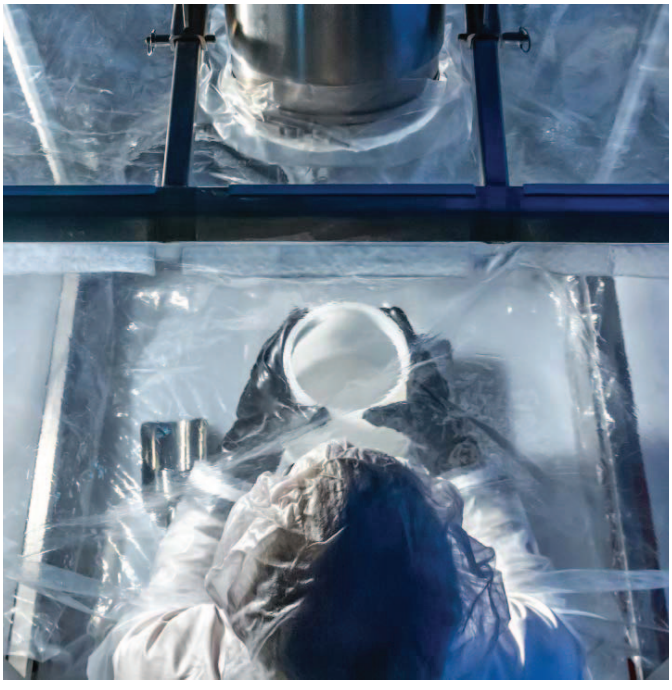
BEYOND BOUNDARIES™

ILC Dover is a world-leader in the innovative design and production of engineered flexible protective solutions, for pharmaceutical and biopharmaceutical, flood protection, personal protection, bulk packaging, and aerospace industries. Our customers will attest to our relentless dedication to high value products, advanced technology, and responsive service, as our visionary solutions have improved efficiency while safeguarding people, product, and infrastructure in hazardous conditions since 1947.

Our focus in the pharmaceutical industry is to facilitate safe and reliable performance in the lab while ensuring maximum productivity with single-use flexible powder solutions for high containment.

Our Single-Use Flexible Powder Solutions for High Containment
CMOs and CDMOs choose our proven solutions for powder transfers and containment over rigid stainless-steel systems, recognizing the significant advantages they bring to the manufacturing process value chain in both chemical synthesis of HPAPI and OSD processing for final drug products. Beyond meeting all regulatory requirements, our solutions reduce the risks of cross-contamination, minimize equipment cleaning and validation between batches, save costs, and maximize productivity, so operators can work uninterrupted at peak performance.

- **EZ BioPac®** is a purpose-built powder containment and transfer system that speeds fill time and makes it easy to adjust contents to precise target weight.
- **DoverPac® Containment Systems** are the global premier products for disposable process and powder containment systems and the global standard for containment, reliability, and service.
- **ArmorFlex® Films** are the premier film for powder handling and containment that provide unmatched performance characteristics, while increasing handling speed and safety. Unlike other films on the market, ArmorFlex® was designed solely for use with powders, meaning there are no additives to discolor product, or slip agents that can cause cell-growth inhibition. Furthermore, its low-residual, antistatic film ensures every bit of product gets where it is going and does not get thrown away inside the bag.
- **Continuous Liners** by ILC Dover are an easy-to-use system that have been proven effective in containing active pharmaceutical ingredients and other hazardous compounds. Continuous Liner System assures a safe and effective transfer of powders, tablets, vials, tools, and trash, and is also used for offloading powders from vessels to drums.
- **Flexible Isolators,** also known as glove bags, by ILC Dover are based on 20 years of designing and building custom isolators for powder containment. These standardized, modular designs allow quick delivery of isolators to handle many contained pharmaceutical powder handling processes.



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Twitter: https://twitter.com/flexintl/
LinkedIn: https://www.linkedin.com/company/flexintl
Facebook: http://facebook.com/flexcorporate/

FAST FACTS

Year Founded: 1969

Number of Employees: 160,000

Number of Facilities: 130 sites in 30 countries, 27 medical sites, 13 FDA registered and 24 ISO 13485 sites

PARTNERING WITH DRUG DELIVERY DEVICE COMPANIES TO CREATE THE EXTRAORDINARY

- Global design, development and manufacturing services provider with nearly 30 years of medical experience across FDA Class I, II and III products and from simple disposables to smart drug delivery systems and complete immunoassay diagnostic systems.
- Global experience across 12 industries gives us insight and expertise in the technologies to be integrated into tomorrow's medical products today.
- Complete vertical integration under one roof from pellet to packout including inline sterilization and final packaging.
- Medical footprint includes multiple plastics tool making and injection molding facilities.
- Global supply chain technology leader with real-time data analysis that drives speed and agility.

COMPREHENSIVE SERVICES

Human Factors Engineering

Generative, formative and summative research to meet user needs and optimize usability.

Full Design & Development

Accelerate and de-risk design and development and integrate advanced technologies. Engineering and development with manufacturability in mind to ensure an outstanding design can be efficiently manufactured at target cost. Expertise in electromechanical drive systems, needle injection systems, miniaturization, and connectivity.

New Product Introduction (NPI)

Expertise in NPI, and collaboration with both design and operations teams results in efficient, validated and scalable production processes that can be easily scaled to high volume manufacturing.

Manufacturing

Our global footprint allows us to match our customers' regional strategies. Tool making, injection molding, PCBA, system integration, full device manufacturing, complex assembly, sterilization and final packaging comprise our full-service manufacturing portfolio.

Supply Chain, Logistics & Distribution

Flex scale drives incredible supply chain strength. Flex Pulse, a sophisticated set of real-time tools enhances speed and impact in supply chain management.

PRODUCT EXPERIENCE

Drug Delivery

Autoinjectors, On-body Injectors, Smart Injection Pens, Pumps, and Infusion Systems.

Medical Equipment

Laboratory Diagnostic Systems, Point of Care Diagnostics, Surgical Generators, OR and ER Equipment, Imaging Systems, Respiratory Care Equipment, and Ophthalmic Diagnostics.

Medical Devices

Diabetes Management, Neural Stimulators, Surgical Tools, Personal Care, Personal Diagnostics and Monitors, Wearables, and Single-Use Disposables.

We see more than manufacturing drug delivery devices.

We see a partnership in making complex drug delivery systems simpler and safer.

As a leading provider of design and manufacturing services for the pharmaceutical industry, we work with you to provide easy-to-use, connected solutions for drug delivery devices. At the same time our eye is on elevating manufacturing efficiencies, accelerating the timeline from production to patient, backed by a global, highly resilient supply chain.

Whether your focus is on autoinjectors, on-body injectors and other wearables, or injection pens, let's partner together to help improve people's lives.

Visit flex.com/health or email healthsolutions@flex.com and find out how we can create the extraordinary together.

Don't miss FlexTalks, our webinar series on hot topics.
Visit **flex.com/connect/flex-talks** to register or view on demand.

- Human Factors and Design
- Advanced Engineering
- Full Product Development
- IP Protection
- New Product Introduction
- Global Manufacturing
- Total Supply Chain
- World Class Quality System
- Digital Health

FOSTER DELIVERY SCIENCE
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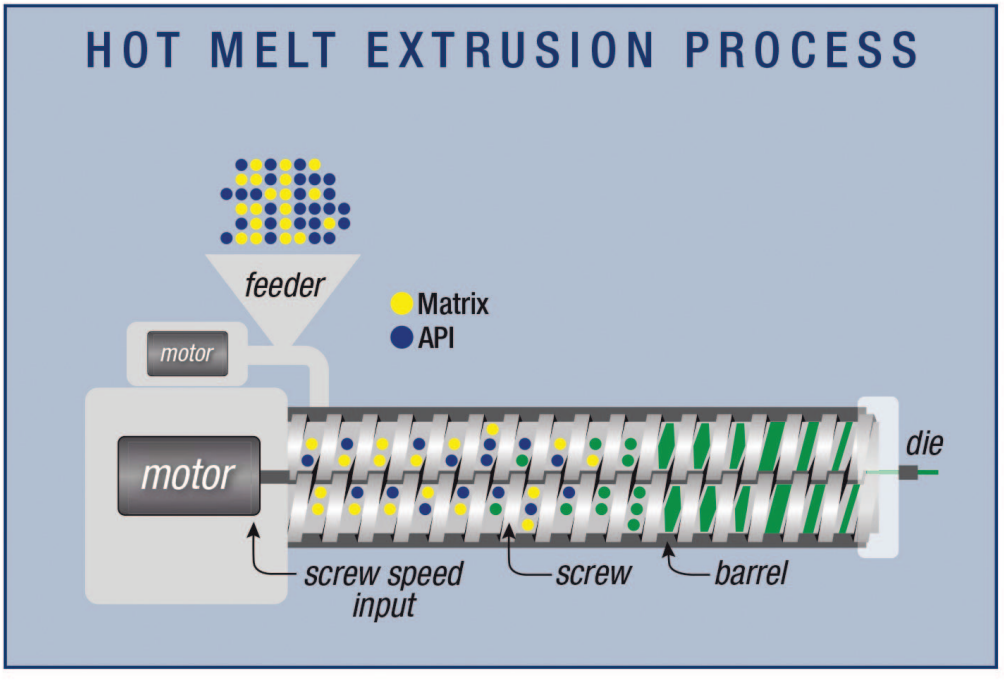
Foster Delivery Science focuses Hot Melt Extrusion and Complex Extrusion, applying our expertise using twin screw extruders not only for traditional solubility enhancement techniques, but to also create Long Acting Implant and film based drug delivery solutions. Our range of services include GMP / Clinical Trial / Commercial Manufacturing supported by formulation development, scale up and optimization of the process. As extrusion is a continuous process by nature, melt granulation programs are also an obvious interest for lifecycle management and new drug development.

Using the industry range of FDA acceptable polymers, we can create permanent and bio-absorbable implants to deliver drugs immediately or over a desired time period. These implants can be micro implants like ophthalmic applications or macro such as intravaginal rings. Excelling in Complex Extrusions Foster Delivery Science can add layers or sheaths to take advantage of multiple API's or deploy rate limiting membranes. We can also deliver effective APIs in a localized manner using transdermal and mucosal films and other polymer shapes, depending on drug need and client interest.

We work with our clients from our facility located just 75 minutes west of Boston in Putnam, CT.



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OF DRUG/POLYMER BLENDS

Now Offering cGMP Milling of Polymers and Extrudates

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DELIVERY SCIENCE

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CORPORATE DESCRIPTION

Founded in 1972 Freund-Vector Corporation is a global market leader in the design, manufacturing of solid dosage processing equipment and services for the processing of powders, particles, beads and tablets. Freund Corporation of Tokyo, Japan, our parent company and a long-time business partner, purchased controlling interest of Freund-Vector Corporation in 1997. Together our two companies now have over 5500 worldwide equipment installations in 55 countries of the world.

MARKETS SERVED

Primary markets served by Freund-Vector include the pharmaceutical, nutritional, food, confectionery, cosmetic and chemical industries. The Freund-Vector product lines include coating pan systems for applying an aqueous, solvent or sugar film coating; fluid bed systems for granulating, fine particle coating, spherization and drying; roll compaction for material densification and granulation; high shear granulators for wet granulation; spray dryers for creating small particles and automated process control systems for all the equipment/systems.

GRANULATION MADE SIMPLE

Freund-Vector offers a complete line of granulation equipment on the market and we have the experience and expertise to direct you to the method that is your best solution. Roll compactors, high shear mixers, fluid bed top-spray and rotor systems are each capable of creating particles with unique characteristics for use in the forming of tablets or filling of capsules. Our equipment lines include laboratory units for product development, larger pilot units for scale-up technology and larger capacity production systems that are all designed with engineered scalability.

COATING MADE SIMPLE

Freund-Vector offers a comprehensive line of tablet coating and fluid bed particle coating systems. Both coating lines are designed for maximum processing flexibility with precision coating capabilities and interchangeable processing drums/inserts. Freund-Vector was the first to manufacture laboratory and pilot tablet coating systems with multiple interchangeable drums and now include production systems to provide maximum processing flexibility and efficiency within a single system.

SPRAY DRYING MADE SIMPLE

Freund-Vector also offers innovative technology in spray drying. With Feasibility, Scalability and Flexibility in mind, with our new VSD-200 Spray Dryer is an enabling technology to create amorphous solid dispersions for the improvement of drug solubility. It is also a great choice for production of biologic substances, pharmaceutical excipients, and API even under containment.

PROCESS SOLUTIONS MADE SIMPLE

The USA laboratory in Marion, Iowa, as well as at our European headquarters in Villasanta, Italy, feature processing equipment ranging from laboratory size to pilot scale to perform feasibility studies and product development.

FREUND-VECTOR CORPORATION
675 44TH STREET
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T: (319) 377-8263
E: sales@freund-vector.com
W: www.freund-vector.com

FREUND VECTOR
Your Global Equipment and Processing Solution

COME SPRAY WITH US!

VSD-200 Lab Scale Spray Dryer

FREUND VECTOR

Your Global Equipment and Processing Solution

What if you could. . .

- ☑ **Produce** "commercial grade" particles with a pressure nozzle on your lab scale spray dryer?
- ☑ **Produce** GMP clinical supplies on a "lab scale" dryer - continuously, without interruptions, and with complete batch documentation?
- ☑ **Obtain** high yield at all scales – and even down to a gram with nearly 100% recovery?
- ☑ **Possess** "future safety" – modular exchangeable components let you tailor today's equipment for tomorrow's new drug innovations?
- ☑ **Plug 'n' spray** in a integrated all-in-one execution on a portable, space efficient platform – minimizes facilities impact?

. . .Now you can!

This spray dryer will change the way you Think, Work and Develop your drug preparations.

FREUND-VECTOR CORPORATION

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GATTEFOSSÉ

About Gattefossé

Gattefossé provides functional excipient and innovative drug delivery solutions to beauty and healthcare industries worldwide. With service and distribution networks that span over 60 countries, Gattefossé prides itself on ensuring products that meet pharmaceutical industry needs from both regional and global perspectives.

Products and Applications

At Gattefossé, each excipient is designed to meet a unique set of formulation and functionality objectives while conforming to the highest safety, quality, and regulatory standards.

Product applications include solubility and bioavailability enhancers; sustained/controlled release matrix formers; protective coatings or taste masking agents for actives; emulsifying bases for topical dosage forms; skin penetration and permeation enhancers; and carriers for suppository bases and vaginal pessaries.

Among our renown products are Compritol®, Labrafil®, Gelucire®, Labrasol®, Capryol®, Lauroglycol™, Precirol®, Tefose™, and Suppocire® series. Globally established for safety and pharmaceutical qualifications, many of these excipients are also found in pediatric dosage forms.

Technical Support

In addition to safety and characterization data, formulation guidelines, and regulatory filing support, we offer formulation assistance. Working closely with drug manufacturers, our Technical Centers of Excellence in Asia, Europe, and North America are hard at work resolving solubility, dissolution, drug release rate, and or dosing options.

Typical customer projects include solubility and compatibility screening, formulation characterization and ultimately the development of prototype formulations for oral, topical, transdermal, and other routes of administration.

It is the aim of Gattefosse to simplify formulation decisions that advance drug pipelines, speed up drug delivery projects, and essentially shorten drug development time.

www.gattefosse.com

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Tel: +33 4 72 22 98 00 - infopharma@gattefosse.com

GATTEFOSSÉ USA Regional Office
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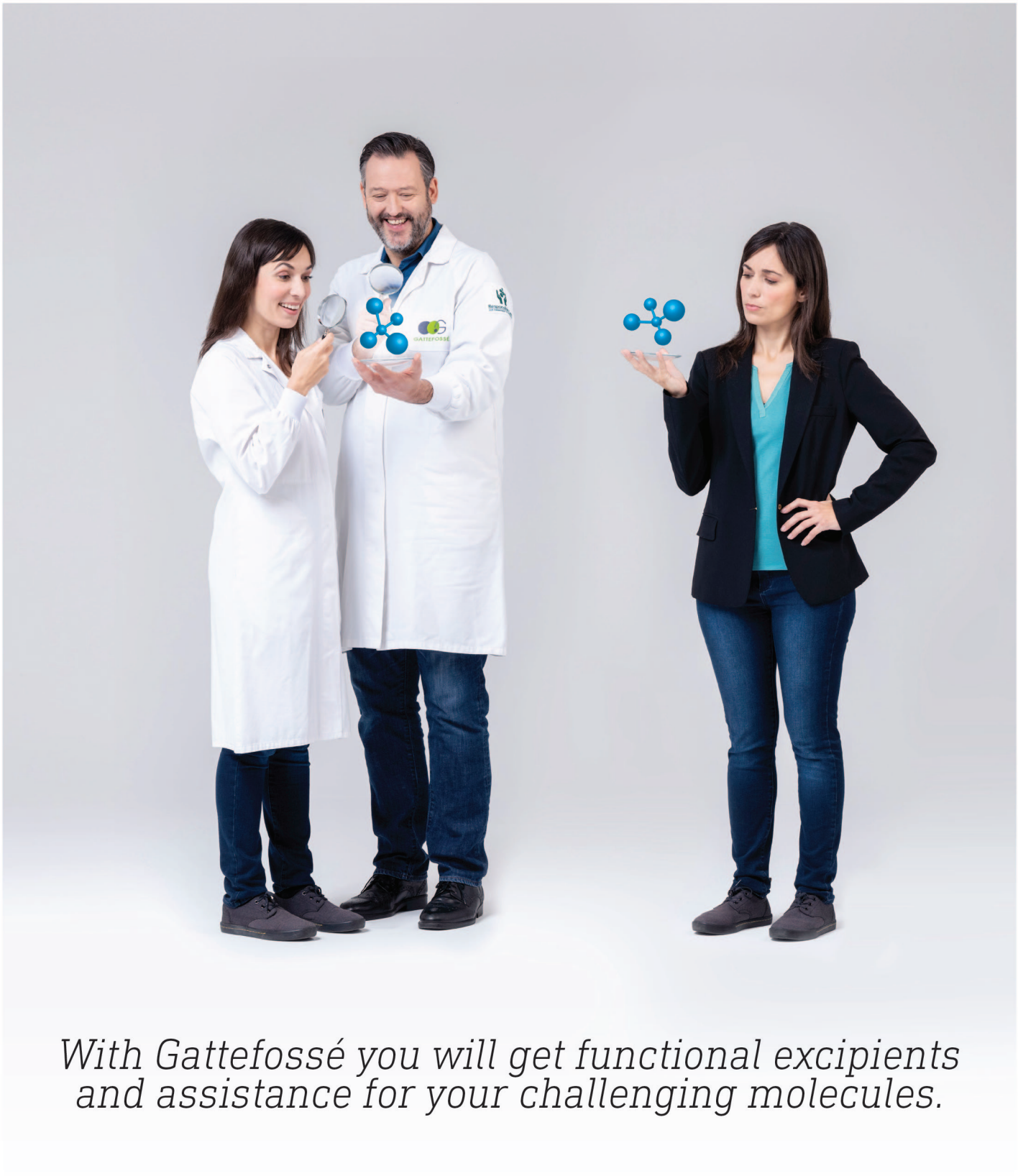

With Gattefossé you will get functional excipients and assistance for your challenging molecules.

www.gattefosse.com

GATTEFOSSÉ

People make our name

HASELMEIER

A Sulzer Brand

Experts in subcutaneous drug delivery systems for self-administration, Haselmeier provides innovative and award-winning system solutions to support patients with a successful therapy. Since October 2020, Haselmeier is a business unit of Sulzer AG, Winterthur, Switzerland.

Our business covers all steps – from design to planning to industrialization – in the creation of high-quality self-injection systems. Our approach is built on a century of experience – and an open, curious mind.

As a leading solutions provider of customized smart drug injection systems, we support reliable, successful therapies. Haselmeier constantly drives innovation for subcutaneous self-injection devices. Our advanced technology, connected devices, and data management solutions improve therapy, and we continuously examine the requirements of therapy efficiency to evolve the technology even further.

We believe that while technology can enhance therapy efficiency, the needs of therapy inspire even better solutions. As a proactive partner, we offer high-tech products and bespoke services, and adapt quickly to evolving engineering opportunities and market changes. We place patient comfort and the needs of our customers at the heart of our approach. Haselmeier works with pharmaceutical and biotechnology companies to improve the lives of patients by manufacturing pens and auto-injectors that are convenient, reliable, and that can be dosed with precision.

Spread across seven global locations on three different continents, the Haselmeier Group employs a workforce of more than 240 people. Our development and operations facility is located in Stuttgart, Germany, with global manufacturing facilities in Germany, Czech Republic, and India. Our manufacturing capabilities include high-volume injection molding, precision machining, manual and fully automated pen assembly.

As a full-service provider, Haselmeier can support you with a lot more than just R&D, product development, and pen assembly. Haselmeier is certified to provide pharmaceutical manufacturing services, so we can offer pharmaceutical and biotechnological companies a comprehensive assembly, labeling, and packaging service. As a result, we are able to support these companies with complete combination product manufacturing and packaging services.

Our innovative reusable and disposable product platforms, connected devices, data management, and related service portfolios assist you every step of the way – leading to an advanced combination of drug and device that is as time-saving and economical for your company as it is safe and convenient. We support you at every stage – from technology to therapy.

Rapid drug development, smooth conduct of clinical trials, and fast time-to-market are high priorities for pharmaceuticals companies. For drugs designed for subcutaneous application, self-injection pens from Haselmeier can help reduce risk and shorten time-to-market.

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E: Terry O'Hagan, t.ohagan@haselmeier.com
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HASELMEIER

A Sulzer Brand

D-Flex – a new generation of manual injection pens

CUSTOMIZED DRUG DELIVERY – FROM TECHNOLOGY TO THERAPY

As a reliable partner, we develop customized solutions for small batch to high-volume production, from clinical trials to long-term commercial use, and from manual applications to connected devices.

For more information, visit
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Wide customizable pen portfolio

HERMES PHARMA

Get the dose right®

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A division of Hermes Arzneimittel GmbH
Georg-Kalb-Strasse 5-8
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W: www.hermes-pharma.com

HERMES PHARMA is the leading expert in developing and manufacturing user-friendly oral dosage forms including effervescent and chewable tablets, instant drinks, lozenges, orally disintegrating granules and HERMES NutriCaps.

ABOUT US

HERMES PHARMA has been working with healthcare companies around the globe for over 40 years to expand their product lines and grow their brands. From new product design and formulation development to manufacturing and regulatory support, HERMES PHARMA offers expert advice and customized solutions at every point along the pharmaceutical value chain. We are the experts in the development and manufacture of user-friendly oral dosage forms, offering a 'one-stop-shop' to meet our customers' needs. Whether they are looking to co-develop a new product, in-license one our products or concepts, or simply outsource manufacturing to our specialists, we can do it.

HERMES PHARMA is a division of Hermes Arzneimittel, a leading German pharmaceutical company that manages a rich portfolio of over-the-counter (OTC) brands.

PRODUCTS & SERVICES

We focus exclusively on user-friendly dosage forms and have more than 40 years of experience in this area. The oral route is generally considered a simple and cost-efficient way of drug delivery, primarily using tablets or capsules. However, recent data suggest that difficulties swallowing tablets and capsules are widespread, occurring across all age groups and potentially impacting treatment success. These findings indicate that conventional solid dosage forms may not be the best option for all individuals, and often fail to keep pace with the evolving needs of modern patients.

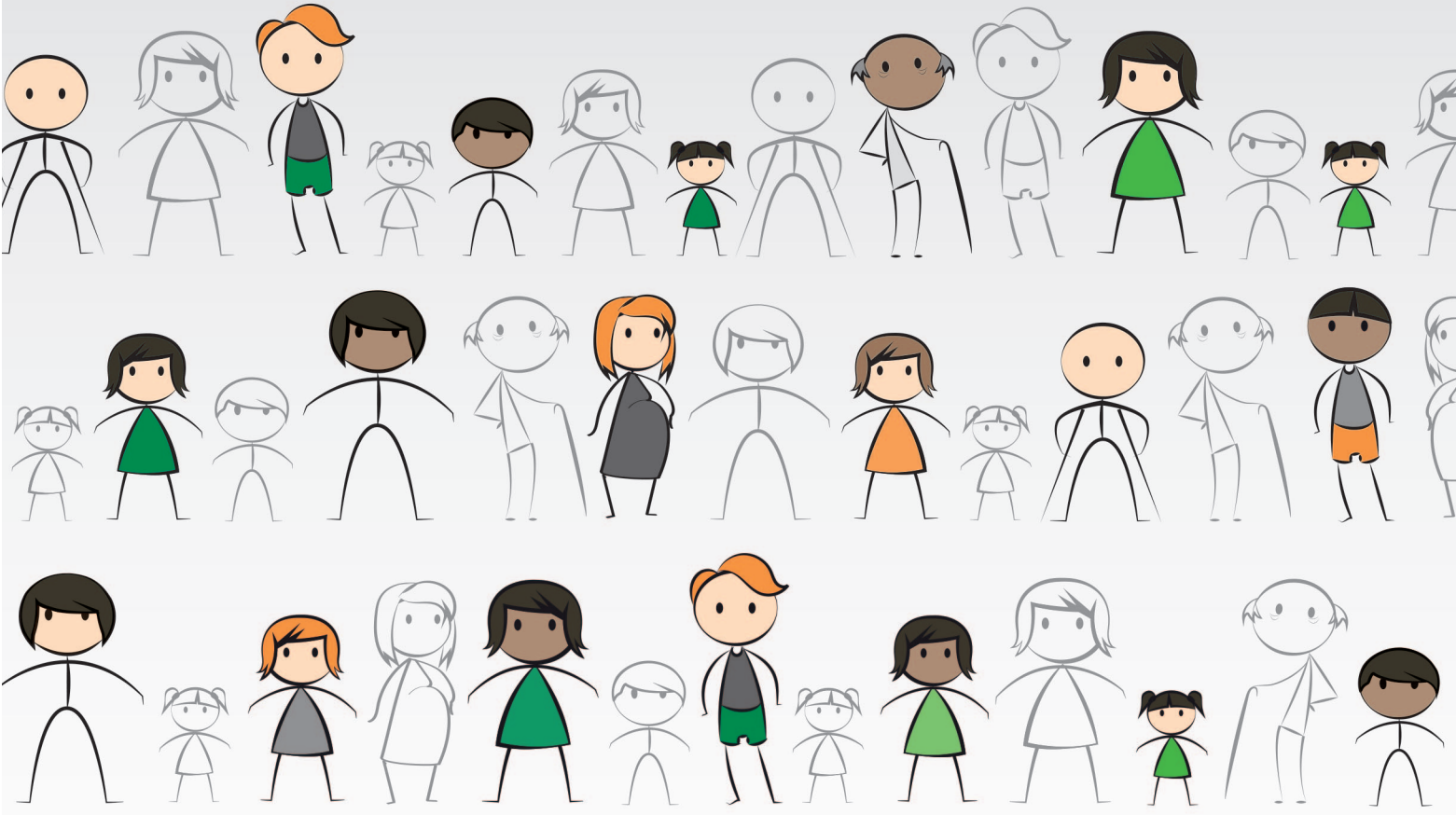
HERMES PHARMA is the leading expert for effervescent and chewable tablets, lozenges, instant drinks, orally disintegrating granules and HERMES NutriCaps. These user-friendly dosage forms:

- Are convenient to use and to take.
- Are easy to swallow – even for people with dysphagia.
- Integrate easily into the busy lives of modern patients.
- Can be taken with or without liquids to suit the individual.
- Taste great and offer a variety of choices in terms of flavor.
- Allow greater amounts and different combinations of API to be delivered in a single dose, simplifying treatment regimens.

User-friendly dosage forms help to increase compliance and improve treatment success. Whilst creating a convenient and enjoyable experience for the patient, they also support healthcare companies to revitalize ageing products and boost brand loyalty.

TAKING A PILL IS AS EASY AS PIE?

50% OF YOUR CUSTOMERS WOULD DISAGREE ...



A recent study proves that more than half of the population has problems swallowing tablets and capsules. From breaking and dissolving to not taking them at all, people invent their own strategies to cope with tablets – which may reduce efficacy and treatment success.

At HERMES PHARMA, we have over 40 years of experience in making medicines easier to take – from product design through to manufacturing and packaging. If you need support with developing new products that are specifically designed to meet the needs of modern patients, contact us:
www.hermes-pharma.com

Scan QR-code or visit
www.swallowingtablets.com
to get a free copy of the market study.

HERMES PHARMA

Get the dose right®

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30 Indian Drive
Ivyland, PA 18974-1431
T: (215) 396-8373 F: (215) 396-8375
E: inquiry@lyo-t.com W: www.lyotechnology.com

WHO WE ARE

Lyophilization Technology, Inc. (LTI) is a Contract Development & Manufacturing Organization (CDMO) focused on all aspects of lyophilization for preparation of health care products.

Clients leverage on our abilities for bringing new products to the clinic and implementing improvements for current products. Capitalize on over 25 years of excellence and our unparalleled capabilities in product development, process engineering, clinical manufacturing, and technical support.

MAJOR MARKETS

Biotechnology and pharmaceutical organizations spanning virtual companies to large multi-national corporations, along with universities and research institutes have engaged our support in successful collaborations for a variety of projects. These projects span initial product and process development for new entities right out of drug discovery through Phase I/II clinical material, to technology transfer to commercial manufacturing with regulatory approval. Gaining a global reputation, LTI has been sought after and completed projects with clients in the European, Middle East, and Asian Pacific regions, as well as North America.

SERVICES OFFERED

Capabilities

- Pre-clinical through Phase II Clinical Materials
- Bulk Lyophilization
- Dedicated/disposable equipment
- Batch sizes: up to 75L
- Vials: 2 to 160 mL
- Dual Chamber cartridges and syringes: 1 to 20 mL
- Novel delivery systems
- Nucleation On-Demand Technology
- DEA license
- US/EU compliant

LTI successfully develops formulations, processes or prepared clinical material for many diverse products, including:

- Biologics (up to BSL-2)
- Oncolytics
- Liposomes
- Anti-Infectives
- Peptides/Polypeptides
- Proteins/mAbs
- Diagnostics
- Nanoparticles/Emulsions
- Vaccines and VLPs
- Controlled Substances
- Highly Potent Compounds
- Antibody Drug Conjugates
- Devices/Delivery Systems
- Small and Large Molecules

Development Sciences

Development Sciences focuses on formulation through finished product characterization. The Process Lab provides capacity for small to medium scale lyophilization. Filtration, filling, stoppering, and loading the qualified pilot-scale lyophilizers are in certified Class A/100 environments, emulating aseptic manufacturing conditions.

- Product Design
- Formulation Development
- Thermal Analysis
- Cycle Design/Refinement
- Product Characterization
- Pilot Plant Scale-up
- Isolation/Containment
- Cartridges

Clinical Manufacturing

US/EU compliant Clinical Manufacturing Area (CMA) for preparation of clinical material enables us to process a wide range of products, including those having unique requirements. The CMA includes an aseptic suite featuring advanced containment/isolation technology using unique disposable negative pressure isolators inspected and approved for handling BSL-2, cytotoxic and highly potent compounds. LTI has also developed the technology that allows us to freeze dry product in both dual chamber cartridges and pre-filled syringes.

- Aseptic compounding
- Pre-clinical through Phase II
- Toxicology Material Processing
- Small to medium batch sizes
- Liquid/diluents
- Dual chamber cartridges/syringes

Technical Services

Technical services are available providing support for all aspects of lyophilization.

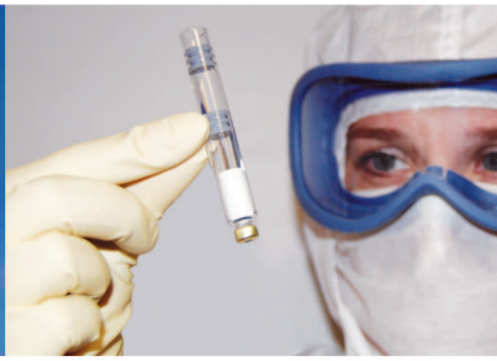
- Customized Training
- Consulting on equipment specifications
- Process requirements
- Guidance on CMC submission
- Support on IQ/OQ and process validation
- Technology transfer
- Process excursions
- Product and process troubleshooting
- Batch record review
- Compliance auditing

Lyophilization TECHNOLOGY Inc.

Integrating Science and Technology

The industry leader with unparalleled capabilites, innovative approaches and effective solutions.





DEVELOPMENT SCIENCES • CLINICAL MANUFACTURING

CONSULTING AND TRAINING

Product Design • Formulation Development • Thermal Analysis • Boundary Studies

Process Engineering • Dual Chamber Processing • Clinical Material Preparation

Quality and Regulatory Support • Technical Services • On-site Training • Consulting

LYOTECHNOLOGY.COM

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METRICS CONTRACT SERVICES
1240 Sugg Parkway
Greenville, NC 27834
T: (252) 752-3800
E: thomas.salus@maynepharma.com
W: www.metricscontractservices.com

COMPANY OVERVIEW

Metrics Contract Services is a science-led, full-service global contract development and manufacturing organization (CDMO) specializing in novel oral dosage forms and providing pharmaceutical development, analytical testing, and commercial manufacturing services to over 100 clients worldwide. We're proud to offer a complete "concept to commercialization" solution under one FDA site registration. For those needing commercial manufacturing services, we deliver seamless scale-up, eliminating the need for costly and time-consuming site transfers. Additionally, we have a comprehensive project management process to streamline and ensure our execution is efficient as possible. A division of Mayne Pharma, we're serious about science and sharply focused on novel drugs that make a difference.

SERVICES OFFERED

Pharmaceutical Development and Clinical Trial Materials Manufacturing

Our Pharmaceutical Development team of veteran formulation scientists delivers materials for all phases of clinical development through to commercial manufacturing. Those comprehensive formulation development services range from preclinical through Phase III CTM including: tableting, immediate release, modified release (including controlled/matrix and sustained release), capsule filling, milling, micronizing, enteric coating, spray drying, extrusion, and spheronization. Our facilities and processes are designed to handle potent products, cytotoxic compounds, and controlled substances.

Analytical Services

With over 150 analytical chemists dedicated to solving complex challenges, Metrics provides a full range of method development and validation services as well as routine testing in state-of-the-art laboratories. We analyze the physical and chemical characteristics of drug substances and drug products through development and validation of methods, release and stability testing. We perform this work in compliance with industry standards and international regulatory guidelines.

Potent Products

Our potent facilities provide engineered containment through customized, hardwall isolation technologies. Containment is achieved at 30 nanograms per cubic meter of room air. Contained equipment and change parts are dedicated exclusively to potent use. The facility features independent entry, exit and equipment double airlocks, decontamination showers, dedicated washroom, dedicated equipment storage and pass through for product/waste.

Fast Track First-Time-In-Human Studies

Metrics Contract Services has successfully delivered materials for over 150 FTIH studies. Our process ensures speed and quality, with a 16-24 week timeline from receipt of well-characterized NCE to shipment to the clinic. Services include stability studies, analytical methods development and validation. Choose simple formulation, blended powder in capsule, or neat API in a bottle.

Concept to Commercialization

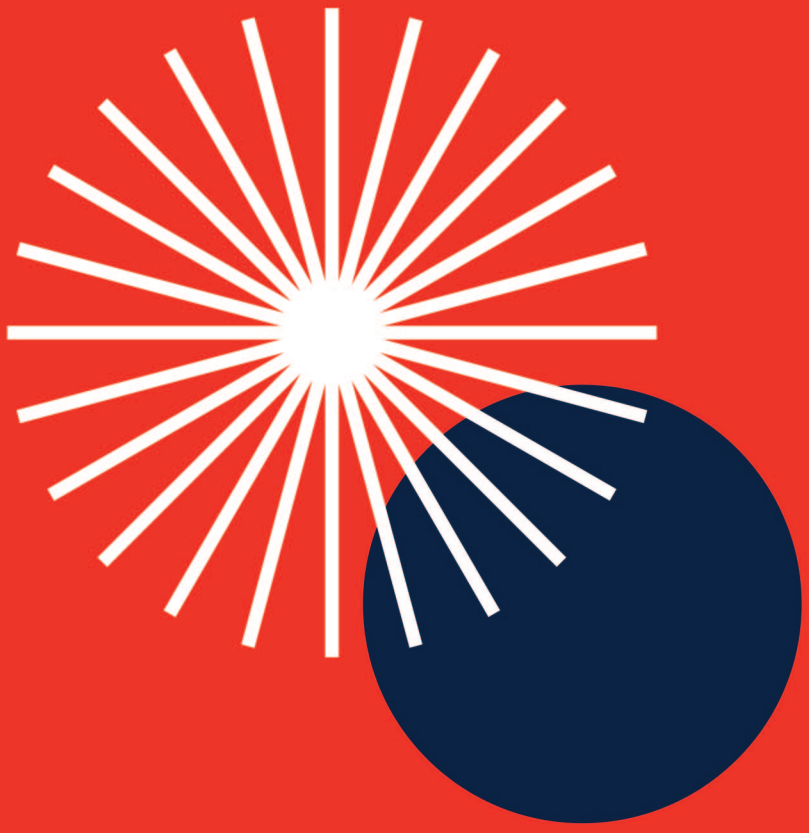
We have invested over $100 million dollars in our Greenville, NC site in the past five years. The most significant component of that investment is our new commercial manufacturing operation, which is 126,000 square feet of oral solid dose manufacturing capability specializing in high potency throughout. This facility enables Metrics Contract Services to offer solutions from initial concept to global commercialization in one contiguous location for clients, providing seamless scale-up and eliminating the need for site transfers.

metrics contract services

With a track record that spans over 25 years, Metrics Contract Services has enabled hundreds of customers to bring complex novel oral solid dose products to patients with confidence.

We are a science-led CDMO engineered around customers. Our scientists and expert operators are experienced professionals who act as an extension of your team to solve your most complex challenges. We specialize in small batch, novel OSD, from early phase development through to commercialization. All from our single campus facility in Greenville, North Carolina.

- Formulation development
- Clinical manufacturing
- Commercial manufacturing
- Analytical testing



Growing with our clients is important to us here. We continue to invest in our facilities to meet client needs. Meet Metrics Contract Services.

www.metricscontractservices.com

MITSUBISHI GAS CHEMICAL

Mitsubishi Gas Chemical (MGC) is a leading company in the field of functional chemicals, such as oxygen barrier and absorbing polymers. MGC established the Advanced Business Development Division in 2015 for tackling a variety of today's problems, and the division created OXYCAPT™ Multilayer Plastic Vial & Syringe to solve some issues of existing primary packaging for injectable drugs.

Products

OXYCAPT™ Vial & Syringe consists of three layers. The inner and outer layers are made of cyclo-olefin polymer (COP), the most reliable polymer in the pharmaceutical industry. The middle layer is made of state-of-the-art polyester developed by MGC. There are 2 types in OXYCAPT™, A and P. OXYCAPT™-A has achieved glass-like oxygen barrier and OXYCAPT™-P has excellent oxygen barrier. OXYCAPT™ also provides an ultra violet (UV) barrier. For example, although about 70% of 300 nm of UV light transmits through glass and COP, only 1.7% transmits through OXYCAPT™. These excellent barrier qualities contribute to the stability of biologics. According to internal studies, OXYCAPT™ surpassed glass and COP in terms of preventing oxidation of antibody. Furthermore, the characteristics of COP used to the drug contact layer bring more advantages to OXYCAPT™. Some studies have shown OXYCAPT™ generates extremely low levels of extractables. Especially, the level from OXYCAPT™ is much less than type 1 glass with regard to inorganic extractables.

OXYCAPT™ Vial & Syringe are produced by co-injection molding technology. Although the technology has been applied to beverage bottles for many years, MGC is the first company that succeeded in coming up with multilayer plastic syringes. MGC has also developed inspection machinery for the multilayer vial and syringe. All of the containers are 100% inspected by the machinery. There are 2-mL, 6-mL, 10-mL, and 20-mL for vials, and 1-mL long and 2.25-mL long for syringes. Regarding the ready to use (RTU) vials and syringes, these are sterilized by gamma and provided with ISO-based nest and tub formats. As customizability is one of the features for plastic, MGC is able to consider developing customized OXYCAPT™ containers if requested. Biologics and cell and gene therapies are a target application for OXYCAPT™ because they are basically sensitive to oxygen, UV, and metals. In addition, OXYCAPT™ can be applied to epinephrine, which is well-known as an oxygen-sensitive drug. MGC believes that OXYCAPT™ contributes to stability of oxygen and UV-sensitive drugs.

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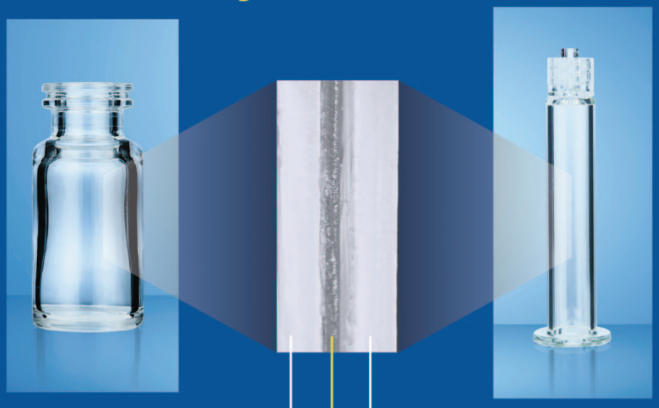
T: +81 3 3283 4913
E: nb3.pharmapackage@mgc.co.jp W: https://www.mgc.co.jp/eng/products/abd/oxycapt.html

OXYCAPT™ Plastic Vial & Syringe

Multilayer Structure



- **Excellent Oxygen Barrier**
- **High Water Vapor Barrier**
- **Very Low Extractables**
- **Low Protein Adsorption**
- **Excellent Ultraviolet Barrier**
- **High Break Resistance**
- **High pH Stability**
- **Silicone Oil Free Barrel**
- **Gamma-sterilized Vial & Syringe**
- **Customizable**
- **For Biologics & Regenerative Medicine**

MITSUBISHI GAS CHEMICAL

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E-mail: nb3.pharmapackage@mgc.co.jp

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E: information@nemera.net W: www.nemera.net

As a world-leading drug device combination solutions specialist, our purpose of putting patients first enables us to design and manufacture devices that maximize treatment efficacy. We are the utmost holistic partner and help our customers succeed in the sprint to market. From early device strategy to state-of-the-art manufacturing, we're committed to the highest quality standards. Agile and open-minded, we work with our customers as colleagues. Together, we go the extra mile to fulfill our mission.

Nemera offers a comprehensive portfolio of products and services covering several key delivery routes:

OPHTHALMIC: 0% PRESERVATIVES IN THE DRUG, 100% EYE PROTECTION

The use of preservatives can cause side effects to the eye, thus jeopardizing adherence to treatments and damaging patients' eyes. Nemera offers a multi-dose closing tip system, **Novelia®, which avoids the need for preservatives in the drug and prevents bacterial contamination over the duration of treatment.**

EAR, NOSE, THROAT: EASY USE, EASY BREATHE

The number of drugs delivered through ear, nose and throat is expanding. Nemera offers various technologies with **a full range of metered pumps and valves platforms, for regulated and unregulated markets: Advancia®, SP270+ and SP370+, SP27, and SP37.** Nemera now also offers **Child Resistant spray system for oral and nasal sprays**, in collaboration with Roy LeClair.

DERMAL & TRANSDERMAL: CONVENIENT DEVICES FOR DERMAL DELIVERY

Some dermal or transdermal drugs can be very sensitive and need to be delivered at a consistent and precise dosage. Nemera offers **high-performance atmospheric or airless delivery devices for Prescription and OTC applications: Sof'bag®, Sof'Airless**, and a wide range of pumps.

PARENTERAL: COMPLEX DEVICES, SIMPLE PATIENT CARE

Parenteral drug administration exposes patients and healthcare professionals to many hazards. To provide a complete set of services, Nemera has integrated pharmaceutical **drug handling capabilities** (ability to assemble a filled primary container with a device). Nemera's experience in drug delivery devices includes: **Insulin Pens, Autoinjectors and Implanters, and Safety devices for prefilled syringes.**

INHALATION: NEMERA, A PARTNER OF CHOICE

Over 10 million patients use devices manufactured by Nemera every day. **From concept generation to large scale manufacturing, Nemera is the key partner for your inhalation device.**

ELECTRONIC: KNOW-HOW & CAPABILITIES TO ANSWER PATIENTS' NEEDS

Nemera also developed **electronic know-how and capabilities** to answer patients' needs. Nemera brings a wealth of knowledge in development, manufacturing and innovation to electronic devices: **e-Novelia®, e-Advancia®, Safe'n'Spray™, wearable systems, and a cloud platform.**

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E: cs@pfanstiehl.com
W: www.pfanstiehl.com

Pfanstiehl is a global leader in the manufacture of cGMP high purity, low endotoxin, low metal injectable-grade excipients and biopharmaceutical components for upstream bioprocessing, downstream formulation, and specialty applications. In addition, Pfanstiehl is a leading contract development and manufacturing organization (CDMO) specializing in the isolation, purification, custom synthesis, and scale-up development of small molecule Active Pharmaceutical Ingredients (APIs), in gram to multi-ton commercial quantities. While most ingredient manufacturers or resellers focus on other industries, such as food, cosmetics, agriculture, and/or nutritional supplements, offering only a subset of 'pharma- grade' ingredients, Pfanstiehl is Pharma Grade through and through. It's all we do. Pfanstiehl's ICH Q7-compliant manufacturing facility is centrally located just north of Chicago, and only 35 minutes by car from O'Hare International Airport.

Pfanstiehl's tried and true, platform-enabling protein and cell membrane stabilizers include Trehalose, Sucrose, Arginine, and Maltose. Parenteral-grade, multi-compendial Mannitol and Sodium Succinate are also offered as key tools for formulation optimization. We are continuing to expand this portfolio to include other key excipients based on feedback from our clients who want real cGMP manufacturing from a company that understands and supports their requirements. Many clients are not simply looking for a high-quality source of consistent ingredients, but seek a partner who can adapt to the ever-evolving regulatory landscape and address emerging formulation challenges collaboratively.

For upstream applications, Pfanstiehl manufactures high purity, low endotoxin, low metal galactose for reduction of lactate and ammonia production. Overall cell culture performance improvements can be achieved with optimized titration of galactose in lieu of other carbon sources. Pfanstiehl offers multiple types of galactose, including a non-animal- derived product. Mannose is also offered as a high purity cell culture supplement to improve native glycosylation and improve consistency in product quality attributes, particularly in high titer processes. Trehalose can be utilized in upstream bioprocessing and cell therapy applications to reduce protein aggregation and improve cell robustness.

Pfanstiehl was founded in 1919 and is celebrating its 100-year anniversary as a leader in carbohydrate and process chemistry. Pfanstiehl's customers include most of the world's leading biopharmaceutical and pharmaceutical companies. Our products are utilized in market-leading drugs that treat life-threatening and debilitating diseases, including cancer, rheumatoid arthritis, STDs, and diabetes. Increasing regulatory and quality requirements are benefiting high integrity biopharmaceutical and pharmaceutical suppliers like Pfanstiehl with high purity, strong cGMP controls and a strong reputation with FDA and other regulatory agencies. In everything we do, Pfanstiehl is motivated by a concern for both product quality and environmental/worker safety. We design and equip our plant, write our procedures and train our people to meet or exceed US FDA, cGMP, OSHA and international regulatory and multi-compendial standards.

Delivering on the Promise of Purity

PACE ANALYTICAL LIFE SCIENCES - IMPROVING OUR HEALTH
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1311 Helmo Avenue North, Oakdale, MN 55128 - T: (651) 738-2728

Puerto Rico
El Retiro Industrial Zone, P.O. Box 325
Calle B&C, San German, PR 00683

PHARMACEUTICAL DEVELOPMENT
GMP LABORATORY TESTING

SUPPORTING PHARMA-BIOLOGICS INNOVATION

Pace Analytical Life Sciences (PLS) is a premier contract development & manufacturing (CDMO) and contract research (CRO) organization helping to improve human health by supporting the Pharmaceutical, Biologics, and Gene Therapy innovators. We help to bring new therapies to market starting with early-phase drug development through successful clinical outcomes and on through commercialization and late-phase manufacturing. We share a common goal to bring real value to people, healthcare professionals and health businesses around the world.

Our Pharmaceutical Development laboratories in Boston, MA, and Philadelphia, PA, provide IND-enabling services to help new therapies progress through the pre-clinical stages, to include: Characterization of new synthetic small molecules, biologics such as proteins, peptides, antibodies, antibody drug conjugates, and gene therapies such as oligonucleotides. Early phase development services include lyophilization process development, spray-drying, phase-appropriate analytical development, Test Article preparation, and Clinical Trial Materials (CTM) Manufacturing.

Technology transfer to Pace Life Sciences' state-of-the art GMP testing facilities enables our clients to seamlessly and confidently advance their programs from preclinical and clinical studies to commercialization in a manner compliant with regulations and industry standards. Strategic partnering with Pace Analytical is a key accelerator for getting your products to market on time and on budget. We provide a real and tangible difference to your customer experience by combining all essential service elements:

Pharmaceutical Development

- Characterization of Novel Molecules & Biologics
- Formulation Development
- Lyophilization Development
- Spray drying
- Analytical Development

GMP Laboratory Testing

- Microbiology
- Raw Materials Clearance Programs
- In-process & Finished Product Support Programs
- ICH Stability Programs
- Reference Standard Programs
- Extractables/Leachables
- Commercial Product Support

Comprehensive Scope of Services: A broad scope of services to support you from early characterization and Pharmaceutical Development through marketed product support.

Capacity: Pace is committed to providing services to all clients, large or small. Our flexible response to demand provides various service models to include fee-for-services, dedicated resource programs, full-time equivalent (FTE) model on-site at PLS, and/or FTE programs at the client site, which allow for economical options to meet business demands.

Quality: Our facilities have long histories of successful regulatory agency, client, and third-party audits. High-quality data and information provides the confidence you need to advance your products quickly.

Reliability: We integrate all critical path components to ensure that programs advance while meeting rigorous scientific demands with flexibility to address dynamic challenges and aggressive timelines.

Pace Analytical®
LIFE SCIENCES

Delivering Science Better

Pace Analytical® Life Sciences provides premier product development/ manufacturing services, with world-class expertise, robust quality systems, and advanced technology tools. We operate four facilities to provide a full range of services to global clientele.

Our services support your product development and commercial manufacturing:

- Small molecules
- Biologics
- Oligonucleotides
- Characterization of Novel Compounds
- Formulation Development
- Product Development
- GMP Clinical Trial Material Manufacturing
- Commercial Product Support
- GMP Laboratory Testing
- Spray Drying
- Lyophilization

See how Pace can be the best solution for your projects.

www.pacelabs.com

YOUR BRIDGE BETWEEN LIFE-CHANGING THERAPIES AND PATIENTS

PCI Pharma Services

PCI Pharma Services is an integrated full service provider, a proven and trusted partner to leading companies in the global healthcare industry. We offer unparalleled expertise and experience in taking compounds from the earliest stages of development through to successful commercialization, delivering speed-to-market and commercial success for our customers.

Our core services support each stage of the product lifecycle, including drug development, clinical trial supply, commercial launch and ongoing commercial supply. We partner with clients in providing innovative technologies, flexible solutions, and an integrated supply network supporting lifesaving medicines destined to over 100 countries around the world.

We support clients with a dedication to providing the industry's leading experience, exemplified in our operational flexibility, delivery, commitment to safety, supported by industry leading technologies and an exemplary quality and regulatory record.

This has allowed us to be the partner of choice for leading pharmaceutical companies around the world, operating as a seamless extension of their business.

Drug Development & Manufacturing Services

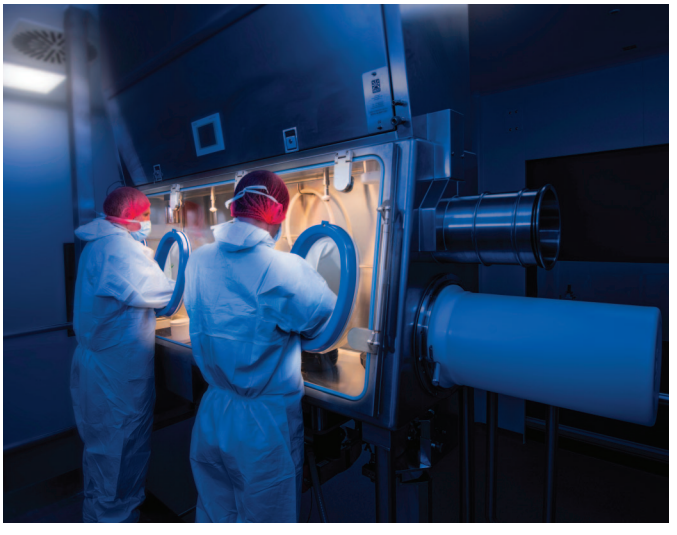
PCI offers full service Formulation Development including Analytical Development/Characterization and Xcelodose® product-in-capsule delivery for early phase clinical trials, as well as an extensive array of sterile and nonsterile delivery forms for early phase studies.

Clinical Trial Services

PCI supports investigational medicines with Tablet, Capsule, Powder and Liquids Manufacturing, Analytical Development, Stability Testing, Clinical Packaging and Labeling including product Blinding and Randomization, Global Storage and Distribution, as well as Returns Management and Destruction.

Commercial Packaging Technology

PCI supports commercial product manufacturing including Commercial scale-up and large-scale manufacturing. Investments include separate suites for large volume tablets manufacture plus roller compaction technology for heat and moisture sensitive formulations. We offer Packaging Services for a broad range of delivery forms including Oral Solids, Powders, Liquids, Creams and Gels, as well as Injectable and Parenteral Delivery forms including Device Assembly. In support of commercial supply we offer Analytical Testing and Stability services.



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F: + 1 215 613 3601
LinkedIn: https://www.linkedin.com/company/pciservices/
E: talkfuture@pciservices.com W: www.pci.com

YOUR BRIDGE BETWEEN LIFE-CHANGING THERAPIES AND PATIENTS

pci PHARMA SERVICES

Excellence in pharmaceutical outsourcing

THE PCI WAY

We are a collaborative partner and an extension to our customers' business, sharing the goal of improving patients' lives.

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pci | CLINICAL TRIAL SERVICES

pci | COMMERCIAL PACKAGING TECHNOLOGY

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E: pfizercentreone@pfizer.com
W: www.pfizercentreone.com

Pfizer CentreOne® is a global CDMO embedded within Pfizer and a leading supplier of specialty APIs. Our global manufacturing network includes more than 35 sites across six continents. Backed by Pfizer resources, we deliver technical expertise, global regulatory support, and long-term supply. For more than 40 years, we've been guiding complex compounds securely and efficiently from development through commercial manufacture.

Working together with our customers, we combine our knowledge with open dialogue to solve challenges. Intelligent collaboration with Pfizer CentreOne. For more information, visit www.pfizercentreone.com.

CORE TECHNOLOGIES, PRODUCTS, AND/OR SERVICES

We offer CDMO services focused on:

- Small molecule APIs
- Oral solids
- Sterile injectable fill-finish
- Biologics

We sell APIs and intermediates manufactured in the US under Pfizer quality standards:

- Steroids
- Hormones
- Antibiotics
- Prostaglandins

A CDMO EMBEDDED WITHIN PFIZER

Embedded within Pfizer and backed by its capabilities, we seek to create more efficient routes to market and deliver the highest quality APIs and drug products.

When a drug is manufactured with Pfizer CentreOne, it benefits from the expertise and world-class facilities of a parent company with over 170 years of experience and hundreds of products to its name. Pfizer invests over $1B annually into manufacturing to continuously improve infrastructure and processes.

From our global manufacturing network, we deliver technical expertise and reliable supply to customers across the globe.

Can Pfizer help with the early development of my complex oral solid?

We sure can. Collaborate with Pfizer CentreOne, and access Pfizer's scientific and product development expertise.

Pfizer CentreOne has a global network offering a suite of development and optimization services.

Collaborating with you, we can help take your molecule all the way from early clinical phases through commercial manufacture and lifecycle management.

Listening. Solving. Guiding.

Backed by Pfizer resources, we deliver technical expertise to overcome oral solid dose challenges.

Intelligent collaboration with Pfizer CentreOne.

Our capabilities include:

- Early stage formulation development
- Process validation and optimization
- Full development of analytical methods
- Scale-up from lab to pilot to commercial
- Specification development
- Regulatory support – pre and post-launch
- Clinical manufacturing Ph I - III
- OEB 1-5 engineering controls
- Tablets, capsules, granules
- Controlled substances

Pfizer CentreOne

www.pfizercentreone.com

The Difference is in the Details

PharmaCircle is a leading provider of authoritative information, global insight, and expert analysis on the pharmaceutical, biotech, drug delivery technology and device, and animal health industries.

PharmaCircle's premier database tracks drugs, biologics and combination products in all stages of development, connecting pipeline and product information with formulation and component details. The database delivers seamless integration of scientific, clinical, safety, regulatory, manufacturing and commercial information, and detailed analyses on over 7,500 drug delivery technologies and delivery devices.

PharmaCircle provides the broad and deep global coverage, and powerful search and analysis tools needed to answer challenging questions so you can uncover new opportunities and make informed decisions.

Key content and capabilities include:

- Pipeline & Products Intelligence
- Drug Delivery Technology Analyses
- Company Capabilities Profiles
- Business Prospecting Tools
- Trial Landscape Insights
- Formulation & Excipient Details
- Strategic Deals Analyzer
- API & Finished Dosage Form Manufacturers Finder
- Global Regulatory Compendium
- Physical Chemical & Pharmacokinetic Data
- Venture Capital Investment Tracking
- Service Provider Comparisons
- Patent Exclusivity Tracking
- Drug Label Comparisons
- Key Product Sales & Forecasts
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To learn more about how PharmaCircle can help your company, please see our ad on pages 7 & 102 and visit our website www.pharmacircle.com.

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- **Integrated Data**
- **Powerful Analysis Tools**
- **Industry Knowledge**

Since 2003, PharmaCircle has been supporting Pharmaceutical Development & Innovation, providing clients with the integrated data, powerful analysis tools, and industry knowledge needed to solve complex, real world challenges in drug delivery and formulation.

PHARMACIRCLE™

The Difference is in the Details

www.pharmacircle.com

Pii
Pharmaceutics International, Inc
Challenges Frame Opportunities

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Hunt Valley, MD 21031
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E: bd@pharm-int.com or pdupont@pharm-int.com
W: www.pharm-int.com

Year Founded: 1994
Number of Employees: 350
Key Personnel: Dr. Kurt Nielsen, President & CEO
Business Development Team: PJ Kim, Head of Commercial and Corporate Development, Kevin Kelly, Head of Sales and Brian Sasaki, Senior Director of Business Development
Marketing: Paul Dupont, Head of Digital Marketing and Devan Patel, Senior Director of Business Development

Concept to Clinic to Commercialization

At Pharmaceutics International, Inc. (Pii), our motto is "challenges frame opportunities." We are a US-based contract development and manufacturing organization (CDMO) that has "walked in your shoes" and has a passion for solving problems efficiently with the highest quality standards. Emphasizing a collaborative relationship with our clients, Pii's experts embrace the art and science of drug development and manufacturing. Our outcome is to deliver better results faster for our clients and their patients.

Pii's Hunt Valley, Maryland campus includes four cGMP and FDA certified facilities, 70 manufacturing suites with all the necessary analytical testing capabilities on site, and four integrated aseptic filling suites delivering quality, safety, and efficiency.

Experienced with small and large molecule compounds, we have special expertise in developing and manufacturing complex parenteral drugs, vaccines, extended-release formulations, and non-aqueous injectable drug products. We can also overcome stability challenges with precision lyophilization cycle development and production.

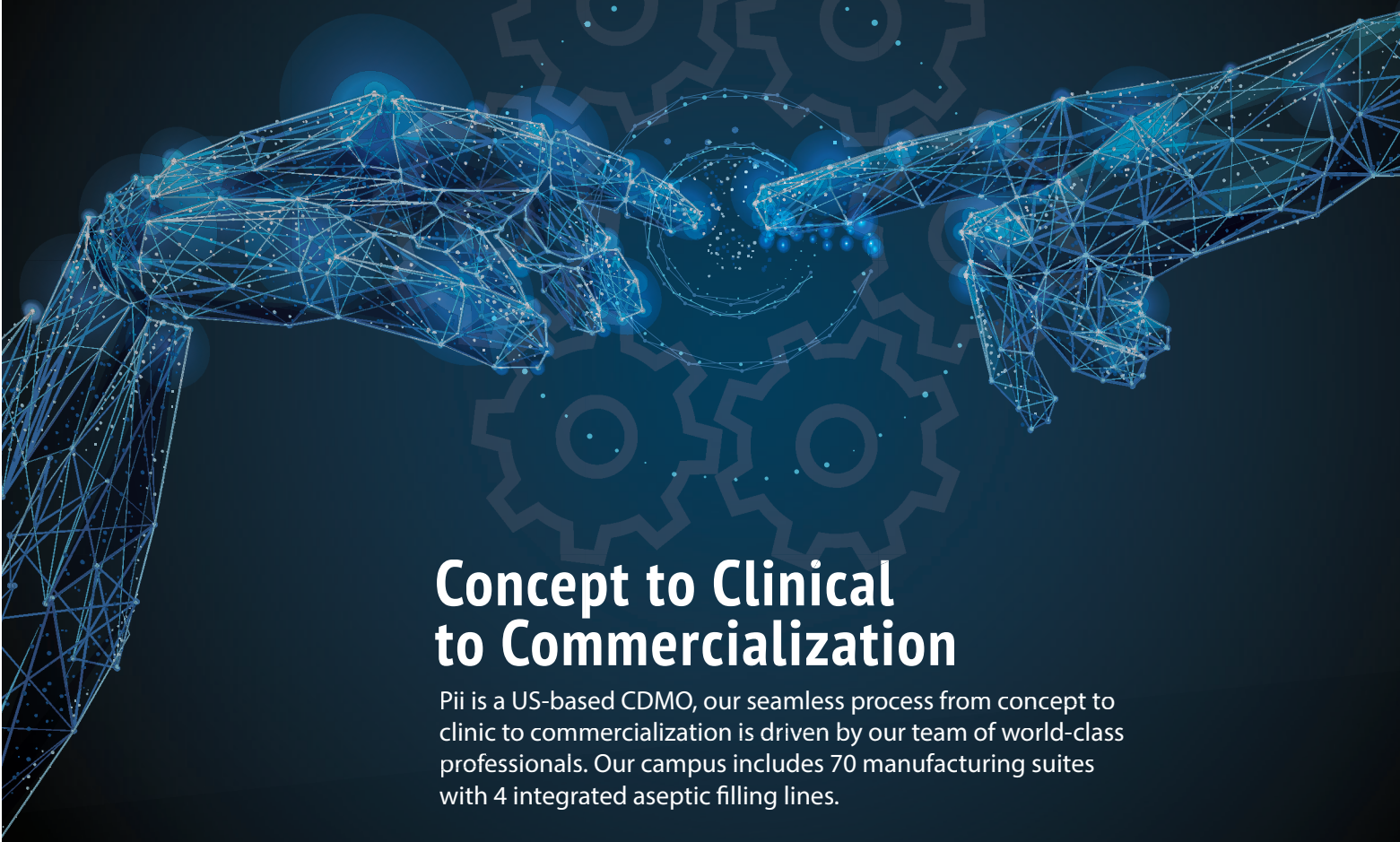
Services

- Formulation and Process Development
- Oral Drug Development
- Parenteral Drug Development
- Bioavailability Enhancements
- Method Development and Validation
- Stability Testing
- Clinical Trial Manufacturing
- Commercial Manufacturing
- Highly Potent Drug Manufacturing
- Analytical Services
- Regulatory Support
- Quality Systems Development

Capabilities

- Development and Commercial Technology Transfer
- Vaccine Fill/Finish
- Steriles-vials, syringes, cartridges
- Lyophilization
- Highly Potent Compounds — hormones, cytotoxins
- Parenterals — aqueous, non-aqueous
- Oral Solids — softgels, tablets, capsules
- Oral Liquids — suspensions, syrups, solutions
- Solid dispersions
- Topicals
- Controlled release formulations
- Fluid-bed processing
- Micro and nanotechnologies
- Coating
- Packaging Serialization
- Enhanced Project Management

The Art and Science of TECH TRANSFER



Concept to Clinical to Commercialization

Pii is a US-based CDMO, our seamless process from concept to clinic to commercialization is driven by our team of world-class professionals. Our campus includes 70 manufacturing suites with 4 integrated aseptic filling lines.

Pii Pharmaceutics International, Inc

TALK TO A Pii PROJECT AMBASSADOR TO START YOUR PROCESS

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410-584-0001

PROVERIS SCIENTIFIC CORPORATION
2 Cabot Road - Hudson, MA 01749
T: (508) 460-8822 E: contactus@proveris.com
W: www.proveris.com

Testing True Product Performance

Leader in spray and aerosol product testing and contract services

Proveris® Scientific's focus is helping its customers unlock the complex relationships between formulation, device, and human usage — knowledge that's essential for timely and effective OINDP development and commercialization. Our industry standard instruments offer rapid insight into critical spray and aerosol parameters, and our team of scientists provide expert consultation and contract test services, taking into account key regulatory and operational nuances of orally inhaled and nasal drug products. As key partners to our clients we help to:

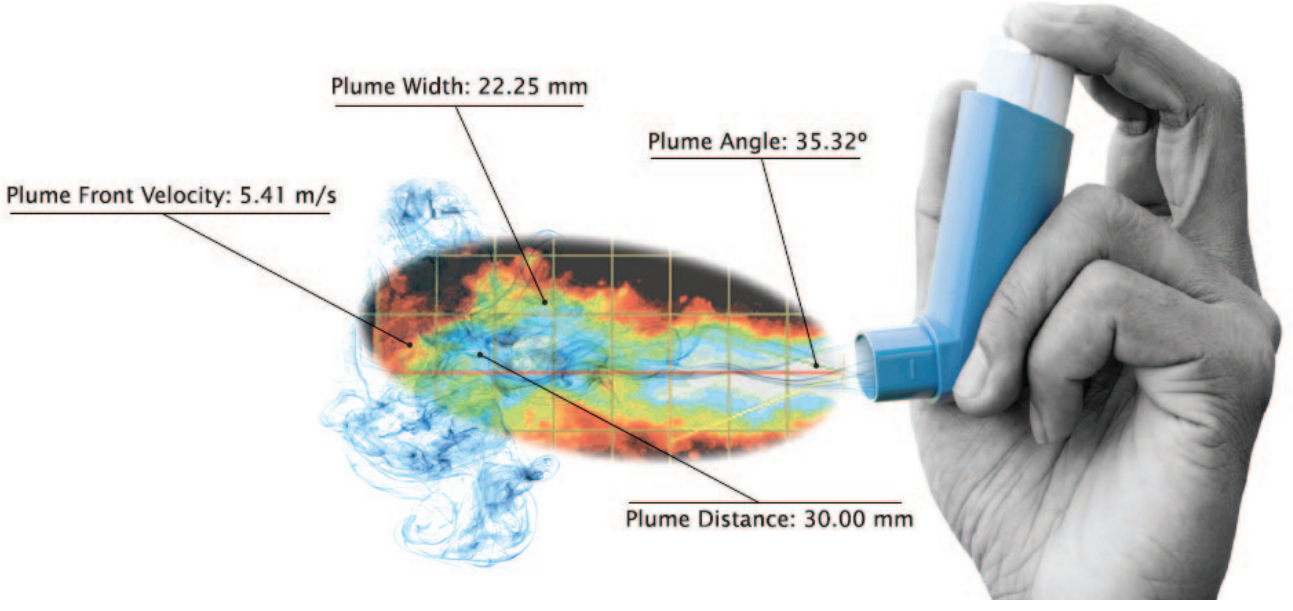
- accelerate successful product development and prevent late-stage development failures
- realize significant savings in time and resources by streamlining testing workflows
- evaluate the suitability of various OINDP delivery devices and optimize device parameters for maximum efficacy
- optimize testing variables to maintain batch-to-batch reproducibility, simplifying regulatory submissions

Proveris Instrumentation

Proveris Scientific manufactures a range of analytical instruments for spray and aerosol characterization, precision automated actuation for through-life testing, automated nasal spray collection systems for spraying, weighing and sample collection, automated shaking and actuation for wasting of pMDIs, as well as powerful software to preserve audit trail and manage your data efficiently.

Contract Services

Proveris Laboratories contract test service offerings include custom packaged studies for method development, formulation and device screening/optimization, human-usage parameters, CMC analytical drug product characterization, device robustness, stability studies, IVIVC studies, and measuring regional drug deposition using physiologically relevant models.



YOUR PARTNER...

FROM DEVELOPMENT TO COMMERCIALIZATION

Scientific expertise and testing strategies for innovator and generic OINDPs

- Human Usage Studies
- Device Selection
- Formulation Screening

Alternative BE Studies

- Regional Drug Deposition
- Plume Velocity
- Evaporation Fraction
- In Vitro Testing
- Drug Product Characterization Studies
- Priming/Repriming
- Temperature Cycling
- Device Robustness
- Stability Studies
- Batch Release Testing
- Long-term Stability Testing
- Root Cause Analysis
- OOS/OOT Investigation

NOW FEATURING cGMP COMPLIANT LABORATORY

LEARN MORE:

www.proveris.com
contactus@proveris.com
+1 508 460-8822

proveris SCIENTIFIC

SGS Life Sciences
E: Us.pharmaqc@sgs.com
W: https://www.sgsgroup.us.com/en/life-sciences

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Lincolnshire, IL
+1 847 821 8900

West Chester, PA
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Mississauga, Ontario
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Markham, Ontario
+1 905 305 0998

SGS gives you convenient access to five North American locations that offer a wide range of life science capabilities and proven processes.

COMPANY OVERVIEW

SGS Life Sciences is a leading contract service organization offering high quality analytical development, biologics characterization, utilities qualification, and quality control testing for over 40 years. Backed by a global network of testing facilities, we can help you to reduce risks, shorten time to market and demonstrate the quality and safety of your products. Our facilities utilize cutting-edge techniques and technologies and are staffed by knowledgeable and experienced personnel who stay abreast on the most recent developments in the field. Our aim is to provide a comprehensive package to support clients from molecule to market, through research, clinical trials product development, quality control testing, manufacture and supply. Whether you need a partner to handle all your testing needs or just an extra hand when your in-house capabilities are restricted, SGS is flexible to meet your needs.

SERVICES OFFERED

cGMP Analytical Testing

- Nitrosamine testing
- Quality control testing of raw materials, APIs, and finished products
- Method development and validation
- Container testing
- Extractable and leachable testing
- Stability testing according to ICH guidelines or customer specifications
- Microbiological testing
- Utilities qualification (air, gas, water and surface)
- Medical device testing
- In vitro toxicology

Biologics Analysis

- Biologics Method Development, Validation, and Quality Control Testing
- GMP Release and Characterization for Drug Substance and Drug Product
- Formal and Accelerated Stability Studies
- Cell Culture for Assays and MCB/ WCB Characterization
- Compendial Testing

LIFE SCIENCES

LIFE INSPIRED, QUALITY DRIVEN

LABORATORY SERVICES

SERVICES INCLUDE:

- Biologics Characterization
- Extractables & Leachables
- Method Development & Validation
- Stability
- Microbiology
- Analytical Chemistry
- In Vitro Toxicology

WANT TO LEARN MORE?

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We work to improve the lives of patients by collaborating with customers to provide leading analytical services, resulting in safer and effective medicines.

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WHEN YOU NEED TO BE SURE

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SINGOTA SOLUTIONS
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Bloomington, IN 47404
T: 812-961-1700
E: solutions@singota.com W: www.singota.com

Singota Solutions is a contract development and manufacturing organization (CDMO) focused on getting products to patients faster by being agile, accountable, and transparent. Founded in 2006, and headquartered in Bloomington, Indiana, Singota provides responsive, quality driven outsourcing services.

Aseptic Manufacturing - Singota can fill parenterals into ready-to-use vials, syringes, or cartridges utilizing our gloveless, robotic, aseptic filling workcell for pre-clinical, clinical, and small commercial therapies. Our manufacturing process ensures freedom from in-process human intervention by not only removing the impact of operators from the initial aseptic environment but also by removing operator variability from the filling process. Some features include:

- Precise, automated, robotic filling allowing repeatability and reduced line loss
- Small volume runs for vials, syringes, or cartridges
- Use of pre-sterilized, nested containers, and pre-sterilized, single use product contact materials
- Customized finishing services, specializing in small-volume clinical batches

Quality Control & Development Laboratory - Our laboratory services include formulation development, process development, and analytical testing. We work with clients in the early phases of development to post-manufacturing support. Our on-site lab saves valuable time on client projects by working seamlessly with our comprehensive services to ensure client milestones are met. Services include:

- Technology/method transfer
- Method qualification
- Thermal characterization
- Particle size reduction
- Lyophilization
- Raw material testing—compendial and other QC release test methods for identity and CoAs
- Release and stability testing (ICH)
- Transport simulation testing, thermal cycling, and thermal excursion studies
- Material compatibility
- Degradation studies

Supply Chain Management & Warehousing - Singota manages a diversified group of materials from APIs and excipients to finished products in our secure cGMP warehouse. We have the capability to handle toxic, potent, flammable, and hazardous materials. Service features include:

- Controlled room temperature (15°C-25°C), cool (2°C-8°C), and frozen (-20°C, and -80°C) storage conditions available
- Clinical trial support and material distribution
- Expertise in temperature-controlled materials management and distribution practices
- Sampling and dispensing capabilities for bulk material forms (liquids, powders, tablets)
- Client accessible material management software
- International supply chain assistance including importer of record services and European storage

Contact us to speak with a Business Development representative to see how we can accelerate your project.

singota®
solutions

Your CDMO

Focused on Faster

We focus on agility and speed while never compromising quality. Our goal is to help you clear your drug development hurdles and meet your pre-clinical and clinical milestones *faster.*

Contact us today

singota.com solutions@singota.com 1.812.961.1700

Stevanato Group: Integrated Capabilities for Pharma & Healthcare

Established in 1949, Stevanato Group is the world's largest, privately owned designer and producer of glass containers for the pharmaceutical industry. From its outset, the Group has developed its own glass-converting technology to ensure the highest standards of quality. The Group comprises a wide set of capabilities dedicated to serving the biopharmaceutical and diagnostic industries: from glass containers with its historical brand Ompi, to high-precision plastic diagnostic and medical components, to contract manufacturing for drug delivery devices, to vision inspection systems, assembly, and packaging equipment. The Group also provides analytical and testing services to study container closure integrity and integration into drug delivery devices, streamlining the drug development process. Thanks to its unique approach as a one-stop-shop, Stevanato Group can offer an unprecedented set of solutions to biopharma companies for a faster time to market and a reduced total cost of ownership.

Global Presence, Local Capabilities

Today, Stevanato Group counts on over 4,000 people in 14 plants & commercial offices across 9 different countries and has an annual turnover of over half a billion Euros. The global growth enabled SG to serve customers with consistent and high-quality products and services close to their operations.

Advanced Glass Primary Packaging & Analytical Services

Stevanato Group boasts unique expertise in providing advanced pharmaceutical containers from glass tubing. Its comprehensive portfolio covers every customer need, from those related to small molecules to highly sensitive drugs. SG produces vials, syringes, and cartridges for different applications, such as vaccines, diabetes care, anesthetics, hormones, anticoagulants, and biologics. Glass containers are available both in bulk SG EZ-fill®, the market-recognized ready-to-fill configuration. SG can also provide container closure and device characterization analytical services through its laboratory US TEC.

Your Specialist in Plastic Molding Solution

Stevanato Group works as a global CMO/CDMO partner, designing, and developing individual plastic solutions for the pharma, diagnostic, and medical market. Its experts are specialists in multi-component precision injection molding and automated system assembly. Stevanato Group can harmonize all the different development processes from the definition phase to the production and global supply of complex products.

Vision Inspection, Assembly & Packaging Technologies: A Modular & Flexible Approach

Stevanato Group capabilities range from modular assembly platforms and packaging lines to advanced vision inspection machines, including manual, semi-automatic, and automatic. SG equipment can inspect a wide range of liquid, emulsions, viscous, gel-like, powder, and lyophilized drugs, catering to the needs of both small firms or big pharma companies producing blockbuster drugs.

STEVANATO GROUP
Via Molinella, 17 35017 Piombino Dese, Padua, ITALY
W: www.stevanatogroup.com

Integrated solutions for pharma & healthcare

Stevanato Group integrates products, technologies, and services providing value-added solutions improving patient's life

Stevanato Group

stevanatogroup.com

CRODA

Pharmaceutical formulators continue to strive to create market leading products with maximum efficacy, quality, and performance. However, the inability to achieve a high level of API solubility and stability are common day-to-day challenges which limit product success. With the help from Croda's superior quality and high purity line of specialty excipients, formulators are able to surpass these barriers, making Croda the supplier of choice in the global pharmaceutical market. With products being manufactured at multiple sites throughout the world, we are able to provide a consistent, local supply of a vast range of high purity surfactants, lipids, and other chemical specialties.

Croda also provides a large selection of products for topical dosage forms, as well as multi-compendial solvents and surfactants suitable for parenteral, oral, ophthalmic, nasal, vaginal, and suppository applications to help formulators maximize the value of their final drug product.

Croda has developed a proprietary line of products called Super Refined™ excipients to help create products of superior quality and purity. These products have undergone intense purification to remove problematic impurities without compromising the fundamental structure of the excipient itself. Super Refined products can help resolve a number of drug development challenges, including formulation instability, inadequate shelf-life, and API degradation. In addition, Croda has been actively investing in GMP API technologies and R&D to ensure the continual delivery of exceptional ingredients, including expertise in drug delivery, vaccine adjuvants, and novel phospholipid ingredients. We consider future health and wellness needs when creating new specialty products.

HIGH-PERFORMANCE PRODUCTS

Croda offers a complete (and constantly growing) range of multicompendial and high purity excipients for various dosage routes and formulations. The company's products include:

- **Super Refined™ Range of Excipients**
  - CCMG 400: high purity caprylocaproyl macrogolglycerides
  - DEGEE: high purity diethylene glycol monoethyl ether
  - Dimethyl isosorbide: high purity solvent for hydrophilic and lipophilic APIs, enhancing skin penetration
  - Oils: sesame, soybean, peanut, corn, olive, safflower, castor, and cottonseed
  - Oleic acid: high-purity, multi-compendial excipient
  - P35 Castor Oil: high-purity polyoxyl 35 castor oil
  - PEGs: high-purity, multi-compendial polyethylene glycols
  - Polysorbates: multi-compendial, high purity Polysorbate 20, 60, and 80
  - Propylene glycol: high purity, multi-compendial solvent
- **Crodacol™ Range:** fatty alcohols
- **Crodamol™ Range:** a range of ester solvents and vehicles
- **Crodesta™ Range:** sucrose esters for mild emulsification and sustainable release in tablet applications
- **Medilan™:** medical grade lanolin designed to surpass USP requirements for lanolin, modified
- **Polawax™:** a complete compendial and self-emulsifying wax
- **Synperonic™ Range:** a range of monograph compliant poloxamers

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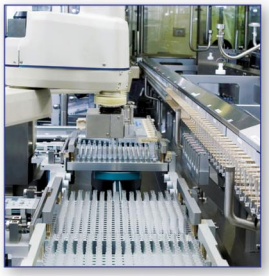
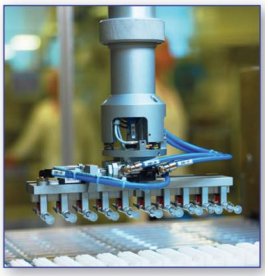
E: infoUS@vetter-pharma.com







YOUR PARTNER IN ASEPTIC FILLING AND PACKAGING

Vetter is a leading contract development and manufacturing organization (CDMO) that specializes in the aseptic filling of syringes, cartridges and vials. Vetter holds numerous patents and has extensive experience with biologics and other complex compounds, including monoclonal antibodies, peptides, interferons, and vaccines. More than 80% of Vetter's active projects are biologics.

Collaborating with biotechnology and pharmaceutical companies both large and small, Vetter supports products from preclinical development through global market supply. Through its US and European facilities, Vetter Development Service provides state-of-the-art support for early stage products, with transfer at Phase III to Vetter Commercial Manufacturing for large-scale production. We offer state-of-the-art technology and innovative processes to promote product quality and maximize API yield.

VETTER AT A GLANCE

- Headquarters in Ravensburg, Germany
- Additional clinical development facility in Chicago, US
- A representative office for Asia Pacific in Singapore and a subsidiary in Japan and South Korea
- Approximately 5,000 employees
- Worldwide specialist in the aseptic production of prefilled drug delivery systems
- Global experience and expertise with regulatory authorities including FDA, EMA, PMDA (Japan), and RP (Germany)
- Lyophilization (freeze-drying) and siliconization specialist

CONTACT US

Visit www.vetter-pharma.com or contact us at info@vetter-pharma.com, infoUS@vetter-pharma.com, or infoAsiaPacific@vetter-pharma.com for more information

Contract Manufacturing

AbbVie Contract Manufacturing has been serving our partners for more than 40 years across ten of our manufacturing facilities located in both North America and Europe. Our contract development and manufacturing capabilities span both small and large molecule API, including classical fermentation, chemical synthetic, biologics, and ADCs. In addition to APIs, we are offering extensive experience and technical solutions in the area of drug product manufacturing, which includes traditional tablet and capsule production with emphasis, potent and hot melt extrusion. Lastly, we can also package your product regionally and offer aseptic fill/finish including prefilled syringe & vial manufacturing capabilities. For more information, visit AbbVie Contract Manufacturing at www.abbviecontractmfg.com or email us directly at **abbviecontractmfg@abbvie.com.**

Lipid-Based Excipients

ABITEC Corporation is dedicated to the advancement of essential bioavailability enhancement and formulation development technology. ABITEC develops and manufactures lipid-based excipients to enhance the bioavailability of poorly water-soluble and poorly permeable Active Pharmaceutical Ingredients (APIs) for the pharmaceutical industry. ABITEC has an expansive portfolio of CAPMUL® bioavailability enhancers, which are medium-chain mono- and di-glycerides and propylene glycol esters. These functional lipid excipients act as solubilizers and emulsifiers in oral, topical, transdermal, and parenteral drug delivery systems. For more information, visit ABITEC at **www.abiteccorp.com.**

Specialty CDMO

Adare Pharma Solutions is a global technology driven CDMO providing turnkey product development through commercial manufacturing expertise focused on oral dosage forms for the Pharmaceutical, Animal Health and OTC markets. Adare's specialized technology platforms provide taste masking, ODTs, and customized drug release solutions. With a proven history in drug delivery, Adare has developed and manufactured more than 40 products sold by customers in more than 100 countries globally. For more information, visit Adare Pharmaceuticals at **www.Adarepharmasolutions.com.**

CDMO Services

Ajinomoto Bio-Pharma Services is a fully integrated contract development and manufacturing organization with sites in Belgium, United States, Japan, and India providing comprehensive development, cGMP manufacturing, and aseptic fill finish services for small and large molecule APIs and intermediates. Ajinomoto Bio-Pharma Services offers a broad range of innovative platforms and capabilities for pre-clinical and pilot programs to commercial quantities, including: Corynex® protein expression technology, oligonucleotide synthesis, antibody drug conjugations (ADC), high potency APIs (HPAPI), biocatalysis, continuous flow manufacturing and more. Ajinomoto Bio-Pharma Services is dedicated to providing a high level of quality and service to meet our client's needs. For more information, contact Ajinomoto Bio-Pharma Services at **www.AjiBio-Pharma.com.**

CDMO Services

Alcami is a contract development, manufacturing, and testing organization headquartered in North Carolina with over 40 years of experience advancing products through every stage of the development lifecycle. Approximately 700 Alcami employees across four campuses in the United States serve biologics and pharmaceutical companies of all sizes, helping to deliver breakthrough therapies to patients faster. Alcami provides customizable and innovative solutions for formulation development, analytical development and testing services, clinical and commercial finished dosage form manufacturing (oral solid dose and parenteral), packaging, and stability services. For more information, visit Alcami at **www.alcaminow.com.**

Contract Laboratory Testing Services

ARL Bio Pharma is a contract laboratory that provides analytical and microbiological testing to pharmaceutical companies and research scientists. Since 1998, ARL has supported the industry-wide commitment to deliver high-quality therapeutic drug products by providing guidance and test services for all phases of the product lifecycle following USP, FDA, and ICH guidelines. Whether you are an innovator or pharmaceutical manufacturer, we provide the testing needed to get your pharmaceutical products to market. Services: USP <61> Microbial Enumeration, USP <62> Specified Organisms, USP <51> Antimicrobial Effectiveness, USP <71> Sterility, USP <85> Endotoxin, Stability Studies, Method Development /Validation, USP Monograph Testing, Y-Site Compatibility Studies, and Dissolution. For more information, contact ARL at (800) 393-1595 or visit **www.arlok.com.**

Formulation Development

Ascendia Pharmaceuticals is a speciality CDMO dedicated to developing enhanced formulations of existing drug products, and enabling formulations for pre-clinical and clinical-stage drug candidates. We specialize in developing formulation solutions for poorly water-soluble molecules and other challenging development projects. Combining our extensive knowledge and experience of formulation capabilities with our suite of nano-particle technologies, we can assess the feasibility of a broad array of robust formulation options to improve a drug's bioavailability. Thusly decreasing the amount of drug and the number of injections and greatly reducing in some cases the daily pill-burden from 20 to 4. Ascendia's expertise spans across (IV, SC, or IM), injection, ophthalmic, transdermal, nasal delivery, along with immediate- and controlled-release products for oral administration and complex generics. For more information, visit Ascendia at **www.ascendiapharma.com.**

Specialized Sterile Injectables

Backed by over 85 years of experience in parenterals, Baxter's BioPharma Solutions (BPS) business collaborates with pharmaceutical companies to support commercialization objectives for their molecules. BPS is a premier CMO with a focus on injectable pharmaceutical manufacturing designed to meet complex and traditional sterile manufacturing challenges with confidence of delivery, service, and integrity. BPS can support your pharmaceutical needs with a broad portfolio of sterile fill/finish production capabilities, and our reputation is built on the high-quality products we manufacture for our clients in a cGMP environment. Our delivery systems include: prefilled syringes, liquid/lyophilized vials, diluents for reconstitution, cartridges, powder-filled vials, and sterile crystallization. For more information, visit Baxter BioPharma Solutions at **www.baxterbiopharmasolutions.com.**

Parenteral Delivery Devices

FOR BETTER TREATMENT OF CHRONIC DISEASES. Across the healthcare continuum, BD is the industry leader in parenteral delivery devices that help health systems treat chronic diseases. We not only continually advance clinically proven, prefillable drug delivery systems, we do so with a vision to help healthcare providers gain better understanding of how patients self-inject their chronic disease therapies outside the healthcare setting. This is why we partner with leading pharmaceutical and biotech companies worldwide to develop digitally-connected self-injection devices — including wearable injectors and autoinjectors — to capture valuable data that can be shared with caregivers. Discover how BD brings new ideas and solutions to customers, and new ways to help patients be healthy and safe. For more information, visit BD Medical – Pharmaceutical Systems at **bd.com/Discover-BD1.**

Small Molecule CDMO

Cambrex is the leading small molecule company for drug substance, drug product, and analytical services across the entire drug lifecycle. With over 35 years' experience and more than 2,100 experts servicing global clients from sites in North America and Europe, Cambrex is a trusted partner in branded and generic markets for API and dosage form development and manufacturing. Cambrex offers an end-to-end partnership for the research, development, and manufacture of small molecule therapeutics along with a range of specialist drug substance technologies and capabilities, including biocatalysis, continuous flow, controlled substances, solid-state science, material characterization, and highly potent APIs. The team has expertise with conventional dosage forms, including oral solids, semi-solids, and liquids, as well as with manufacturing specialized dosage forms, such as modified-release, fixed-dose combination, pediatric, bi-layer tablets, stick packs, topicals, controlled substances, and sterile and non-sterile ointments. For more information, visit Cambrex at **www.cambrex.com.**

Platform Technology

Captisol is a patent-protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Captisol was invented and initially developed by scientists in the laboratories of Dr. Valentino Stella at the University of Kansas' Higuchi Biosciences Center for specific use in drug development and formulation. This unique technology has enabled 11 FDA-approved products, including Onyx Pharmaceuticals' Kyprolis®, Baxter International's Nexterone®, and Merck's NOXAFIL IV. There are more than 30 Captisol-enabled products currently in clinical development. For more information, visit Captisol at **www.captisol.com.**

Early Phase Drug Development

From its three early phase drug development centers of excellence in Nottingham, UK, Somerset, NJ, and San Diego, CA, Catalent offers its customers a number of solutions including analytical, pre-formulation, and formulation technologies. With its comprehensive bioavailability-enhancing technology toolkit, including lipid formulation, spray drying, and hot melt extrusion, Catalent supports the development and launch of over 100 new products every year. Catalent's proprietary OptiForm® Solution Suite platform assists in the development of optimized and innovative dose forms to improve a drug's efficacy and success. OptiForm Solution Suite integrates multiple technologies and tools, and is fast, flexible, and fact-based to deliver data to ensure the right decisions are made at each stage of development and accelerate molecules to Phase 1 clinical trials. For more information, contact Catalent Pharma Solutions at (888) SOLUTION or visit **www.catalent.com.**

Differentiated Injectable Delivery

Credence MedSystems is a medical technology company focused on delivering medications safely for the benefit of our patients, caregivers and partners. The Companion Safety Syringe System was born from Credence's core philosophy of *Innovation Without Change.* By providing passive safety and reuse prevention while using existing primary package components, the Companion offers best-in-class drug delivery with a vastly simplified path to market for our biotech and pharmaceutical partners. The Companion is available in luer needle, staked needle and dual chamber reconstitution configurations. In all cases, the user performs the injection, receives end-of-dose cues and then the needle automatically retracts into the syringe, which is then disabled. For more information, contact Credence MedSystems at 1-844-CMEDSYS, email info@credencemed.com, or visit **www.CredenceMed.com.**

Super Refined™ Excipients

CRODA

Croda manufactures a complete range of high purity excipients and delivery aids, offering superior quality for the global pharmaceutical market. These excipients are ideal for multiple dosage forms, including topical, parenteral, oral, and ophthalmic formulations as well as advanced delivery systems. Croda's Super Refined™ excipients go through a proprietary process to remove the polar and oxidative impurities that can cause performance and stability issues. These excipients are ideal for use when working with sensitive drug actives, helping to maximize the stability and overall performance of the drug product. Excipients in the Super Refined range include PEGs, polysorbates, oils, and triglycerides, propylene glycol, castor oil, and a range of topical penetration enhancers, such as oleic acid and dimethyl isosorbide. For more information, contact Croda at (732) 417-0800 or visit **www.crodahealthcare.com.**

Datwyler Healthcare

Datwyler Sealing Solutions is a leading industrial supplier and key player in the healthcare industry. The Swiss-based company provides state-of-the-art solutions for parenteral drug and medical device packaging which are built on over 100 years of experience. Datwyler's product portfolio, service offering, and manufacturing capabilities can meet a variety of different needs, ranging from early phases of drug development through commercial scale production. Datwyler is the preferred solution partner to pharmaceutical companies and offers one of the most extensive product portfolios for vials, cartridges, and prefilled syringes in the pharmaceutical and biotech markets worldwide. The offering includes a variety of rubber and aluminum seals, plungers, combiseals, tip caps, and needle shields. Our mission: to ensure patients' safety and improve patients' lives. BECAUSE WE CARE. For more information, visit Datwyler Sealing Solutions at **www.sealing.datwyler.com.**

Testing Services

DDL®

Testing experts.
Service specialists.

DDL is an independent third-party, ISO 17025-accredited testing laboratory that provides package, medical device, and combination products testing. For nearly 30 years, DDL has provided extraordinary service and specialized testing expertise to the medical device and pharmaceutical industries. We employ a team of engineers, technical, and quality experts devoted to helping our customers bring medical device and combination products to market. Our single source, totally integrated approach enables organizations of all sizes from start-ups to globally recognized corporations maximize product performance, reliability, and safety while seamlessly achieving regulatory compliance. We work hard to build strong partnerships with our clients and have an unwavering commitment to assist in getting products to market on time. For more information, visit DDL at **www.DDLTesting.com.**

Pharmacovigilance Conference

DIA

For pharmacovigilance professionals, the complexity of safety and pharmacovigilance efforts is heightened by the rapid development of multiple vaccines and treatments, the emergent nature of knowledge about the etiology of the corona virus disease, and pervasive misinformation about prevention and treatment practices. The current challenges are ongoing and will have lasting impact on safety, pharmacovigilance, and risk management. DIA's virtual Pharmacovigilance and Risk Management Strategies Conference, January 26-28, provides the foundation for strong strategic planning and practical decision-making in pharmacovigilance programs. Developed by recognized experts from the biopharmaceutical industry and global regulatory agencies, this conference provides the background, context, and opportunities to discuss current challenges and to problem-solve around issues that matter most to professionals working in the field. For more information, visit DIA Global at **www.DIAglobal.org/PVRMS21.**

Drug Delivery Laboratory

DRUG DELIVERY EXPERTS

Drug Delivery Experts (DDE Labs) is a contract R&D drug delivery laboratory located in San Diego's emerging biotech sector that specializes in drug product development. We have the expertise to integrate drug delivery formulations with the appropriate device to maximize commercial potential. DDE Labs was created in 2014 to address the gap of good outsourcing partners in the formulation and drug delivery technology landscape. We specialize in drug-device combination product development and integration of formulation and delivery system approaches with commercial strategy and life-cycle plans. We work in the injectable products space as well as alternate delivery systems. For more information, visit Drug Delivery Experts at **www.ddelabs.com.**

Formulation Technology

Enteris BioPharma is an independently operated and wholly owned subsidiary of SWK Holdings Corporation [NASDAQ: SWKH]. The organization's headquarters and 32,000- square-foot cGMP manufacturing facility is based within the heart of New Jersey's "Life Sciences Corridor." Through its pioneering and proprietary Peptelligence® technology, Enteris BioPharma partners with pharmaceutical and biotech organizations to develop bespoke solutions, including robust oral formulation development and clinical cGMP manufacturing. For more information, visit Enteris BioPharma at **www.enterisbiopharma.com.**

Global Manufacturing Partner

Flex is a global manufacturing partner that helps a diverse customer base design and build products that improve the world. Through the collective strength of a workforce across 30 countries and responsible, sustainable operations, Flex delivers technology innovation, supply chain, and manufacturing solutions to various industries and end markets. Flex Health Solutions provides design, engineering, manufacturing, real-time supply chain insight, and logistics services to pharmaceutical and medtech companies. It focuses on medical device and drug delivery design, development and manufacturing solutions, including extensive work in injection pens, auto-injectors, wearable pumps, and smart inhalers. Our approach is supported by FDA-registered and ISO 13485- compliant and ISO 11608-1-accredited faciilties, with a world-class single quality system across sites. For more information, visit Flex Health Solutions at **www.flex.com/health.**

GMP & Formulation Development

Foster Delivery Science specializes in hot melt extrusion of drugs and polymers for pharmaceutical and combination drug-device applications. The company's cGMP facility is equipped with state-of-the-art melt extrusion equipment to support pharmaceutical clients from small-scale proof-of-concept to formulation development through clinical supplies and commercial manufacturing. Foster's equipment inventory includes downstream processing equipment and post extrusion equipment to manufacture many different dosage forms. For more information, visit Foster Delivery Science at **www.deliveryscience.com.**

Solutions Made Simple

Freund-Vector Corporation is a world leader in the design, manufacturing of solid dosage processing equipment and services for the processing of powders, particles, beads, and tablets. Primary markets served by Freund-Vector include the pharmaceutical, nutritional, food, confectionery, cosmetic, and chemical industries. The Freund-Vector product lines include coating pan systems for applying an aqueous, solvent, or sugar film coating; fluid bed systems for granulating, fine particle coating, spherization, and drying; roll compaction for material densification and granulation; high shear granulators for wet granulation; spray dryers for creating small particles, and automated process control systems for all the equipment/systems. For more information, visit Freund Vector Corporation at **www.freund-vector.com.**

Formulation Support, Lipid-Based Technologies

With application and R&D Centers in the United States, France, India, and China, the **Gattefossé** group is providing formulation support for oral, topical, transdermal, and other routes of administration. Equipped with state-of-the-art analytical and processing instruments, we are able to support your development efforts and stay at the forefront of research both in basic and applied sciences pertaining to lipids and related drug delivery technologies. Our support covers all stages of development, from solubility screening and preclinical to late-stage formulation and "proof-of-concept" studies. Moreover, we provide extensive regulatory support, sharing toxicological and safety data, and analytical/characterization methods. For more information, visit Gattefossé at **www.gattefosse.com.**

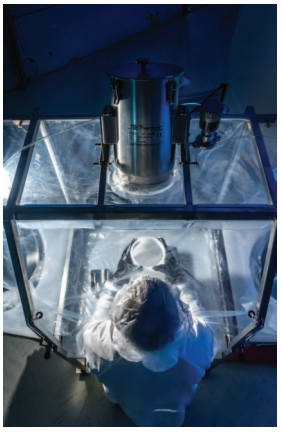
High-Quality Self-Injection Systems

Experts in subcutaneous drug delivery systems for self-administration, Haselmeier provides innovative and award-winning individual system solutions to support patients for a successful therapy. This family-owned business covers all steps – from design to planning to industrialization – in the creation of high-quality self-injection systems. In 2020, this well-established company will be able to look back on a 100-year-old success story. As a leading solutions provider in customized smart drug injection systems, we support reliable, successful therapies. For more information, visit Haselmeier at **www.Haselmeier.com.**

User-Friendly Dosage Forms

HERMES PHARMA is the expert in developing and manufacturing user-friendly oral dosage forms, including effervescent and chewable tablets, instant drinks, lozenges, orally disintegrating granules, and HERMES NutriCaps. The company offers customized solutions at every point along the value chain, from new product development and formulation to manufacturing and regulatory support. For more than 40 years, leading healthcare companies around the globe have been working with HERMES PHARMA to expand their product lines and grow their brands. User-friendly dosage forms are not only a smart solution for people who cannot swallow tablets. Whilst creating an enjoyable experience for the patient, they support healthcare companies to revitalize ageing products and differentiate products from the competition. HERMES PHARMA is a division of Hermes Arzneimittel, a leading German provider of high-quality medicines and supplements marketed under its proprietary, well-established brands. For more information, visit HERMES PHARMA at **www.hermes-pharma.com.**

Atmospheric Control Module



JetVent™, ILC Dover's atmospheric control module, provides safe, automatic, and pressurized containment for higher-potency active pharmaceutical ingredients (HPAPIs) within manufacturing-area isolators, lab areas, and for GMP chambers where airflow, temperature, humidity, and pressure differentials exist from room to room. Designed for use with isolators, including ILC Dover's ArmorFlex® Flexible Isolator, the module's precise fan speed controls negative air pressure to ensure proper flow into flexible-wall isolators, while reducing the risk of worker exposure. Key features include: Portable & Compact, Fully Automated Control, Features Vacuum Control, Includes Breach Response, and Works With Air or Nitrogen. For more information, visit ILC Dover at **www.ilcdover.com.**

Lyophilization Services & Solutions

Founded 1992, **Lyophilization Technology, Inc.** is a Contract Development and Manufacturing Organization providing development services and technical support focused on lyophilized products. Experience with a wide variety of products, including small molecules, cytotoxics, biologics, highly potent compounds, vaccines, medical devices, and diagnostic agents, LTI has provided services and support spanning start-up, virtual, and multinational companies. A comprehensive range of services consists of product design, formulation development, process engineering, and clinical supplies manufacturing for pharmaceuticals, biologics, diagnostics, and biopharmaceuticals. Technical support encompasses consultation on technology transfer, validation, product and process evaluation, troubleshooting, streamlining operations, compliance auditing and training. When your needs are lyophilization, our focus is on your product. For more information, visit **www.lyotechnology.com** or call (215) 396-8373.

The Right Equipment for Your Project

With our new high-shear mixer, the QUEST HSM III granulator, **Metrics Contract Services** can transition formulations from initial development to the process validation stage and, ultimately, to commercial production. Developed jointly by ACG and Xertecs, the flexible QUEST HSM-III granulator can use three different size bowls to accommodate granulation batch sizes from 3 kg to approximately 25 kg. Moreover, its slip ring technology affords us the ability to measure the force acting on the rotating impeller shaft. It provides a sensitive measure of granulation endpoint and, just as important, provides scale-up data during tech transfer. The new granulator further expands our portfolio of manufacturing and service capabilities including pharmaceutical formulation development, preclinical and Phases I-III clinical trial materials manufacturing & comprehensive analytical testing. For more information, visit Metrics Contract Services at **www.metricscontractservices.com.**

Functional Chemicals

Mitsubishi Gas Chemical (MGC) is a leading company in the field of functional chemicals, such as oxygen barrier and absorbing polymers. MGC established the Advanced Business Development Division in 2015 for tackling a variety of today's problems, and the division created OXYCAPT™ Multilayer Plastic Vial & Syringe to solve some issues of existing primary packaging for injectable drugs. OXYCAPT Vial & Syringe consists of three layers. The inner and outer layers are made of cyclo-olefin polymer (COP), the most reliable polymer in the pharmaceutical industry. The middle layer is made of state-of-the-art polyester developed by MGC. The oxygen-barrier property is almost equivalent to glass and much better than COP. OXYCAPT also provides an ultra violet (UV) barrier. For more information, visit Mitsubishi Gas Chemical at **www.mgc.co.jp/eng/products/abd/oxycapt.html.**

Patient-Focused Delivery Devices

With over 1,600 people and four plants across two continents, **Nemera** is a world leader in the design, development, and manufacturing of drug delivery devices for the pharmaceutical, biotechnology, generics industries. Nemera's services and products cover several key delivery routes: Ophthalmic (multidose eye droppers for preservative-free formulations), Nasal, Buccal, Auricular (pumps, valves, and actuators for sprays), Dermal & Transdermal (airless and atmospheric dispensers), Parenteral (autoinjectors, pens, safety devices, and implanters), and Inhalation (pMDIs, DPIs). Nemera always puts patients first, providing the most comprehensive range of devices in the industry, including off-the-shelf innovative systems, customized design development, and contract manufacturing. For more information, contact Nemera at information@nemera.net or visit **www.nemera.net.**

Analytical Testing

Pace Analytical Life Sciences is a network of full-service contract CMC development and GMP analytical testing laboratories. CMC development, chemistry, and microbiology central lab testing services are provided to the Pharmaceutical, Biopharmaceutical, Medical Device, and Combination Product manufacturing industries. Our investment in state-of-the-art facilities and highly trained personnel emphasizes our commitment to delivering positive customer experiences across all channels of our business. We are well-equipped to handle almost any project regardless of scope or complexity. Pace Analytical operates FDA-registered laboratory testing facilities in Oakdale, MN, San German, Puerto Rico, Woburn, MA, and Somerset, NJ. Pace Analytical Services is the largest, American-owned environmental testing company in the US. For more information, visit Pace Analytical Life Sciences at **www.pacelifesciences.com.**

Integrated Full Service Provider

PCI Pharma Services is an integrated full service provider, a proven and trusted partner to leading companies in the global healthcare industry. We offer unparalleled expertise and experience in taking compounds from the earliest stages of development through to successful commercialization, delivering speed-to-market and commercial success for our customers. Our core services support each stage of the product lifecycle, including drug development, clinical trial supply, commercial launch and ongoing commercial supply. We partner with clients in providing innovative technologies, flexible solutions, and an integrated supply network supporting lifesaving medicines destined to over 100 countries around the world. For more information, visit PCI Pharma Services at **www.pciservices.com.**

Specialized Products & Services

Pfanstiehl is a leading cGMP manufacturer of parenteral grade excipients and highly potent APIs. Pfanstiehl develops and manufactures high-purity, low-endotoxin (HPLE) carbohydrates such as trehalose, sucrose, mannitol, galactose, and mannose utilized as injectable excipients for the stabilization of proteins, mAbs, and vaccines. These HPLEs are also used as supplements for industrial cell culture, cell therapy, and cryopreservation media. Pfanstiehl also works closely with some of world's largest multinational pharmaceutical and biopharmaceutical firms, as well as with virtual pharmaceutical companies, to synthesize proprietary and commercial compounds in quantities ranging from grams to MT quantities. Manufacturing and development occur at Pfanstiehl's a 13-building campus located near Chicago, IL. For more information, visit us at **www.pfanstiehl.com.**

Global Contract Manufacturer

Pfizer CentreOne® is a global CDMO embedded within Pfizer and a leading supplier of specialty APIs. Our global manufacturing network includes more than 35 sites across six continents. Backed by Pfizer resources, we deliver technical expertise, global regulatory support, and long-term supply. Working together with our customers, we combine our knowledge with open dialogue to solve challenges. For more information, visit Pfizer CentreOne at **www.pfizercentreone.com.**

Global Data & Analytics

PharmaCircle is a leading provider of global data and analysis on the pharmaceutical, biotechnology, and drug delivery industries. PharmaCircle's premier database delivers an integrated scientific, regulatory, and commercial landscape view with unprecedented access to hundreds of company, product, and technology attributes. PharmaCircle connects product and pipeline information for drugs and biologics with formulation and component details, and provides due diligence level data on nearly 6,000 drug delivery technologies and devices. Drug label comparison tools and full-text document search capabilities help to further streamline research. No other industry database matches PharmaCircle's breadth of content and multi-parameter search, filtering, and visualization capabilities. To learn more, email contact@pharmacircle.com, call (800) 439-5130, or visit **www.pharmacircle.com.**

Specialty CDMO

Pharmaceutics International, Inc. (Pii) is a US-based contract development and manufacturing organization (CDMO) with a passion for solving problems efficiently with the highest quality standards. Pii's Hunt Valley, Maryland campus includes 70 manufacturing suites with 4 integrated aseptic filling lines delivering quality, safety, and efficiency. Our professionals have extensive experience with small and large molecule compounds, developing and manufacturing complex parenteral drugs, extended-release formulations, non-aqueous injectable drug products, and lyophilization. For more information, visit Pii at **pharm-int.com.**

OIND Development

Proveris Scientific is an instrument and laboratory service company that creates today's most advanced testing solutions for orally inhaled and nasal drug product (OINDP) development and manufacturing. We are known worldwide for our expertise in spray characterization, studies for predictive *in vitro/in vivo* correlation, precision automated actuation for through-life testing, and streamlined software solutions to aid in regulatory submission. Our products and services meet strict regulatory standards, including FDA, EMEA, CFDA, ANVISA and ASTM. Our contract test services laboratory is cGMP compliant. For more information, visit Proveris Scientific at **www.proveris.com**.

Contract Service Organization

SGS Life Sciences is a leading contract service organization providing analytical development, biologics characterization, biosafety and quality control testing. With a wholly-owned network of 20 laboratories in 11 countries, services include: analytical chemistry, microbiology, stability studies, bioanalysis, extractables/leachables, virology and protein analysis. Additionally, we offer Phase I-IV clinical services. For more information, contact SGS Life Sciences at Lss.info@sgs.com or visit **www.sgs.com/lifescience.**

Agile CDMO

Singota Solutions is focused on getting your product to patients faster by being an agile, accountable, and transparent CDMO. Our clients can reach their preclinical and clinical milestones more quickly with our shorter lead times and industry expertise. Singota's formulation development, analytical testing, finishing, and supply chain services all support our robotic aseptic filing operation. This completely gloveless, highly repeatable, and precisely controlled process is beneficial for filling your high-value drug product into vials, syringes, or cartridges. Whether a virtual company or large pharma, our team at Singota is here to collaborate with you and customize our services to meet your needs and hit your milestones. Contact us at 812.961.1700 to schedule a visit. For more information, contact Signota Solutions at (812) 961-1700 or visit **www.singota.com.**

Glass Primary Packaging & Analytical Services

Established in 1949, **Stevanato Group** is the world's largest, privately owned designer and producer of glass containers for the pharmaceutical industry. From its outset, the Group has developed its own glass-converting technology to ensure the highest standards of quality. The Group comprises a wide set of capabilities dedicated to serving the biopharmaceutical and diagnostic industries: from glass containers with its historical brand Ompi, to high-precision plastic diagnostic and medical components, to contract manufacturing for drug delivery devices, to vision inspection systems, assembly, and packaging equipment. For more information, visit Stevanator Group at **www.stevanatogroup.com.**

Full-Service CDMO

Vetter is a leading contract development and manufacturing organization (CDMO) that specializes in the aseptic filling and packaging of syringes, cartridges, and vials. The company has extensive experience with biologics and other complex compounds. Collaborating with pharma/biotech clients worldwide, Vetter supports products from preclinical development through global market supply. Through its US and European facilities, Vetter Development Service provides state-of-the-art support for early stage products, with transfer at Phase III to Vetter Commercial Manufacturing for large-scale production. For US inquiries, contact +1-847-581-6888 or infoUS@vetterpharma.com. For Japan inquiries, contact +81-3-6717-2740 or infoAsiaPacific@vetter-pharma.com. For Asia Pacific inquiries, contact +65-6808-7766 or infoAsiaPacific@vetter-pharma.com. For EU and other international inquiries, contact +49-751-3700-0 or info@vetter-pharma.com. For more information, visit **www.vetter-pharma.com.**

Versatile Platform

Sonceboz core competencies consist of design, development, and production of mechatronic drive systems. Since 1936, our focus has been on innovation, best-in-class quality, and service, which is our key to success for worldwide OEM customers. Sonceboz is ISO 13485 certified and active in wearable drug delivery, medical devices, and laboratory industry. Pharma companies looking for Large-Volume Injectors for high- viscosity drugs, Dual-Cartridge, or Auto-Reconstitution Injectors will find interesting solutions in Sonceboz's new drug Delivery Device Platform. Sonceboz's activity in medical devices is based on a long experience in industry, where top quality, reliability, and cost effectiveness is key. For more information, visit Sonceboz at **www.medical.sonceboz.com.**

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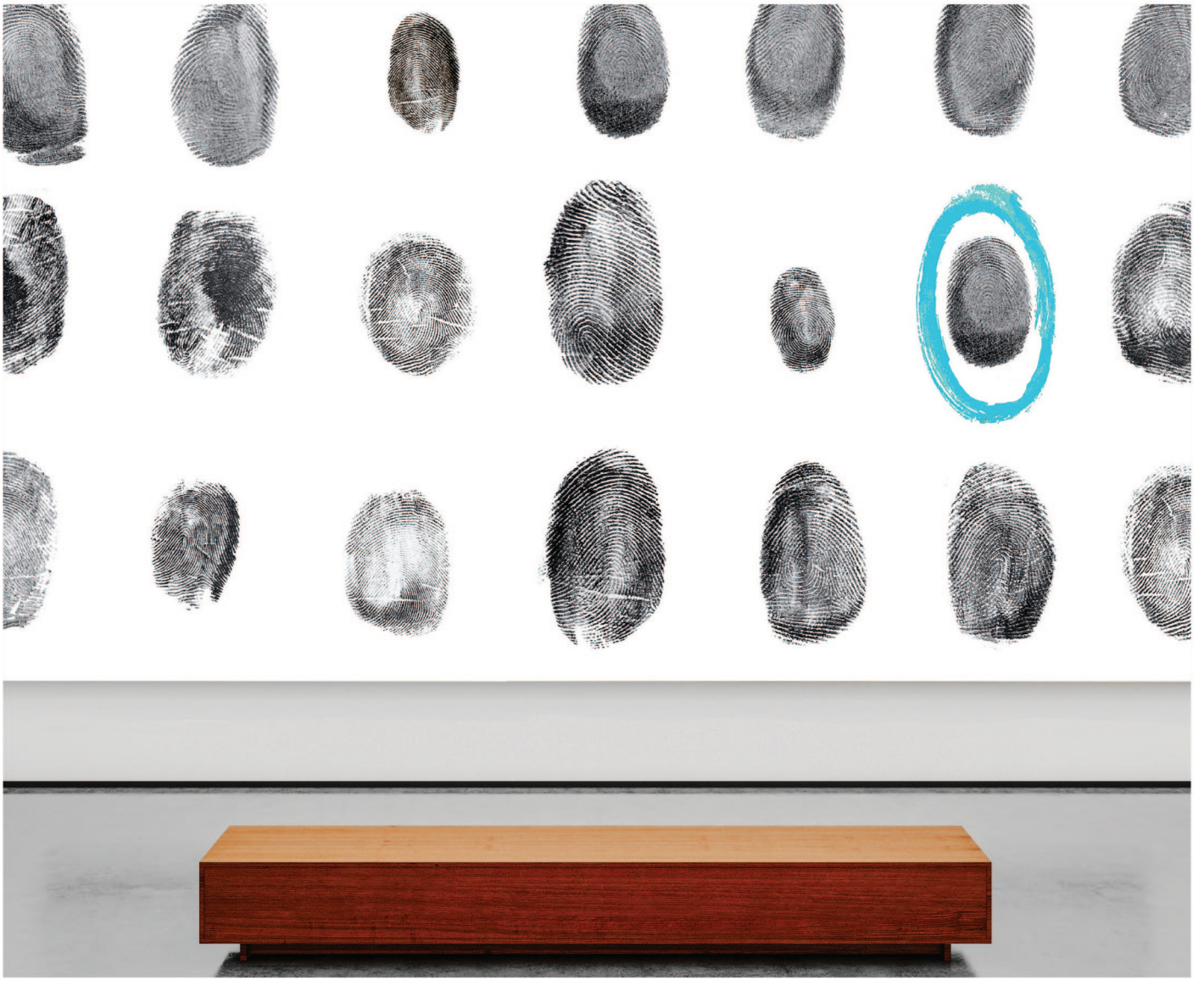
ABITEC Corporation	40,41	acoulter@abiteccorp.com	www.abiteccorp.com
Adare Pharmaceuticals	42,43	BusDev@adarepharma.com	www.Adarepharmasolutions.com
Ajinomoto Bio-Pharma Services	44,45	info@US.AjiBio-Pharma.com	www.AjiBio-Pharma.com
Alcami Corporation	46,47	sales@alcaminow.com	www.alcaminow.com
ARL Bio Pharma	14,48	info@arlok.com	www.arlok.com
Ascendia Pharma	9,50	732-640-0058	www.ascendiapharma.com
Baxter BioPharma Solutions	52,53	biopharmasolutions@baxter.com	www.baxterbiopharmasolutions.com
BD Medical Pharmaceutical Systems	54,55	US: 800-225-3310 - Europe: +33 4 76 68 36 36	www.drugdeliverysystems.bd.com
Captisol	5,56,57	cdinfo@captisol.com	www.Captisol.com
Catalent Pharma Solutions	58, 59,116	888-SOLUTION (USA)	www.catalent.com
Celanese	60,61	healthcare@celanese.com	www.healthcare.celanese.com
Credence MedSystems	51	info@CredenceMed.com	www.CredenceMed.com
Croda	13, 106	Marketing-USA@croda.com	www.CrodaHealthcare.com
Drug Delivery Experts	12, 65	info@ddelabs.com	www.ddelabs.com
DDL	10,64	DDLinforequests@DDLtesting.com	www.DDLtesting.com
DIA	62,63	Americas@diaglobal.org	www.diaglobal.org
Drug Development & Delivery	4,49	rvitaro@drug-dev.com	www.drug-dev.com
Enteris Biopharma	11,66	info@entrisbiopharma.com	www.enterisbiopharma.com
FLEX Health Solutions	68,69	healthsolutions@flex.com	www.flex.com/health
Foster Delivery Sciences	70,71	rsterling@deliveryscience.com	www.deliveryscience.com
Freund-Vector Corporation	72,73	sales@freund-vector.com	www.freund-vector.com
Gattefosse	2, 74,75	info@gattefossecorp.com	www.Gattefosse.com
Haselmeier	76,77	t.ohagan@haselmeier.com	www.Haselmeier.com
Hermes Pharma	78,79	+49 - 89 79102 261	www.Hermes-pharma.com
ILC Dover	8,67	800 631 9567	www.ilcdover.com
Lyophilization Technology	80, 81	inquiry@lyo-t.com	www.lyotechnology.com
Metrics Contract Services	82,83	thomas.salus@maynepharma.com	www.metricscontractservices.com
Mitsubishi Gas Chemical	3,84,85	Nb3.pharmapackage@mgc.co.jp	www.mgc-a.com
Nemera	15,86	information@nemera.net	www.nemera.net
PCI Pharma Services	90,91	talkfuture@pciservices.com	www.pci.com
PACE Analytical Life Sciences	88,89	781 305 4940	www.pacelabs.com
Pfizer CentreOne	92,93	224-212-2267	www.pfizercentreone.com
Pfanstiehl, Inc.	16, 87	cs@pfanstiehl.com	www.pfanstiehl.com
PharmaCircle	7,94,95	contact@pharmacircle.com	www.pharmacircle.com
Pii – Pharmaceutical International Inc	96,97	bd@pharm-int.com	www.pharm-int.com
Proveris Scientific	98,99	contactus@provaris.com	www.proveris.com
SGS Life Sciences	100,101	US.pharmaqc@sgs.com	www.sgsgroup.us.com/en/life-sciences
Singota Solutions	102,103	solutions@singota.com	www.singota.com
Sonceboz	17		www.medical.sonceboz.com
Stevanato Group	104,105		www.stevanatogroup.com
Vetter Pharma International	106	info@vetter-pharma.com	www.vetter-pharma.com



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