Drug Development & Delivery

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Company Profiles & Capabilities

The Science & Business of Pharmaceutical and Biological Drug Development

IN THIS ISSUE

INTERVIEW WITH QUOTIENT SCIENCES' EXECUTIVE DIRECTOR, PEDIATRIC SERVICES

NAZIM KANJI

GATTEFOSSÉ

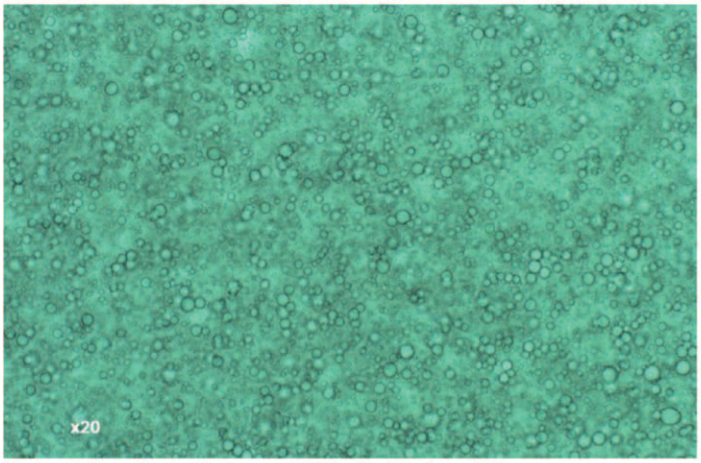
Innovate with bi-gels using Emulfree® Duo

New functional excipient in Gattefossé portfolio

Gattefossé widens its range of high quality, functional excipients for skin delivery with Emulfree® Duo, a stabilizing agent.

Enabler of bi-gel

Emulfree® Duo is a ready-to-use system. It has been designed to stabilize the oil phase within the bi-gel, by ensuring fine and homogeneous dispersion in the aqueous phase. Bi-gels can be adapted to obtain a wide range of consistencies from fluid lotions to rich creams.



Microscopic observation of a bi-gel prepared with Emulfree® Duo (magn. 20)

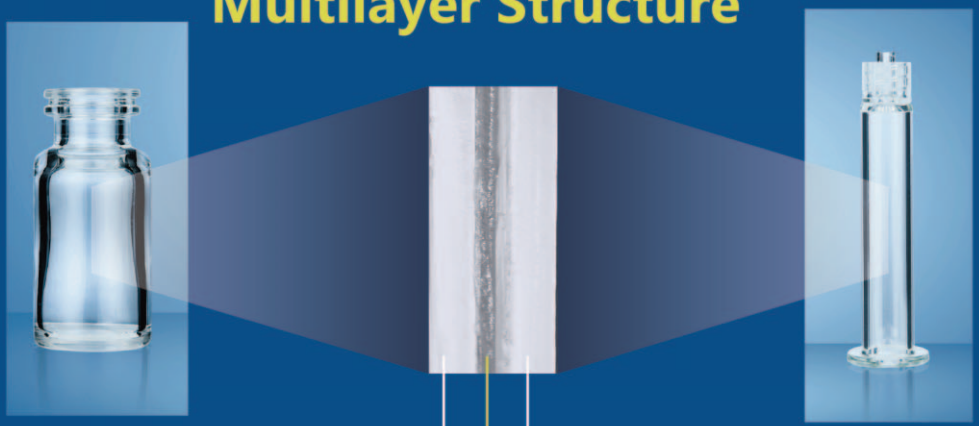
Key benefits

- Ready-to-use stabilizing agent
- Processable at room temperature
- Suitable for hydrophilic, lipophilic and heat sensitive APIs
- PEG-free excipient for sensitive skins and mucosae
- Mixture of propylene glycol monolaurate EP/NF, propylene glycol isostearate and ethylcellulose EP/NF
- Enabler of bi-gel, an emerging and innovative pharmaceutical topical dosage form

https://www.gattefosse.com/pharmaceuticals-products/Emulfree-duo

OXYCAPT™ Plastic Vial & Syringe

Multilayer Structure



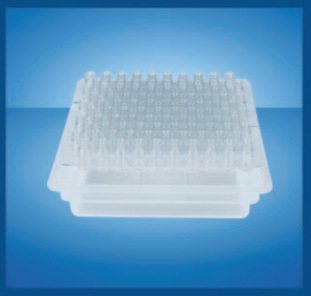
Water Vapor Barrier Layer (COP)

Oxygen Barrier Layer (New Polymer)

Drug Contact Layer (COP)

- 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 & Gene/Cell Therapy

2, 6, 10, 20mL Vial



Nest & Tub for Vial

1, 2.25mL Syringe

Nest & Tub for Syringe

MITSUBISHI GAS CHEMICAL

Mitsubishi Gas Chemical Company, Inc.
https://www.mgc.co.jp/eng/products/abd/oxycapt.html
Mitsubishi Gas Chemical America, Inc.
http://www.mgc-a.com
Mitsubishi Gas Chemical Europe GmbH
https://www.mgc-europe.de

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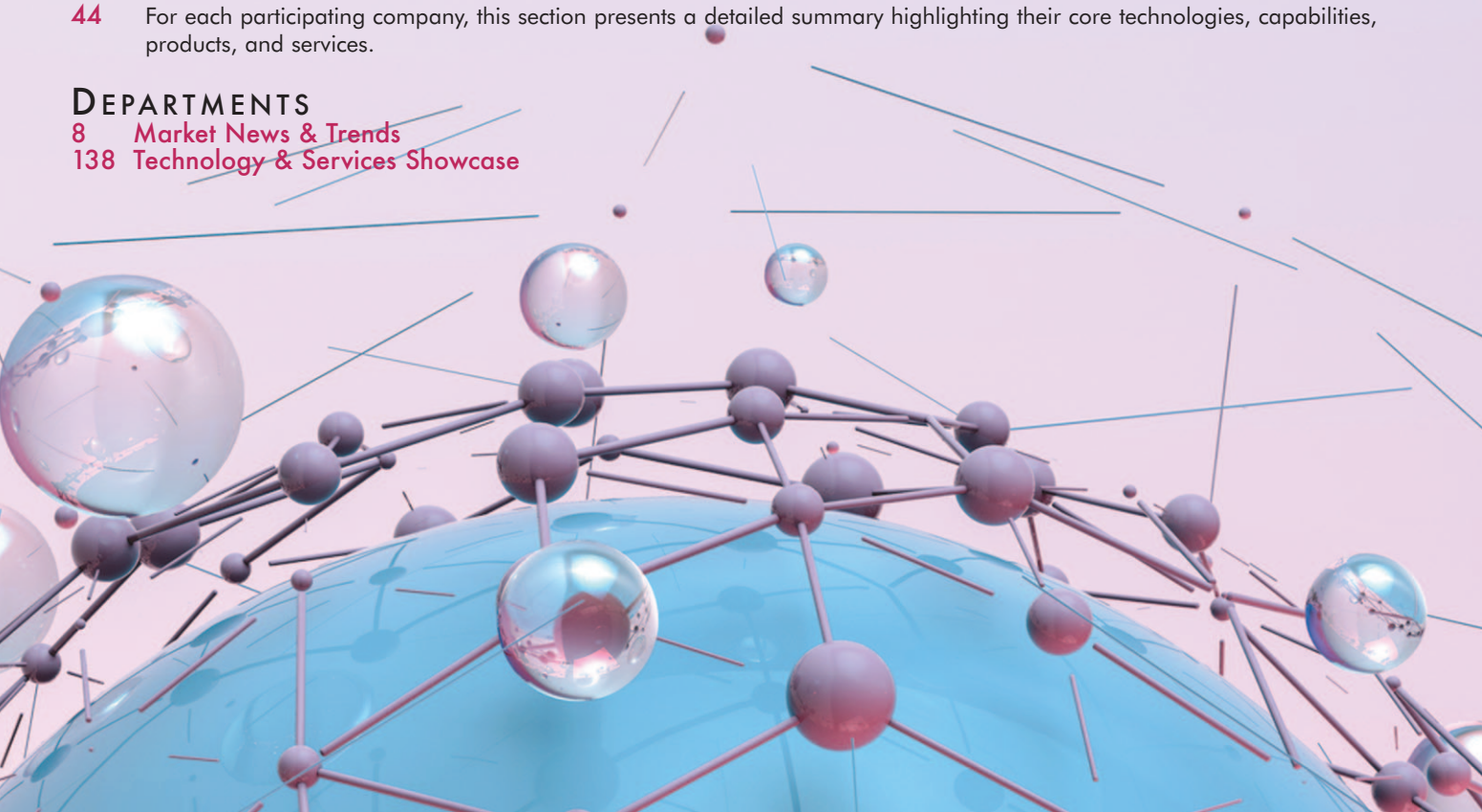
Table of Contents



A TECHNOLOGY-DRIVEN CDMO DELIVERING END-TO-END PATIENT-CENTRIC SOLUTIONS

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Revive Therapeutics Files for FDA Orphan Drug Designation for Bucillamine in the Prevention of Ischemia-Reperfusion Injury During Liver Transplantation

Revive Therapeutics Ltd. recently announced it has filed an application with the US FDA to receive Orphan Drug Designation (ODD) for Bucillamine for the prevention of ischemia–reperfusion injury (IRI) during liver transplantation.

Currently, there is no approved treatments available for IRI. Liver ischemia-reperfusion injury is a major complication of liver transplantation and is one of the leading causes for post-surgery hepatic dysfunction leading to an increased risk of post-operative morbidity and mortality. According to the United Network for Organ Sharing ("UNOS") there were 8,906 liver transplants in 2020 and at the time of the ODD submission there were 11,664 on the waiting list for a liver transplant. Although many therapeutic strategies have been shown to be effective in controlled experimental models, most have yielded equivocal results in clinical practice or have yet to reach human clinical trials.

Revive believes the use of Bucillamine during liver transplantation has the potential to be a safe and effective approach to address the unmet medical need for a novel strategy to limit or prevent IRI. Bucillamine, a cysteine derivative that contains two donatable thiol groups, in the context of IRI is capable of replenishing the thiol group in glutathione, thereby reactivating this endogenous defense against oxidant injury. In addition, Bucillamine appears to have anti-inflammatory effects unrelated to its antioxidant effect. Bucillamine has the potential to address the shortage of quality organs by reducing the susceptibility to IRI of steatotic livers thereby making these livers available for transplants. Bucillamine also has the potential to improve graft function and patient outcome by preventing or lessening IRI.

Michael Frank, CEO of Revive, said "We are continuing to advance novel uses of Bucillamine not only as a treatment for infectious diseases, but also for rare conditions that have no treatment options such as IRI. The FDA orphan drug application for Bucillamine as a potential solution in preventing IRI during liver transplantation and subsequently to other organ transplants complements our overall strategy of developing Bucillamine as a strong platform for other conditions."

Revive is a life sciences company focused on the research and development of therapeutics for infectious diseases and rare disorders, and it is prioritizing drug development efforts to take advantage of several regulatory incentives awarded by the FDA such as Orphan Drug, Fast Track, Breakthrough Therapy and Rare Pediatric Disease designations. Currently, the Company is exploring the use of Bucillamine for the potential treatment of infectious diseases, with an initial focus on severe influenza and COVID-19. With its acquisition of Psilocin Pharma Corp., Revive is advancing the development of Psilocybin-based therapeutics in various diseases and disorders. Revive's cannabinoid pharmaceutical portfolio focuses on rare inflammatory diseases and the company was granted FDA orphan drug status designation for the use of Cannabidiol (CBD) to treat autoimmune hepatitis (liver disease) and to treat ischemia and reperfusion injury from organ transplantation.

Diffusion Pharmaceuticals Doses First Participants in Altitude Trial

Diffusion Pharmaceuticals Inc. recently announced it has dosed the first participants in its Altitude Trial. The trial will evaluate the company's lead product candidate, trans sodium crocetinate (TSC), in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to hypoxic and hypobaric conditions, or "simulated altitude."

The Altitude Trial is a double-blind, randomized, placebo-controlled crossover study designed to evaluate the effects of TSC on maximal oxygen consumption, or VO2, and partial pressure of blood oxygen, or PaO2, in normal healthy volunteers subjected to incremental levels of physical exertion while exposed to "simulated altitude." Diffusion intends to enroll 30 healthy volunteers and give each volunteer a single dose of TSC at one of three different doses. This study will evaluate the effectiveness of TSC in enhancing oxygen delivery to the blood and tissues during exercise under hypoxic conditions. The company anticipates completing the study in late December 2021 or early January 2022, subject to the pace of participant enrollment, and reporting topline results within two months of study completion.

The Altitude Trial is the second in a series of three, short-term studies Diffusion is conducting intended to provide the company with additional information regarding TSC's mechanism of action and dose-response characteristics. The results of the Altitude Trial, together with the results of the company's TCOM Trial (announced in June 2021) and its ILD-DLCO Trial, expected to commence in December 2021, will be used to further inform the design of clinical trials aimed at supporting the commercialization of TSC as a treatment for conditions complicated by hypoxia.

While the company intends to continue developing data to support TSC's broad potential uses, it recently announced that its near-term focus will be the design and execution of a clinical program to support the use of intravenously administered TSC as a treatment for hypoxic solid tumors, and that it intends to obtain input from the US FDA on the program's design in early 2022.

Diffusion Pharmaceuticals Inc. is a biopharmaceutical company developing novel therapies that enhance the body's ability to deliver oxygen to areas where it is needed most. Diffusion's lead product candidate, TSC, is being developed to enhance the diffusion of oxygen to tissues with low oxygen levels, also known as hypoxia, a serious complication of many of medicine's most intractable and difficult-to-treat conditions, including hypoxic solid tumors. In November 2021, based on the preclinical and clinical data accumulated to date and the significant unmet medical need, Diffusion announced that its near-term focus will be the design and execution of a clinical program to support the use of intravenously administered TSC as a treatment for hypoxic solid tumors.

Decibel Therapeutics Announces Extension of Research Term Under Strategic Collaboration With Regeneron to Discover & Develop Gene Therapies for Hearing Loss

Decibel Therapeutics recently announced that Regeneron has extended the research term of its collaboration with the company to discover and develop gene therapies for hearing loss. The research term will be extended to November 15, 2023, and Regeneron will pay Decibel an extension fee of $10 million in Q4 of 2022.

Under the collaboration launched in 2017, Decibel is developing three gene therapy programs targeting congenital, monogenic hearing loss with Regeneron. Decibel plans to initiate in 2022 a Phase 1/2 clinical trial of DB-OTO, the Company's lead gene therapy product candidate, designed to provide hearing to individuals born with profound hearing loss due to mutation of the otoferlin gene. Decibel is also advancing AAV.103 and AAV.104, gene therapy programs targeting other monogenic forms of hearing loss, with Regeneron. AAV.103 aims to restore hearing in individuals with mutations in the GJB2 gene, and AAV.104 aims to restore hearing in individuals with mutations in the STRC gene.

"Decibel and Regeneron scientists have worked closely to advance our gene therapy pipeline for the treatment of congenital, monogenic hearing loss, bringing our lead program, DB-OTO, within sight of the clinic. We are pleased that Regeneron has elected to extend the research term, which extends our access to Regeneron's world-leading genomic and genetic technologies, and therapeutic discovery and development expertise," said Laurence Reid, PhD, Chief Executive Officer of Decibel. "This collaboration, which plays to each party's strengths, is an important part of our ability to accelerate the discovery and development of innovative genetic therapies for patients in need."

"The inner ear is a highly promising frontier for gene therapy, and we believe that the programs being developed in collaboration with Decibel could lead to novel medicines that help people with congenital, monogenic hearing loss," said George D. Yancopoulos, MD, PhD, Co-Founder, President and Chief Scientific Officer, Regeneron. "We're pleased to extend this successful collaboration, which is an important component of Regeneron's growing genetics medicine portfolio. Regeneron and Decibel will continue to work together to combine novel gene therapy technologies with deep biologic expertise, so as to bring life-changing medicines to those suffering with hearing loss."

Through the collaboration, Regeneron provides Decibel with broad access to its proprietary suite of technologies to support Decibel's goal of discovering new medicines for congenital, monogenic hearing loss. Regeneron also directly participates in and provides financial support for Decibel's research and development efforts under the collaboration through milestone payments and reimbursement intended to fund approximately half of the costs of the collaboration programs. Decibel retains worldwide development and commercialization rights to the product candidates being developed in the collaboration and will pay Regeneron tiered royalties based on net sales.

Decibel Therapeutics is a clinical-stage biotechnology company dedicated to discovering and developing transformative treatments to restore and improve hearing and balance, one of the largest areas of unmet need in medicine.

Sever Pharma Solutions Acquires Foster Delivery Science

Sever Pharma Solutions (SPS) recently announced it has entered into a definitive agreement to acquire the assets of Foster Delivery Science (FDS) located in Putnam, CT.

The acquisition of FDS, which is expected to be completed in November, will significantly expand SPS's ability to leverage its expertise in the development of high-potent pharmaceutical products by incorporating the Long-Acting Implantable delivery system capabilities of FDS.

The capabilities of the FDS facility and staff will complement those of SPS's operations in Sweden and the Netherlands. Further development of the FDS facilities is expected to result in a commercially licensed operation within the next few years.

"At Sever Pharma Solutions, we are very pleased to welcome FDS into our group and recognize the expertise in extrusion based implantable drug delivery that will complement our capabilities very well. This will provide clients the opportunity to take advantage of end-to-end services in extrusion" says Kenneth Stokholm, CEO of Sever Pharma Solutions.

"SPS has turned out to be the perfect acquirer for FDS. We share the same vision and philosophies regarding technological leadership, customer service excellence, quality, safety, and putting people first. SPS plans to make significant investments in FDS operations and its Putnam, CT, facilities. I am excited about the future prospect for this business" says Larry Acquarulo CEO of Foster.

For this transaction, PharmaBioSource, Inc. served as the exclusive advisors to SPS and FDS was advised by Covington Associates LLC.

Sever Pharma Solutions brings pharmaceutical ideas to life by offering expertise in high-potent drug development, a drive to enhance performance, a passion for perfection, and a commitment to be your partner through the whole journey. As a committed long-term partner with a strong focus on creating a commercial product, Sever Pharma Solutions will put all its resources to work for its customers. The company also provides global cGMP compliance, regulatory services, and market access strategies to ensure that its customers' products will benefit patients all over the world. For more information, visit www.severpharmasolutions.com.

Foster Delivery Science focuses on hot melt extrusion and complex extrusion, applying its 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. FDS's range of services include GMP/clinical trial/commercial manufacturing supported by formulation development, scale up and optimization of the process. As extrusion is a highly tailorable, continuous process by nature, melt granulation programs are also an obvious interest for lifecycle management and new drug development. For more information, visit www.fosterdeliveryscience.com.

SOTIO Expands Its Antibody-Drug Conjugate Pipeline With Exclusive Collaboration & License Agreement With LegoChem Biosciences

SOTIO Biotech recently announced an exclusive, target-specific license and option agreement with LegoChem Biosciences Inc in which SOTIO will obtain rights to deploy LCB's ADC technology for up to five therapeutic programs targeting distinct tumor-associated antigens.

The deal enables SOTIO to combine its proprietary antibodies with LCB's ADC technology platform in order to deliver novel therapeutics for the treatment of solid tumors and includes LCB's proprietary conjugation technology ConjuAll™ and potent linker-payload platform including multiple different payloads.

Under the terms of the multi-target agreement, LCB is eligible to receive upfront and potential milestone payments worth up to $1027.5 million, payable based on certain developments and regulatory achievements, plus royalties on net sales. The deal includes upfront and near-term milestones worth up to $29.5 million, subject to exercise of the options and achievement of success-based milestones. No further financial details are disclosed.

"At SOTIO we are building an innovative pipeline of ADC programs and plan IND filing for our lead program SOT102 by the end of 2021. The licensing agreement with our new, experienced partner LegoChem allows us to broaden our oncology pipeline with additional programs and solid tumor targets. We are looking forward to using the potential of LegoChem's ADC technology platform and to develop innovative ADCs for patients in need," said Radek Spisek, MD, PhD, Chief Executive Officer of SOTIO.

SOTIO will be responsible for research, development, manufacturing and commercialization of the ADC products, while LCB will support and work closely with SOTIO for the research activities and the manufacturing of components that are specifically related to its proprietary ConjuAll and the linker-payload technologies.

Dr. Yong-Zu Kim, CEO and President of LCB, added "This collaboration is yet another example that illustrates how the value proposition of the LCB platform can increase the competitive position of our partners within the ADC space. SOTIO is an ideal partner for LCB due to its expertise and strategic focus on innovative antibody drug conjugates, and we look forward to working closely together on multiple innovative programs."

LegoChem Biosciences is a clinical-stage biopharmaceutical company focusing on the development of next-generation novel therapeutics utilizing its proprietary medicinal drug discovery technology LegoChemistry and ADC platform technology ConjuAll. Since its foundation in 2006, LCB has focused on the research and development of Antibody-Drug-Conjugates (ADCs), antibiotics, anti-fibrotic and anticancer therapeutics based on proprietary platform technologies.

SOTIO Biotech is shaping the future of cancer immunotherapies by translating compelling science into patient benefit. The robust SOTIO clinical pipeline includes a differentiated superagonist of the attractive immuno-oncology target IL-15, SOT101, currently being tested phase II clinical trials. Three programs will enter phase I clinical testing within the next 12 months, including SOT201, an IL-15-based immunocytokine, BOXR1030, a GPC3-targeted CAR-T based on proprietary technology designed to improve on the efficacy of CAR-T therapies in the tumor microenvironment and SOT102, a next-generation Claudin18.2-targeted antibody-drug conjugate (ADC). SOTIO is a member of the PPF Group.

Baxter Announced $100-Million Investment in BioPharma Solutions Halle/Westfalen, Germany Sterile Fill/Finish Manufacturing Facility

Baxter International Inc. recently announced an approximately $100-million expansion of its sterile fill/finish manufacturing facility located in Halle/Westfalen, Germany. This facility is operated by BioPharma Solutions (BPS), a business unit of Baxter that specializes in partnering with leading pharmaceutical and biotech companies on the development and contract manufacturing of drug product for parenteral (injectable) pharmaceuticals. Construction on the new manufacturing building is expected to begin in 2022 and be completed in 2024.

This strategic investment will expand the BPS manufacturing footprint and add state-of-the-art equipment designed to help products achieve stability and improved shelf life through lyophilization (freeze drying). Construction will also add an aseptic syringe filling line, enabling BPS to meet the growing demand for this delivery platform in both Europe and the United States. Pre-filled syringes can enhance efficiency and ease-of-use for clinicians and have potential to minimize microbial contamination and reduce medication dosing errors during medication preparation, which are key considerations for patient safety.

"Baxter's manufacturing site in Halle/Westfalen is one of the most advanced facilities in our global network and has seen significant growth over the last several years," said Marie Keeley, General Manager, Baxter BioPharma Solutions. "By making this investment, we are building on recent expansions to help ensure this facility can serve our partners at the highest level now and well into the future."

Baxter's Halle/Westfalen, Germany site has more than 60 years of experience and is recognized as a world-class manufacturer of cytotoxic and highly potent drugs, offering dedicated clinical development through commercial production with integrated technologies and services, including barrier technology that helps maintain a high level of containment when manufacturing sensitive and sophisticated drugs. The site also has broad sterile manufacturing capabilities and areas of focus, complies with current good manufacturing practices (cGMP) regulations, features dedicated production areas and is designed to deliver products with optimum efficiency and speed to market. Baxter's Halle/Westfalen facility was previously expanded in 2015, which added capacity and new technologies to stay on the leading edge of manufacturing parenteral oncology therapies. In addition, Baxter's Halle/Westfalen facility is engaged in multiple collaborations to provide sterile manufacturing services for COVID-19 vaccines.

Baxter's BioPharma Solutions business supports leading pharmaceutical companies in meeting their commercialization objectives by providing scientific expertise, sterile manufacturing solutions, parenteral delivery systems and customized support services needed to meet the unique challenges that parenteral products face. For more information, please visit: biopharmasolutions.baxter.com.

OWP Pharmaceuticals Announces IND Authorization for the First-Ever Oral Liquid Formulation of Atomoxetine Hydrochloride for the Treatment of ADHD

OWP Pharmaceuticals, Inc. recently announced it has received IND authorization from the FDA for the first-ever oral suspension of atomoxetine hydrochloride. Offering an important delivery alternative for a drug often used for attention deficit hyperactivity disorder (ADHD), this represents the fifth of several oral liquid medications in neuroscience that the company hopes to commercialize over the next several years via a 505(b)(2) application, in keeping with its pipeline of reformulated, approved therapeutics with no currently available liquid formulation.

Atomoxetine hydrochloride is a selective norepinephrine reuptake inhibitor and the capsules, for oral use, were first approved in the US in 2002. The medication is widely prescribed by healthcare providers in psychiatry for ADHD, and it is indicated for treatment in children 6 years and older and adults. The efficacy of atomoxetine hydrochloride capsules was established in seven clinical trials in outpatients with ADHD: four 6 to 9-week trials in pediatric patients (ages 6 to 18), two 10-week trials in adults (age 18 and older), and one maintenance trial in pediatric patients (ages 6 to 15). In capsule form, US prescriptions for atomoxetine hydrochloride are approximately 3 million total prescriptions annually.

The term attention deficit hyperactivity disorder (ADHD) refers to a neurodevelopmental disorder characterized by inattention, or excessive activity and impulsivity, which are otherwise not appropriate for a person's age. Some individuals with ADHD also display difficulty regulating emotions or problems with executive function. For a diagnosis, the symptoms should appear before a person is 12 years old, be present for more than six months, and cause problems in at least two settings (such as school, home, or recreational activities). In children, problems paying attention may result in poor school performance. Additionally, it is associated with other mental disorders and substance misuse. Although it causes impairment, particularly in modern society, many people with ADHD can have sustained attention for tasks they find interesting or rewarding (known as hyperfocus).

Scott Boyer, Founder and Chief Executive Officer of OWP, said "Today we are pleased to have received IND authorization for our unique formulation of a drug widely used in neuroscience for patients challenged with ADHD. As with our other potential entrants, this alternative dosage form may be preferred by patients of many ages who have trouble swallowing tablets or capsules or who experience swallowing difficulties. Healthcare providers may also find that in this form, the medication may be easier to administer, and it may simplify dosage titration. This fifth important strategic initiative, closely following the releases of our oral liquid formulations for lamotrigine, topiramate, quetiapine, and duloxetine, aligns well with our goal of expanding our business model of single source and multisource generics to include more complex 505(b)(2) branded products in our pipeline."

First Own Gerresheimer Autoinjector – Gerresheimer & Midas Pharma Announce Strategic Partnership

Gerresheimer recently announced it has acquired the IP of a new generation cartridge-based autoinjector from Midas Pharma. This is the start of a strategic partnership. The joint project comprises the development and marketing of the new generation autoinjector. The go-to-market approach for the autoinjector combines the complementary strengths of both companies – Gerresheimer as a solution provider for medical devices and primary packaging solutions and Midas Pharma as experienced facilitator for global pharma projects and provider of products and services along the pharmaceutical value chain.

The new Gerresheimer autoinjector offers biotech and pharma companies as well as patients new opportunities in the treatment of various diseases. The new-generation autoinjector is suitable for subcutaneous injection with up to 3-ml injection volume. The patient-friendly, robust cartridge-based autoinjector will serve as a flexible and adaptable platform for a range of different products in a variety of therapeutic areas. These include highly viscous formulations of biological APIs like new biological entities and biosimilars. With this autoinjector development – based on own IP- Gerresheimer enhances its existing broad portfolio of medical devices such as various on-body injector solutions and wearable injector systems.

The two companies will offer biotech and pharma customers a one-stop-shop around the autoinjector solution: Starting with the selection and delivery for the best solution of a medical device and associated primary packaging plus sourcing of the active pharmaceutical ingredients, through the entire development (technical, pharmaceutical and clinical) and registration. It also includes commercial manufacturing and supply of the ready filled, sterilized and assembled drug-device-combination, supported by a full range of complementary services, eg, quality, technical and analytical, regulatory, IP or project management.

Gerresheimer is the global partner for pharma, biotech, healthcare and cosmetics with a very broad product range for pharmaceutical and cosmetic packaging and drug delivery devices. The company is an innovative solution provider from concept to delivery of the end product. Gerresheimer achieves its ambitious goals through a high level of innovative strength, industrial competence, focus on quality and customers. In developing innovative and sustainable solutions, Gerresheimer relies on a comprehensive international network with numerous innovation and production centers in Europe, America and Asia. Gerresheimer produces close to its customers worldwide with around 10,000 employees and generates annual sales of more than ⇔1.4 billion. With its products and solutions, Gerresheimer plays an essential role in people's health and well-being.

Midas Pharma is a pharmaceutical company based in Ingelheim, Germany, that offers products, services and expertise along the entire pharmaceutical value chain – from Starting Materials and Active Pharmaceutical Ingredients to market ready Finished Products and Devices. Since over three decades the family-owned company has successfully contributed to the Pharma sector and has step by step expanded its competencies.

Dunad Therapeutics Enters Strategic Collaboration With Novartis to Develop Next-Generation Oral Targeted Protein Degrader Therapies

Dunad Therapeutics recently announced it has entered a strategic collaboration and license agreement with Novartis to generate orally bioavailable covalent and protein degrading small molecule drugs. Under the terms of the agreement, Dunad will apply its tunable and highly selective platform to generate novel covalent and targeted protein-degrading small molecule drugs focusing on up to four drug targets agreed with Novartis. Dunad will also be responsible for program execution up to lead optimization. Novartis will contribute target and ligand knowledge as well as access to unique assays and models and will fully fund the research collaboration.

Novartis has an exclusive option to develop and commercialize products resulting from the research programs directed against up to four drug targets. Upon exercise of this option, Novartis will assume responsibility for future development, manufacturing and global commercialization of the small molecule therapeutic products generated against the agreed targets.

Dunad's unique platform uses mono-valent small molecules to induce selective degradation of disease-causing and often undruggable proteins via direct modification of the target. The company's novel molecular approach is fully tunable to be selective and is underpinned by a target-class agnostic mechanism of action that is clearly differentiated from other targeted protein degradation technologies. Dunad's platform has the potential to generate orally bioavailable degrader therapeutics that significantly expand the frontiers of protein degradation targets.

Under the terms of the agreement, Dunad will receive $24 million in an upfront payment and equity investment, as well as significant research funding. Dunad will also be eligible for milestone payments that could aggregate to up to $1.3 billion and royalties.

Alongside the equity investment of Novartis, and the founding investor Epidarex Capital, BioGeneration Ventures (BGV) is joining Dunad as a new investor. Oskar Slotboom, General Partner at BGV, has joined Dunad's Board of Directors.

Prof. Patrick Gunning, Dunad's Co-founder, acting Chief Executive Officer, and Chief Scientific Officer, said "We are thrilled to have entered this collaboration with Novartis, which has already established a world leading position in the protein degradation space. This deal highlights the clear benefits our platform promises for the development of next-generation targeted protein degrader therapeutics. We are confident that with our approach of inducing degradation via direct modulation of target proteins with mono-valent small molecules, we can significantly expand the boundaries of targeted protein degraders as a therapeutic modality."

Dr. Diana Kraskouskaya, Co-founder and Chief Operating Officer of Dunad, added "This collaboration is an important milestone for Dunad. It allows us to rapidly expand the impact of our platform technology to additional target classes and therapeutic areas, beyond Dunad's own internal target pipeline. Our growing team is committed to advancing our internal pipeline and partnered programs directed against the most sought-after and previously intractable targets."

FORMULATION FORUM

Amorphous Nanoparticles for Drug Delivery of Poorly Water-Soluble Compounds

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

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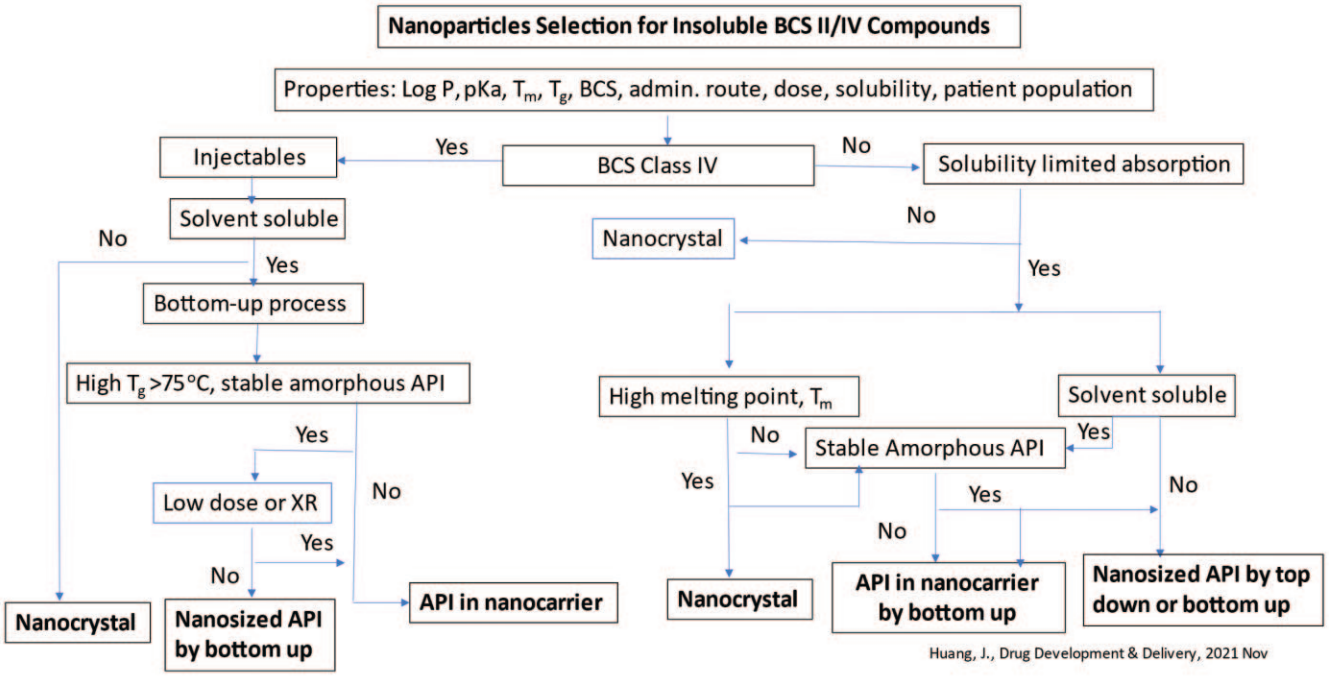
INTRODUCTION

A pharmaceutical amorphous nanoparticle is a solid particle, wherein amorphous drug is nanosized and surrounded by stabilizer(s) or is dispersed in a nanosized carrier at a molecular level. Amorphous nanoparticles are relatively a new class of pharmaceutical dosage forms, possessing the advantages of both nanoparticles and amorphous materials in enhancing solubility and bioavailability of insoluble drugs. Nanosizing offers the advantages of enhancing the rate of drug release by increasing surface area for dissolution, whereas amorphous formation could significantly increase the solubility of poorly soluble drugs in aqueous medium. The saturated solubility and dissolution rate of amorphous nanoparticles could potentially be increased by more than thousand-folds relative to its crystalline counterpart. As a result, the GI absorption and bioavailability of orally administered drugs could be significantly enhanced, particularly for poorly water-soluble drugs classified as BCS IIa and IIb. BCS II compound possess drug biopharmaceutical properties with high GI permeability and low water solubility, which is subdivided into BCS IIa (dissolution limited absorption) and BCS IIb (solubility limited absorption).

The advantages of amorphous nanoparticles include improving solubility and

FIGURE 1



bioavailability, suitable for injectable dosage forms, eliminating food effect, increasing drug loading, eliminating cosolvents, dose reduction, better dose flexibility and accuracy, and easy swallowing for pediatric or geriatric populations.

RATIONAL DESIGN OF AMORPHOUS NANOPARTICLE DOSAGE FORMS

Despite the aforementioned advantages of amorphous nanoparticles, intrinsic solid state metastability of amorphous materials and colloid nature of nanosuspension dosage forms warrant a rational design of amorphous nanoparticles dosage forms in order to extend their application from discovery to clinical testing and ultimately to commercial application. A good understanding of compound properties (T_g, T_m, log P, PKa, solubility, permeability, stability), solvent solubility, miscibility/compatibility with carrier/stabilizer, therapeutic dose in relevant to drug loading, route of administration, and patient population, etc, will help define the target product profile and design a stable dosage form with enhanced drug solubility and bioavailability.

A good candidate for amorphous nanosuspension has the characteristics of BCS Class II and IV compounds: low solubility, amorphous form with a high T_g, a requirement for injectable with high drug loading/solubility ratio, oral dosage form with low bioavailability, and a strong tendency of food effects. A decision guide to decide the suitable form of the nanosuspension and selection of process technology are outlined (Figure 1).

SELECTION OF FORMULATION PRINCIPLE

Based on solid state properties of the API, there are two options for amorphous nanoparticles: 1) nanosized amorphous drug surrounded by stabilizer(s); 2) API dispersed in a nanosized carrier at a molecular level. If the amorphous API can be reproducibly manufactured, and it possesses characteristics that could maintain its physical-chemical properties during process, storage, and in-vivo physiological conditions, eg, a high transition point, (T_g-$T_{storage}$>50°C), strong glass former, non-hygroscopicity, and ability to maintain supersaturation in GI fluid within the transition time period without recrystallization, it is possible that amorphous APIs can be nanosized by traditional top-down milling process with the help of polymers and surfactants as the stabilizers. Top-down technology involves the disintegration of larger particles into nanoparticles, examples of which are being used in Ascendia Pharma include high-pressure homogenization, micro-fluidization, sonication, and wet milling methods, etc.

If an API forms a fragile glass, which has a T_g of <75°C, and readily recrystallizes out during storage or *in-vivo* dissolution, it is often necessary to utilize excipients to form a multiple-component amorphous system (ie, amorphous solid dispersion) to stabilize and inhibit the amorphous drug from crystallization at its solid or aqueous states. An amorphous nanoparticle with a carrier such as polymer, lipid, surfactant, or others will be needed to disperse API at a molecular level in the matrix to stabilize the amorphous API; a bottom-up process could be selected to facilitate the dispersion of drug in the carrier and formation of amorphous nanoparticles, wherein API is molecularly dispersed. Bottom-up technology is an assembling method to form nanoparticles by dissolving the AI in a solvent and then undergoing a solvent removal process, examples of which are being used by Ascendia Pharma include precipitation, coprecipitation, or nano-emulsification methods.

FORMULATION & PROCESS DEVELOPMENT

For nanosized amorphous drug nanoparticles prepared by the top-down process, formulation and process development are similar to crystalline nanosuspension as outlined in a previous Formulation Forum.[1] A formulation screening study is conducted under a miniature scale to find the suitable stabilizer(s), ie, a polymer, a surfactant, or a combination of polymer/surfactant for the nanosuspension. Different surface properties of API, such as surface charge, hydrophobicity, functional groups responsible for ionic, hydrogen bond, and Van der Waal interactions, may demand different types and levels of stabilizers. The performance of nanosuspensions should be confirmed by in-vitro studies such as stability, re-dispersibility, and *in-vivo* performance in animal models.

For amorphous nanoparticles in which drug is dispersed in a nanosized carrier at a molecular level, the initial screening studies to select carrier and stabilizer is similar to that of amorphous solid dispersions as outlined in a previous Formulation Forum.[2] The primary goals of a screening study are to find a polymer and/or surfactant that is physically miscible and chemical compatible with drug, can load reasonable amount of drug in nanoparticle matrix, and to enhance solubility and stability of insoluble compound *in-vitro* and *in-vivo*. Matrix-type amorphous nanoparticles can be prepared using a bottom-up process, high-shear mixing, high-pressure homogenization, or combination of a bottom-up process with a bottom-down nanosizing process. Drug is dissolved in organic solvent(s) together with

other stabilizer excipients, which are induced to precipitate by introduction of non-solvent(s). Variation of formulation and process parameters can generate amorphous drug nanoparticles of different particle size that can be further incorporated into dosage forms by a downstream process.

PROCESS FOR AMORPHOUS NANOPARTICLES

Antisolvent Precipitation/ Co-Precipitation Method

Antisolvent precipitation/coprecipitation method is one of the commonly used bottom-up techniques to prepare amorphous nanoparticles. This method involves dissolving of API and stabilizer(s) in a common solvent, induction of nanoprecipitation by mixing the solvent solution containing API/polymer with an antisolvent, removal of solvent by evaporation or ultrafiltration, and optionally nanosizing using a high shear/pressure/ultrasonic/extrusion process. Different parameters, such as mixing speed, solvent/nonsolvent ratio, drug to stabilizer ratio, drug and stabilizer concentration, and mixing temperature, etc, can be optimized to generate amorphous nanoparticles with a desired particle size distribution and stability profile. Rapid mixing of solvent solution with nonsolvent creates a supersaturation condition that generates precipitation of API as amorphous nanoparticles with or without a carrier. This method is suitable for compounds that are solvent soluble, poorly water soluble, hydrophobic, form stable amorphous forms, or have a high glass transition point.

Nano-Emulsification Method

Nano-emulsification is the process by dispersing one liquid phase into another immiscible liquid phase that generates a uniform mixture of nanodroplets. In the pharma industry, these two immiscible liquids typically consist of an organic (oil/solvent) phase and an aqueous (water) phase in the presence of stabilizer such as surfactant, cosurfactant, and polymer (W/O emulsification). Traditionally, nano-emulsification has been achieved by high shear homogenization, microfluidization, and ultrasonication for nanocapsulation of amorphous hydrophobic compounds, followed by solvent evaporation process if solvent is used. In a modified way, amorphous nanoparticles of hydrophilic drug can be manufactured by a W/O/W emulsification process followed by high pressure homogenization and solvent evaporation process.

Wet Milling Technology

Wet milling (top-down process) is a milling technique commonly used for nanocrystal suspension preparation. It can be also used to wet mill amorphous APIs into nanoparticles if the amorphous drug has enough stability during the process and storage. Another application of wet milling technology used to generate amorphous nanoparticles is by a combination of wet milling with a bottom-up antisolvent precipitation process.

High Pressure/High Shear Technology

Similar to wet milling technology, high pressure homogenization or microfluidization can also achieve nanosuspensions with narrow particle size distribution as a top -down process. Alternatively, a combination of bottom-up and top- down process, ie, solvent dissolution of API, precipitation by non-solvent, and then homogenization of freshly formed particles, could be utilized.

Ultrasonication

Ultrasonication (>20 kHz) is a process of applying sound energy to agitate particles in a liquid. Ultrasonication creates cavitation that improves mixing and mass transfer locally at the contact surface. Ultrasonication can be conducted using an ultrasonic bath or an

FIGURE 2

A high-level flow chart for amorphous nanoparticles prototype formulation development.

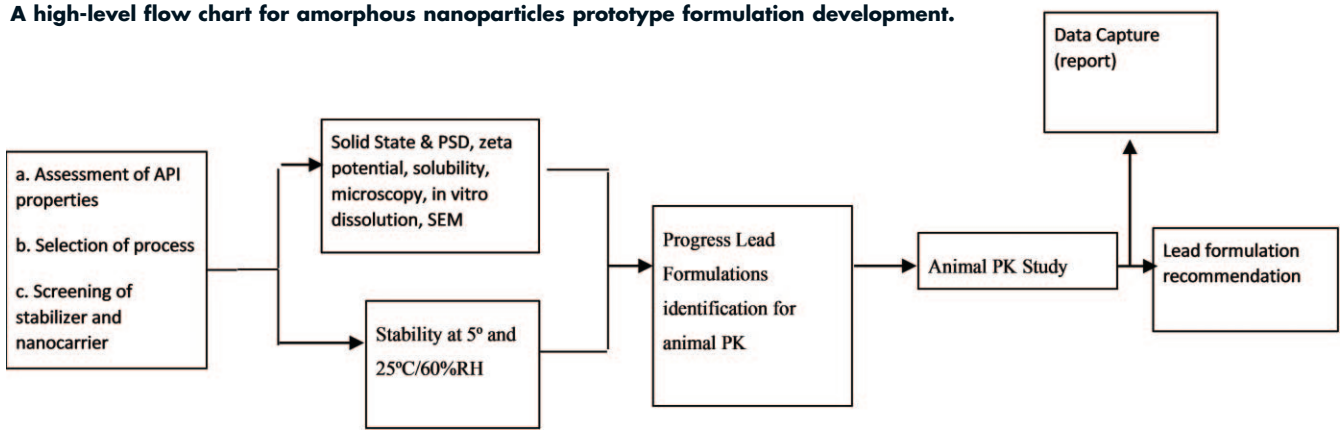
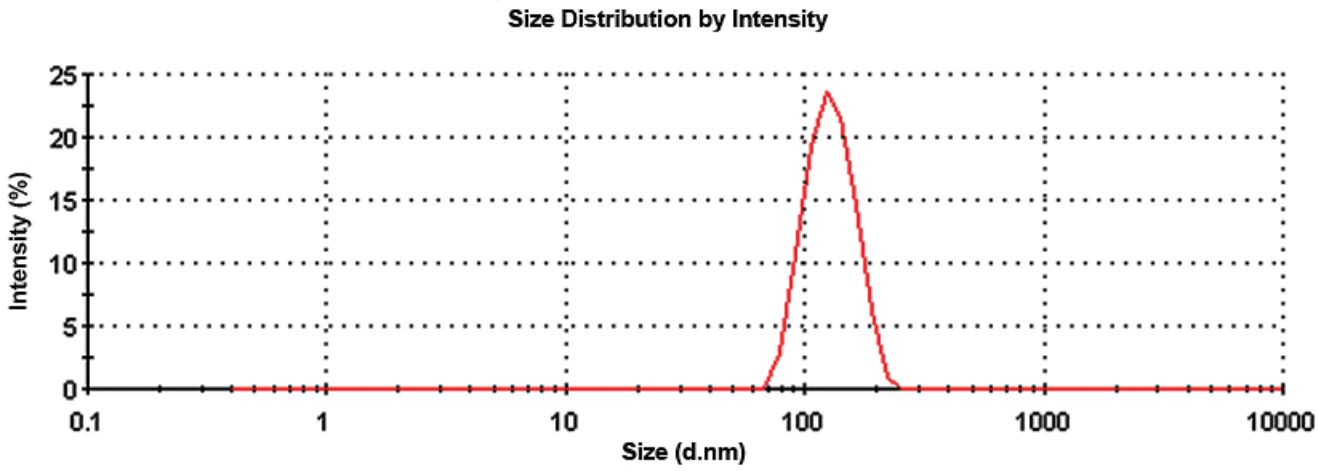


FIGURE 3



PLGA Nanoparticle Size Distribution Used for IV Infusion

ultrasonic probe. Ultrasonication could be used in both the top-down (reducing suspension particle size) and bottom-up method (to control particle size and crystallinity at time of solvent/nonsolvent mixing) for preparation of nanoparticles. Depending on API intrinsic solid state properties, ultrasonic energy intensity, ultrasonic exposure time, mixing mode (on line mixing or post mixing of solvent to nonsolvent), solvent/nonsolvent ratio, type, and level of stabilizer, etc, the ultrasonic process may generate crystalline or amorphous nanoparticles with varied particle size distribution.

A CASE STUDY-PLGA NANOPARTICLES FOR IV INFUSION

A compound was classified as BCS IV (low solubility, low permeability). The compound was targeted for IV infusion due to low oral bioavailability. Because it has a narrow therapeutics index, a sustained-release nanoparticle formulation was desired to enable IV infusion, to reduce Cmax, and to increase half-life for the purpose to reduce compound toxicity and to increase drug exposure at the target organ. Based on the assessment of the compound properties, Ascendia's Nanosol® Technology was utilized for screening and in-vitro assessment of the nanoparticle sustained-release formulation. An O/W nano-emulsification was explored using biodegradable PLGA polymers as the nanocarrier for the compound. Several nanosuspension prototype formulations with in-vitro release rate ranging from <1 day to >2 weeks were developed and tested for stability and animal PK. The particle size of the lead nanoparticles was determined to be ~100-200 nm (Figure 3). The lead prototype nanosuspensions achieved a corresponding in-vivo long half-life up to 1 day to 2 weeks that decreases the drug toxicity and increases drug exposure at the target organ site in animal models.

SUMMARY

Amorphous nanoparticles are a new class of pharmaceutical dosage forms, which have been increasingly used in pharmaceutical compounds with solubility and bioavailability enhancement at discovery, preclinical, and early clinical development phases. Thorough understanding of their amorphous stabilization and nano colloidal properties in relationship to *in-vitro* and *in-vivo* performance will help advance this interesting dosage form into human clinical testing and commercialization.◆

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MARKET BRIEF

Navigating the Evolving Landscape of Rare Cancer Trials

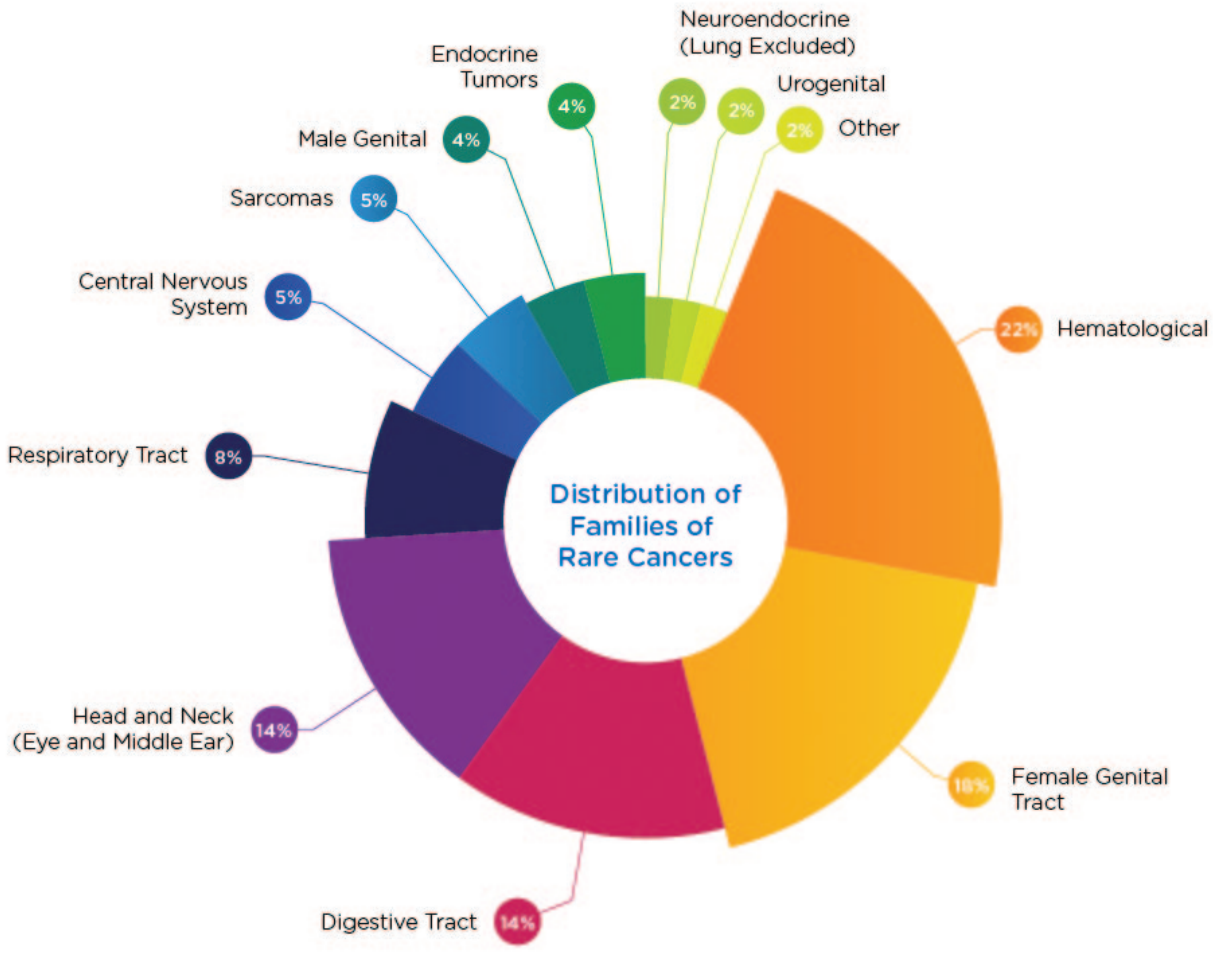
By: Rupa Doshi, PhD, and Sameena Sharif, PhD

INTRODUCTION

Rare cancers account for 27% of all new cancer diagnoses in the US and 22% of all new cancer diagnoses in the EU.[1] With the shift toward grouping cancer based on molecular subtypes rather than by location and tissue type, some common cancers are now categorized as groups of rare cancers. For example, melanoma as a whole is not considered a rare cancer, but when divided into molecular subtypes, it can be viewed as a collection of rare cancers. When grouped as families, the most common rare cancer types are hematological, female genital tract, gastrointestinal, and head and neck malignancies.[2]

Grouping cancer based on molecular subtypes has changed not only how tumors are categorized, but also how novel thera-

FIGURE 1



Adapted from Rare Cancers Europe

Distribution of families of rare cancers.[3]

peutics are studied in clinical trials. In this discussion, we explore the landscape of rare cancer clinical trials, from key considerations for study design and the value of biomarkers to the importance of the patient perspective and the options for speeding much-needed therapies to market.

DEFINING RARE CANCERS

There is no universally accepted definition for a rare cancer. In the US, rare cancers are defined as those with fewer than 15 cases per 100,000 per year. In the EU, however, cancers are considered to be rare if they occur in six cases per 100,000 per year.

While rare cancers are sometimes called the rare diseases of oncology, the terms are not synonymous. From a clinical trial perspective, there is some overlap between rare cancers and rare diseases — namely small and geographically dispersed patient populations, diagnostic challenges, poorly understood natural histories, and statistical hurdles stemming from small sample sizes. There are, however, some key differences:

How they are defined – Rare diseases are defined by prevalence, while rare cancers are defined by incidence.

The role of genetics – 80% of rare disease have a genetic basis, whereas few rare cancers have a well-defined genetic component.

How they affect children – 75% of rare diseases affect children, and while childhood cancers are less common than adult cancers, every pediatric cancer is considered rare.

The approach to target discovery - Rare diseases comprise a heterogeneous collection of diseases with unique targets, while rare cancers fall under the larger cancer umbrella and may benefit from discoveries in common cancers.

RARE CANCERS & PRECISION MEDICINE

Surgery, radiation, and chemotherapy were the mainstays of cancer treatment for many decades, but precision medicine has transformed the oncology landscape. With advances in genetics and technology, it is now possible to offer customized care based on the molecular characteristics of a particular tumor. In recent years, there have been breakthrough developments of tumor- or tissue-agnostic therapeutics. Three such therapies have received regulatory approval to date:

Pembrolizumab – for tumors with microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR).

Larotrectinib – for tumors with neurotrophic tyrosine receptor kinase (NTRK) gene fusions, which are found in approximately 0.3% of patients across various cancer histologies.

Entrectinib – also for tumors with NTRK gene fusions.

Larotrectinib is the first drug developed entirely using an agnostic approach. Its approval was based on efficacy data derived from three separate open-label, single-arm trials. Designed as basket studies, these trials included patients with 12 different solid tumor indications, all with the same NTRK gene fusion and all of whom were treated with larotrectinib. The overall response rate was 75% across all three trials. Approval was based on pooled data from only 55 patients and the time from Phase 1 to accelerated approval was only 3 years, highlighting the potential efficiency of adopting a biomarker-driven approach to innovative drug development.

MOVING TOWARD SEAMLESS DRUG DEVELOPMENT

An increasing number of rare oncology programs have transitioned from a traditional, sequential drug development pathway to a seamless one. In seamless drug development, pharmacology, therapeutic exploratory, and therapeutic confirmatory studies are combined, with the goal of achieving accelerated approval.

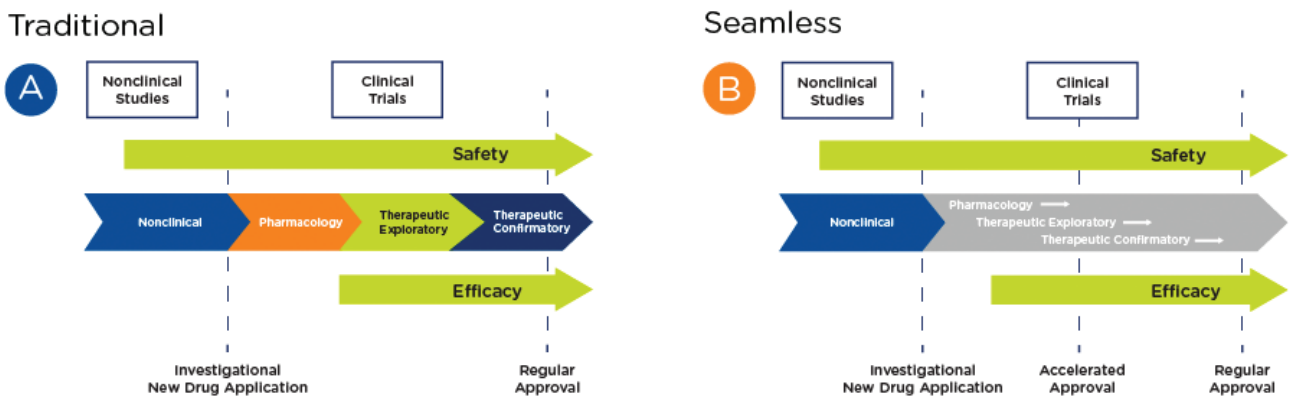
Cross-functional alignment across clinical, regulatory, manufacturing, and marketing is essential for meeting the shortened timelines of seamless drug development. Rare oncology sponsors who are considering this approach will need to account for the following:

Population size – The number of patients in the final dataset will be low, so innovative trial designs and statistical methods for data analysis may be required.

Recruitment strategy – For successful enrollment, broad geographic reach will likely be necessary, increasing study cost and complexity.

Study design – It is critical to define the study population and subgroups, methodology for response assessment, and endpoints. Biomarkers may be more sensitive than tumor measurements for gauging response, especially with targeted therapies

FIGURE 2



Adapted from American Association for Cancer Research and Theoret MR, et al. Clin Cancer Res. 2015;21:4545-4551.

Traditional versus seamless drug development.[4]

and immunotherapies. If overall survival is an endpoint, it is also important to determine how to manage patients who progress after initial treatment.

Genetic or biomarker testing – Sponsors will need to identify an appropriate testing kit and testing methodology early in the program. The kit and methodology should be fit for purpose based on the development phase, but also scalable for late-stage studies and commercialization.

Manufacturing – With an accelerated program, manufacturing will need to scale quickly while remaining compliant with regulatory requirements.

THE ROLE OF ADAPTIVE DESIGNS IN RARE CANCER TRIALS

Adaptive designs are study designs that allow for prospectively planned, predefined modifications to be made based on analysis of accumulating data at predetermined points in the trial. These designs can be used to optimize rare cancer trials, allowing for additional flexibility, increased efficiency, and more targeted study populations. Adaptive designs commonly used in rare oncology trials include:

Seamless Phase 1/2 – where a Phase 1 study focused on dose-finding transitions directly into a Phase 2 expansion study focused on efficacy.

Biomarker enrichment – which uses biomarkers as inclusion/exclusion criteria, with the goal of identifying patients who are most likely to respond. An alternative to this approach is biomarker stratification, where biomarkers are measured on all patients and are used as stratification variables.

Umbrella – which evaluates multiple targeted therapies for a single disease by stratifying patients into subgroups based on tumor molecular characteristics.

Basket – where a single targeted therapy or therapy combination is investigated in a variety of cancer types that share common underlying molecular alterations.

Notably, adaptive designs are not mutually exclusive, and multiple methods may be used in a single trial.

THE BENEFIT OF BIOMARKERS

Use of biomarkers for patient selection and treatment response monitoring has increased significantly. Research has shown that studies using biomarkers for patient selection are both more likely to advance at every stage of development and more likely to gain regulatory approval. In Phase 3 trials, studies employing biomarkers are nearly twice as likely to succeed as those that do not.[5]

Biomarker testing methodologies are myriad. Next-generation sequencing (NGS), which enables a broad spectrum of genomic alterations to be analyzed simultaneously, has been a driver of precision medicine in oncology. NGS can be applied to specific genes, off-the-shelf or custom gene panels, whole exomes, or even the entire genome. Coupled with decreases in sequencing costs and increases in efficiency, NGS has fueled a paradigm shift in biomarker discovery and targeted drug development.

NGS generates a massive amount of data, but not all genomic information is

"Grouping cancer based on molecular subtypes has changed not only how tumors are categorized, but also how novel therapeutics are studied in clinical trials. In this discussion, we explore the landscape of rare cancer clinical trials, from key considerations for study design and the value of biomarkers to the importance of the patient perspective and the options for speeding much-needed therapies to market."

clinically relevant. It is, therefore, important for sponsors to develop a strategy for sifting through and interpreting the data to assess its clinical significance. In addition to leveraging online genomic knowledge bases, sponsors may find it useful to create precision medicine teams or molecular tumor boards to assist in data interpretation. Liquid biopsies — which may be blood, plasma, or other bodily fluids — are also poised to be indispensable biomarker tools. Traditional tissue biopsies are associated with certain limitations such as availability, invasiveness, cost, and inability to perform multiple assessments. With liquid biopsies, it is possible to perform cost-effective serial sampling for longitudinal assessment and downstream analysis.

INCORPORATING THE PATIENT PERSPECTIVE

Successful rare cancer studies require strong patient advocacy and engagement. Imatinib, a type of chemotherapy, is a classic example of how the internet can inspire patient activism and impact drug development. When reports of remission with imatinib treatment in a Phase 1 study circulated in the early 2000s, patients clamored for increased clinical trial activity and drug production, spurring a Phase 2 trial and, ultimately, approval.

Technology has been a powerful enabler of patient involvement in drug development. Social media platforms facilitate knowledge sharing at scale and offer opportunities for sponsors to learn more about the patient perspective. This is especially important in rare cancer research, in which patients are searching for options and might be willing to accept different levels of treatment-related risk. Facebook groups and other online forums bring together patients with rare cancers, allowing sponsors to reach out to patients for feedback. An increasing number of nonprofit organizations such as Count Me In are seeking to connect patients with researchers to accelerate discovery and development of novel treatments. The ability to interact with geographically dispersed patients not only facilitates recruitment but also broadens access.

ACCELERATING THE PATH TO APPROVAL

Given the limited arsenal of treatment options available for most rare cancers, time is of the essence in drug development. The 2020 approvals of tazmetostat for advanced epithelioid sarcoma and selumetinib for neurofibromatosis type 1 signal the FDA's commitment to prioritizing the unique needs of rare cancers. Recognizing that certain aspects of drug development for common diseases may not be feasible for rare cancers, the agency has demonstrated a willingness to offer additional flexibility.

In the US, there are a number of regulatory mechanisms available to help expedite rare oncology program, including:

Fast track designation - To qualify for fast track designation, a therapeutic must be intended to treat a serious condition, and there must be nonclinical or clinical data demonstrating its potential to address an unmet medical need. Alternatively, the therapeutic must be designated as a qualified infectious disease product. This designation can be rescinded if the therapy no longer meets the qualifying criteria.

Breakthrough therapy designation – Like the fast track designation, the breakthrough therapy designation applies to therapeutics intended to treat a serious condition and can be rescinded. To qualify as a breakthrough therapy, however, there must be preliminary clinical evidence indicating that the product may demonstrate substantial improvement on at least one clinically significant endpoint over available therapies.

Accelerated approval – This pathway is intended for therapeutics that treat a serious condition, provide a meaningful advantage over available therapies, and demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint. Sponsors who are interested in pursuing accelerated approval should discuss their plans with the FDA review division early on in development. In general, the FDA will request that confirmatory studies be underway at the time of accelerated approval.

Priority review designation – The priority review designation requires that a drug is intended to treat a serious condition and, if approved, provide a significant improvement in safety or effectiveness. Other submissions that might qualify for priority review include supplements that propose a labeling change pursuant to a pediatric study, applications for drugs designated as qualified infectious disease products, and submissions accompanied by a priority review voucher.

PRIME – In the EU, PRIME is the main mechanism for expediting development of medicines targeting unmet medical needs. PRIME provides enhanced interaction and early dialogue with regulators to help ensure generation of robust data and enable accelerated assessment of marketing authorization applications. Key benefits of PRIME include appointment of a rapporteur for continuous support, organization of a kick-off meeting for guidance on the regulatory strategy and overall development plan, assignment of a dedicated contact point, and provision of scientific advice at key development milestones.

SUMMARY

Rare cancers represent a significant unmet need in oncology. Globally, more than one in five cancer patients is living with a rare cancer and faced with limited treatment options. With advances in genomic testing, immunotherapy, and precision medicine, progress is being made, bringing new treatment alternatives to the patients who need them. ◆

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Dr. Rupa Doshi is Vice President, Program Strategy, Oncology at Premier Research. With more than 23 years in the industry, she is an experienced professional with demonstrated leadership skills in clinical operations, global project/program management, customer management, and strategy development. Her experience spans the clinical development spectrum from pre-IND to NDA. She has also led global teams to execute full-service complex clinical trials across all phases. She brings drug discovery and clinical development experience with biologics and small molecules as well as cell and gene therapy products over a range of indications. Her doctoral research focus was on breast cancer, while her post-doctoral research was in site-directed mutagenesis. She holds patents in angiogenesis and has also supported three products resulting in agency approval.

Dr. Sameena Sharif is President, Regulatory Professionals, A Division of Premier Research. She is a strategic thought leader in drug development, alliance, project, and portfolio management. She has broad experience in managing projects at all stages of drug development — from the target selection and pre-investigational new drug stages through new drug application/marketing authorization application submissions and commercial planning. She has led large, cross-functional teams in global alliances with Amgen, Otsuka, Genentech, Novartis, Onyx, and AstraZeneca, with a particular interest in optimization of the drug development and alliance management process in small and midsize companies. She earned her Bachelor of Pharmacy from the University of Bradford and her PhD in Pharmaceutics from the University of Nottingham.

APTAMER TECHNOLOGY

From Postal Codes to GPS: Building Better Drug Conjugates With Aptamers

By: David Bunka, PhD and Emily Robinson, PhD

INTRODUCTION

Orthoclone OKT3 was the first therapeutic monoclonal antibody brought to market in 1986 for the treatment of kidney transplant rejection.[1] Following this, the biotherapeutic market has continued to expand, representing the fastest-growing pharmaceutical market sector. Predicted annual growth of 14% with annual sales of over $120 billion in this sector compares favorably to growth of just 6.8% for traditional pharmaceuticals.[2,3] Indeed, last year, five of the top-ten best-selling drugs were antibody therapeutics, and antibody technology has a proven track record in developing effective therapies with good safety profiles across oncology, hematology, cardiology, immunology, and autoimmunity.[4-6] The increased interest in this sector has spurred advances in immunotherapy, gene and cell therapies, and affinity reagent technologies. However, these advances have also revealed limitations in antibody technology that prevent these molecules from meeting the developing potential of precision medicine.[2,3] Such

FIGURE 1

Size comparison of an antibody (left) versus an aptamer (right). Antibodies are approximately 10 times the size of aptamers. The larger size and molecular weight of antibodies (~150 kDa) can impede tissue penetration compared to the smaller size and molecular weight of aptamers (~5-18 kDa).

limitations include the large size of antibody molecules (Figure 1), which hampers their ability to penetrate tissues *in vivo*, and their structural complexity, which requires expensive and difficult to optimize mammalian manufacturing systems.

A new breed of affinity binders that can be used as an alternative to antibody therapeutics has the potential to reshape the industry, delivering new medicines with improved safety and efficacy profiles and reduced healthcare costs.

ANTIBODY-DRUG CONJUGATES: THE PROBLEMS

Conjugating drug molecules to an affinity ligand produces targeted therapies that can enhance the selectivity and hence the performance of the therapeutic agent while simultaneously reducing off-target interactions, which lead to adverse side effects.[7] Antibody-drug conjugates (ADCs) allow the combination of the targeted precision of antibodies with:

1. the potency of small molecules for targeted therapy
2. oligonucleotide therapeutics (such as siRNA) - for the targeted cellular delivery of gene therapy
3. an additional affinity reagent as a bispecific modality for increased therapeutic targeting and receptor activation

From the introduction of the first ADC in 2001, these molecules have undergone multiple rounds of refinement, including developing new toxic payloads, increasing the linker stability, and assessing the potential for antibody alternatives.[8] Though the high target binding affinities of monoclonal antibodies reduce off-target effects, the large size of these biologics has been shown to restrict their diffusion through tissue *in vivo* and limit the accessibility of ADCs to certain epitopes.[9] Their high molecular weight also reduces the rate of renal clearance. While this can be beneficial in that it reduces dosing frequency, it can also be detrimental in that long circulation times increase the potential for off-target effects and the development of anti-drug antibodies.

Antibodies are composed of multiple polypeptide chains that are variably glycosylated and connected through numerous disulfide bonds. This structural complexity poses a significant challenge to the scale-up of their manufacture, requiring expensive mammalian expression systems and often leading to batch consistency issues.[10] Additionally, for ADC production, the final antibody must be further modified with the therapeutic payload. Site-specific chemistries, such as maleimide linkages on cysteine residues, can still lead to problems in generating a homogenous product due to the number of cysteine residues present in the antibody molecule and their varying accessibility and chemical reactivity. While there has been considerable progress in this area, significant challenges remain in controlling the antibody:drug ratio and purification of the final product.

Delivery of the final ADC cargo to the cell's cytoplasm for its effector function is not straightforward with antibodies. Due to the large size of antibodies, cellular internalization can be retarded, requiring highly stable linkers to prevent premature linker cleavage and release of the cargo before it reaches the intended site of action.[11]

ADVANCING BIOLOGICS WITH APTAMER TECHNOLOGY

The use of nucleic acid aptamers as the targeting moiety overcomes many of these pitfalls. Aptamers are small, single-stranded oligonucleotide molecules isolated from large libraries, using highly tunable *in vitro* processes. Based upon their nucleotide sequences, aptamers form a variety of structures and can be selected to specifically bind to their target molecules in the same way as antibodies. However, aptamers also offer manufacturing advantages as they are generated via well-defined solid-phase synthetic processes, for batch consistency and simple modification with a range of cargo.[12] Due to their small size, aptamers have a short half-life *in vivo*, offering reduced toxicity concerns compared to antibodies, which can stay in the patient's circulation for weeks. To delay renal clearance, strategies must be adopted, such as PEGylation, which increase half-life where required.[13] Aptamer-drug conjugates (ApDCs) are offering new potential for this therapeutic approach to provide effective treatments for a range of diseases.

The first aptamer therapeutic, pegaptanib sodium (Macugen) was licensed in 2004 for the treatment of neovascular (wet) age-related macular degeneration.[14] A further 10 aptamer therapeutics have successfully entered clinical development for conditions ranging from oncology and inflammation to diabetes and coagulation.

NOXXON Pharma's unique aptamer-based Spiegelmers® are L-enantiomers and consequently not subject to nuclease activity for increased retention. Ongoing trials for Spiegelmer therapeutics include Phase 1/2 trials for the treatment of pancreatic cancer and brain cancer in differ-

TABLE 1

Aptamer Target	Therapeutic Cargo	References
Protein tyrosine kinase 7	Chemotherapeutics Photosensitizers Immunotherapeutics	18-20
Nucleolin	Chemotherapeutics siRNA	21, 22
Prostate-specific membrane antigen	Chemotherapeutics siRNA/shRNA	23, 24
Rat and human osteoblasts	siRNA	25
HIV-1 gp120	siRNA	26
PDGFRα	siRNA	27
EpCAM	Chemotherapeutics siRNA	28, 29

Examples of aptamer-drug conjugates used in targeted drug delivery.

ent combinations and Phase 1 trials for the treatment of solid tumors.[15] Iveric Bio have progressed their complement 5 targeting aptamer-based therapeutic for the treatment of age-related macular degeneration to Phase 3, and for the treatment of autosomal recessive Stargardt disease to Phase 2.[16]

The advantages that aptamer therapeutics hold over standard antibodies and antibody-related binders, have led to them being investigated as direct therapeutics and as delivery vehicles for a range of cargo.[17] Many examples of ApDCs have been generated with cargo ranging from chemotherapeutics and photosensitizers to siRNA (Table 1).[7]

BREAKING THE BARRIERS TO CLINIC

Despite more than three decades since the discovery of the first aptamers, development of these molecules through the clinic has been limited. This lag period is not unexpected in the uptake of a new technology, and many of the perceived limitations of therapeutic aptamers have been addressed through new advances:

Susceptibility to ubiquitous nucleases within the body - The issue of stability has been largely overcome by modifying the nucleic acid backbone with the substitution of 2′-hydroxyl groups in RNA aptamers with 2′-fluoro, 2′-amino or 2′-O-methyl groups, and through 3′-end capping with inverted thymidine, other blocking molecules or the circularisation of aptamers.[30]

Rapid clearance by renal filtration - Chemical conjugation with high molecular weight polyethylene glycol (PEG), cholesterol or other carrier molecules helps to reduce the rate of renal clearance and improve aptamer retention *in vivo*. In some cases this strategy has been shown to extend aptamer half-life beyond 48 hours, thus improving their pharmacokinetic properties.[30] However, for situations such as the development of imaging reagents or "hit-and-run" treatments with highly toxic payloads (where long retention times are detrimental) rapid clearance may be beneficial for ApDCs. The ability to tune aptamer therapeutic half-life in this way is beneficial.

DEVELOPING APTAMERS FOR DRUG DELIVERY

As aptamer technology is increasingly explored for its therapeutic potential, there are a number of additional advantages to these molecules that make them particularly efficient for drug delivery.

Biomarker-Free Selection & Screening

The *in vitro* selection process for cell-targeting aptamers allows the discrimination of cell phenotypes, such as diseased versus healthy. Each cell type can be included in the aptamer selection strategy as part of multiple positive and negative selection rounds, removing the need for *a priori* knowledge of disease-specific biomarkers. Aptamers that bind to the diseased cells and not to the healthy cell population can subsequently be used to pull-down the specific biomarker that they target.[31] In this way, aptamer selection can be used for biomarker discovery and validation in one complete step.

Simple, Cost-Effective Manufacturing

Aptamers can be synthesized using well-defined and characterized chemical processes, with no requirement for cell systems. This makes aptamer production more cost-effective and simpler to scale up than comparative protein-based therapeutics. For ApDCs that are delivering oligonucleotide therapeutics, such as siRNA or antisense oligonucleotides, there is also the potential to synthesize the ApDC as a single contiguous molecule, removing the need for additional conjugation and purification of the final aptamer with the

drug cargo. This greatly reduces the production costs, increases standardization of the product and improves yields relative to processes requiring post synthesis conjugation.

Rapid Internalization for Drug Delivery

As aptamers are approximately one-tenth the size of antibodies, they can be readily taken up by cells through a number of mechanisms, most commonly endocytosis and micropinocytosis.[32] Aptamer uptake is ultimately determined by the specific interaction with their target, making them very appealing for the delivery of cargo to the cell interior for targeted chemotherapy or gene therapy applications.

Delivery to Challenging Tissues *In Vivo*

Delivery of therapeutics across the blood-brain barrier has long been challenging, resulting in limited treatment options for many brain and central nervous system diseases. Many targeted antibody therapeutics for neurological conditions have failed to show clinical benefit and pose serious risk of eliciting an immune response. Aptamers have shown to be a promising class of therapeutic for the potential treatment of brain disorders, as they are small, non-immunogenic, and able to permeate the blood-brain barrier with relative ease compared to larger antibody molecules.[28,33]

A second challenging site for targeted delivery of oligonucleotide therapeutics is the kidney.[34] Despite increased approval of oligonucleotide therapeutics, targeting these molecules to extrahepatic tissues remains challenging. Due to the small size of oligonucleotides, targeting to the kidney is difficult as it promotes the rapid renal filtration of the intended therapeutic, limiting the potential effect. To overcome this problem, siRNA and antisense oligonucleotides can be conjugated to aptamers that are both highly specific for targeted delivery, and with high affinity to prevent the therapeutic being cleared from the kidney. Aptamer Group is currently working in collaboration with AstraZeneca to develop such solutions for the treatment of kidney disease using aptamer technology.[35]

LOOKING TO THE FUTURE

As the potential of biotherapeutics continues to expand and the limitations of antibody technologies are increasingly being highlighted, a new breed of oligonucleotide-based affinity binders is showing their value as more molecules progress steadily toward clinical application. Aptamers offer many advantages over antibodies and protein-based binders, including ease of formatting and production, improved cell internalization, and the ability to target new diseases, such as in the CNS. With many of the perceived limitations of aptamers having been successfully addressed, aptamers are coming of age. These novel therapeutics have the potential to deliver effective treatments that can transform patients' lives whilst offering essential cost savings for healthcare providers who urgently need alternatives in the face of the high cost of antibody therapeutics. ◆

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BIOGRAPHIES

Dr. David Bunka is the CTO of Aptamer Group. He has spent over 20 years developing nucleic acid aptamers against a wide variety of targets, including small molecules, disease-associated proteins, several cancer-associated cell-lines, viruses and tissue biopsies. He earned his PhD in Molecular Biology from University of Leeds.

Dr. Emily Robinson leads the therapeutic development team at Aptamer Group to support early drug discovery for partners and collaborators. She has research experience in the evaluation of dysregulated signaling pathways in cancer and the identification of novel drug targets. She earned her PhD in Cancer Immunology from University of Leeds.

Drug Development
EXECUTIVE

Nazim Kanji

Executive Director, Pediatric Services

Quotient Sciences

Quotient Sciences

Molecule to cure. Fast.™

Quotient Sciences: Unique Considerations & Challenges When Developing Palatable Pediatric Formulations

The demand for pediatric dosage forms continues to increase; however, the number of approved pediatric drug treatments on the market remains substantially less than those for adults. Developing drug products for pediatric patients brings a whole set of unique challenges for development teams. Formulation scientists must consider the route of administration, the safety profile, overall taste and palatability, the child's age, weight, physiologic condition, and the treatment plan's requirements. All these key factors must be balanced for developing a pediatric product that garners clinical, regulatory, and commercial success.

Quotient Sciences, a drug development and manufacturing accelerator, has extensive experience in developing palatable pediatric formulations on behalf of pharmaceutical and biotech customers globally and has successfully developed customized pediatric pharmaceutical formulations that have received regulatory approval.

Drug Development & Delivery recently spoke with Nazim Kanji, Executive Director, Pediatric Services at Quotient Sciences, about the unique considerations and challenges when developing palatable pediatric formulations, so that molecules can become cures, fast.

Q: What are the regulatory considerations when developing a pediatric formulation, including US and EU incentives, guidance, and requirements?

A: Historically, drug products used in children were generally only approved for adults. They were rarely tested in pediatric populations, and product labelling did not

include directions for safe and effective use in pediatric patients. Furthermore, the correct dose and excipient safety were generally not determined for target age groups, and there was a distinct lack of age-appropriate formulations, which meant that in many cases, manipulation of the adult product would be required to dose children.

Pediatric legislation in the form of The Best Pharmaceuticals for Children Act and Pediatric Research Equity Act in the US and the Paediatric Regulation in the EU came into effect between 2002 and 2007. The aim of these regulations was to increase the number of products that were approved for pediatric use, and they sought to do this by mandating companies to undertake pediatric research and development as well as providing financial incentives for them if they invested in doing this work.

Both the US and EU regulations require the submission of pediatric plans at given points in the adult development - in the EU, a Paediatric Investigation Plan (PIP) is to be submitted no later than the end of human pharmacokinetic (PK) studies in adults, while the US requires a Pediatric Study Plan (PSP) to be submitted within 60 days of the end-of-Phase 2 meeting. These documents give a commitment to the studies that will be conducted and also the timeframe.

Q: What are some key strategies and product considerations when developing patient-centric dosage forms that are acceptable and palatable for pediatric populations?

A: In order to meet patient needs and regulatory expectations, there are several key steps for consideration in the development of a pediatric dosage form. First is the design stage, to understand the target product profile for the defined population(s) along with associated challenges and risks. Formulation development is then required to identify acceptable, age-appropriate dosage form(s). Depending upon the active pharmaceutical ingredient (API) characteristics and formulation strategy, a key factor here of course may be taste masking. Next is typically a clinical assessment of the proposed pediatric formulations in adult panels to understand, optimize, and clinically validate dosage forms based on taste and/or PK attributes prior to proceeding into pediatric trials. These efficacy studies often present the development team with unique challenges given bespoke patient requirements that can put a strain on traditional product manufacturing and supply logistics. Finally, there may also be the need to identify a long-term manufacturing partner for what may be low-volume commercial products. Clearly, there is plenty to think about on this journey!

There are many factors influencing dosage form design and selection, which are not just centered around drug and formulation needs, but importantly, should also reflect patient, clinical, and regulatory considerations.

The inherent properties of the drug itself are clearly influential, for example, in regard to taste/palatability and, in the context of the required dose form, the solubility.

Broader formulation considerations are important, arguably more so than in adult development. The choice and levels of excipients have to be carefully considered in relation to the target age groups to ensure safety and avoid the risk of adverse effects.

Additionally, patient-related factors are also influential, for example, in terms of broader acceptability criteria, such as swallowability of solid oral dosage forms. The container closure system and dosing devices should ensure ease and accuracy of administration by the parent or caregiver. Some formats may require sprinkling/co-administration with foodstuffs, requiring sponsors to show appropriate diligence in performing representative food-compatibility studies to inform the product labelling.

Finally, there are a host of clinical and regulatory factors. Typically there will be a target pharmacokinetic (PK) profile to drive efficacy, which can be a challenging prospect in terms of extrapolating adult-to-child data for dose selection, as well as any unique pediatric biopharmaceutics features affecting *in vivo* drug delivery and bioavailability. The intended dose and posology of the drug product should also be considered when justifying the levels of excipients to be included within the formulation.

Q: How can physiologically based pharmacokinetic (PBPK) modelling and simulation be used for dose extrapolation from adults to children and to predict drug product performance in children?

A: There are unique biopharmaceutics considerations in regard to *in vivo* drug and formulation performance in pediatrics given differences in anatomy and physiology when compared to adults - gastric and intestinal factors around pH, transit, surface area, enzyme expression, and microflora can all influence oral bioavailability of some drugs differently in the pediatric population.

At Quotient Sciences, we use GastroPlus® to build PBPK

models. In order to build a robust model for pediatric dose predictions, there is firstly a need to build a robust PBPK model to represent the adult situation.

The PBPK model is built on clinical data from a range of studies, eg, SAD, MAD, DDI, food effect, and where possible, different formulations and dosing regimens along with supporting *in vitro* data. The model must be validated with clinical data independent to that used to build the model to ensure robustness. It is very important the metabolic clearance routes, especially the enzymes responsible, as well as any transporter interactions, are fully understood, given the changes of enzyme and transporter expression with age, especially for those under 2 years old.

To scale down to the pediatric physiology, the software takes into account the different expression levels of metabolizing enzymes and transporters relative to age and is thus able to factor these changes into predictions.

Other factors, such as varying percentage of body water and body fat (which influence tissue distribution kinetics), differences in protein binding, relative blood flows, and size of organs relative to total body weight, are also taken into account in the pediatric physiologies used in PBPK modelling.

For the pediatric physiologies of interest, exposure in plasma can be simulated to determine the predicted dose that matches the target product profile (TPP), for example, similar AUC and/or Cmax as observed in adults.

PBPK models allow the gastrointestinal environment to be tailored so it more closely represents the pediatric physiology and can be used to predict exposure in children from alternative dose formats and/or formulation attributes.

Q: What are some challenges drug developers should be aware of when dealing with taste masking, taste modification, and alternate dosage forms?

A: A common problem in pediatric drug development is that drug substances can be very bitter or have other aversive taste attributes. A key challenge is understanding how to effectively mask these taste properties in order to ensure patient compliance, especially if the end drug product is intended for pediatric populations who are not able to swallow conventional dosage forms such as tablets and capsules. This can impact drugs across all therapeutic areas and can be influenced by several factors, including the chemical structure of the drug substance, solubility, and dose.

It is therefore important to understand the taste characteristics of a drug substance early in the development of a pediatric dose form in order to aid the selection of an age-appropriate formulation and associated taste-masking strategy.

For dose forms, such as solutions, suspensions, powders for reconstitution, and orally disintegrating tablets, flavors and sweeteners may be sufficient to achieve appropriate taste masking. Complexing agents may also be utilized to prevent the drug molecule from interacting with the taste receptors.

Barrier coatings can be applied to solid dose formats, such as tablets, mini-tablets, and multiparticulates, to prevent drug release in the buccal cavity.

Q: How can an integrated development, manufacturing, and clinical testing approach be leveraged to optimize taste and pharmacokinetic performance?

A: To avoid the risks from the use of surrogate *in vitro* tools or preclinical models, the most effective method of confirming or indeed optimizing palatability and PK attributes prior to moving into pediatric subjects is to perform rapid and flexible assessments in healthy adults.

At Quotient, we have the ability to integrate formulation development, real-time adaptive manufacturing, and clinical testing workflows. This makes it possible for us to manufacture drug products immediately prior to dosing, creating the ability to modify compositions in response to arising clinical data, enabling formulation technology platform(s) to be assessed in identification of the best technology to achieve the desired TPP.

Following the pharmaceutical development work, regulatory submissions or updates can be made using representative technical and engineering batch data, including short-term stability results, which are sufficient to cover the cycle time between manufacturing, release, and clinical dosing. The first clinical batch is then made and dosed, and we enter a make-test cycle, whereby arising clinical data informs the next formulation to be made and then dosed every 7-14 days.

Additional flexibility can come from the definition of a formulation design space in the regulatory submission for formulation variables, which are anticipated to be critical to *in vivo* performance. By bracketing compositional ranges for these formulation components in the submission, it provides freedom to operate in this space during the clinical study.

The key benefits of this approach address the challenges around time, cost, and flexibility. Quotient Sciences has performed over 400 clinical studies using this model to assess and optimize drug product performance with safety, PK, or taste

data driving decisions.

Quotient undertakes taste assessment and palatability studies in our Phase 1 clinics using healthy adult volunteers from our clinical trial panel. Subjects are trained in the tasting technique regarding how to sample the product and retain in the oral cavity before expectorating.

Multiple formulations can be screened in a single day, approximately one hour apart with a defined rinsing and cleansing procedure. The volunteers complete taste questionnaires to assess product attributes, such as bitterness, sweetness, flavor, texture, and aftertaste, as well as overall acceptability. This provides representative data on acceptability of formulations to the general population and avoids complexities and expense of accessing highly trained subjects while still providing relevant data in identifying an acceptable pharmaceutical drug product.

While taste assessments can be used as the sole clinical endpoint, they can also be combined with PK measurements as part of the same study.

Q: What are some adaptive clinical manufacturing and product supply strategies for global pediatric trials?

A: There can be a number of CMC and logistical challenges in getting the right product to the right patient at the right time. Typical challenges can include (1) Challenging and sporadic patient recruitment across multiple sites and countries, (2) Patient weight variability may require dose flexibility during the trial, (3) Formulation stability may be limited and, (4) Small batch sizes may be required.

These problems are magnified by increasing research also being performed in rare and orphan diseases. Industry is not well positioned to respond to these needs given the historical practice of larger batch sizes and long cycle times to get product manufactured, released, labelled, packaged, and shipped. Implicit in this is also a lack of ability to customize the drug product around unique, individual patient needs.

By an extension of the rapid make-test cycle, it is possible to develop a way of bringing flexibility to patient supplies via real-time adaptive manufacturing. Using Quotient's integrated services model, within 1-3 weeks of subject eligibility being confirmed into a trial, the manufacture of a bespoke product under GMP conditions can be performed, with the product being made available to the caregiver for dosing in any global location. Furthermore, the product can then be adjusted and re-supplied during the treatment phase, also within a 3-week window if an adjustment is required.

In summary, there are many factors that need to be considered for the successful development of pediatric products. With the demand for pediatric dosage forms continuing to increase, the industry must adapt and diverge from the traditional drug development paradigm to find better solutions for drug developers in order to increase the number of approved pediatric treatments on the market. For Quotient Sciences, it's about providing unique expertise with our extensive experience with having of delivered pediatric programs and our end-to-end integrated solution across the design, development, and supply continuum in order to get these life-changing medicines to pediatric patients in need.

For more information about Quotient's pediatric development capabilities, contact us directly at HYPERLINK "mailto:info@quotientsciences.com" info@quotientsciences.com or visit: https://www.quotientsciences.com/solutions/pediatrics/ ◆

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INHALATION THERAPY

An Overview to Drug-Nebulizer Combination Development With Biologics

By: E. Hernan Cuevas Brun, MBA

BENEFITS OF INHALATION THERAPY FOR DELIVERY OF BIOLOGICS

Biologic drugs have been shown to provide great contribution to the treatment of several rare diseases in the past few years. When looking at the number of new drugs approved by the US FDA, biologics have accounted for approximately 27% of new approvals since 2014.[1] Although their administration is traditionally performed via intravenous injections, research has revealed that for the treatment of diseases that affect the respiratory airways, more specifically the lower airways, direct administration for topical delivery through inhalation has presented itself as a more suitable approach.

Two of the major benefits of inhalation therapy to support the delivery of biologics are the reduction of potential systemic side effects and the need for lower doses to achieve therapeutic effect. Currently, the most common route of administration, intravenous administration, has been reported to increase systemic exposure of different parts of the body to the biologic components, hence only allowing a small amount of the initially injected drug to reach the lungs. Conversely, inhalation therapy has demonstrated that by directly delivering biologic drugs into the lungs, active pharmaceutical ingredients can be successfully uptaken via topical delivery and further avoid systemic circulation. Moreover, while clearance of biologic components from the lungs mostly takes about 24 hours, plasma half-lives of antibodies may be clear only after 21 days or longer. [2]

In recent years, biologic drugs are increasingly being investigated for delivery with inhalation therapy, which has initiated more in-depth discussions about the implications of formulation development and their pairing with adequate inhaled devices for more efficient treatment outcomes.

IMPLICATIONS OF DEVICE SELECTION TO DELIVER BIOLOGICS

Biologic drugs are particularly susceptible to several factors, such as high temperature, shear forces, and extreme pH, which may lead to the denaturation of their structure or result in aggregation. Due to the aforementioned nature of biologic drugs, selecting the most suitable delivery system is vital to ensure that the functionality of the drug remains highly active when reaching the airways to effectively treat respiratory diseases.

The additional processing required to administer biologic drugs via dry powder inhalers (DPIs), which may require the formulation to be freeze or spray dried, exposes the biologic drugs to extreme conditions that can easily lead to their degradation. On the other hand, metered dose inhalers (MDIs), which permit the formulation to be in the liquid state, may also degrade the structure of proteins by allowing them to be in a liquid environment for extended periods of time and in contact with hydrofluoroalkane (HFA) propellants further risking their integrity. Although in recent years it has been possible to overcome some of the issues previously mentioned, the large doses required to reach therapeutic treatment may also lead to disregard DPIs and MDIs when selecting a fitting device, leaving nebulizers as the most suitable delivery system.[3]

Nebulizers, devices that transform liquid medication into aerosol, are usually divided in three categories: jet, ultrasonic, and mesh nebulizers. The formerly developed jet nebulizers operate by generating aerosol by the means of pushing air pressure into a container filled with liquid medication. The shear forces produced during this process are highly detrimental to biologic drugs that can readily aggregate during the aerosolization process. Similarly, the heat generated by ultrasonic nebulizers that produce aerosol with ultrasonic waves, which are driven by a piezoelectric component, can also lead to denaturation of biologics, making them inactive. Only the newest type of nebulizers, mesh nebulizers, have been shown to provide one of the most adequate mechanisms for the delivery of biologics, with low shear forces and heat generation.[4]

As a result of this scenario, several of the new developments involving inhaled biologics are in combination with mesh nebulizers, covering indications ranging from asthma and chronic obstructive pulmonary disease (COPD) to cystic fibrosis and non-cystic fibrosis bronchiectasis.

FORMULATION CHARACTERISTICS & THEIR EFFECT ON AEROSOL CHARACTERIZATION

One of the key elements for the successful delivery of biologics is the selection of excipients. The addition of excipients can help protect the structure of biologic compounds, and subsequently aid them to retain their stability and activity in aqueous solutions and even after nebulization. Unfortunately, when it comes to inhaled biologics, the number of approved inhaled excipients by the US FDA remains limited.[5] Surfactants, such as polysorbate, as well as sodium chloride and arginine, are commonly used in biologic formulations to regulate the physicochemical characteristics that will later influence the aerosol characterization when in combination with nebulizers.

To achieve desired aerosol characteristics and target high lung deposition, some of the main properties that are related to aerosolization of the liquid medication are viscosity, surface tension, and osmolality. Several biologic formulations tend to present higher levels of viscosity, especially at high concentrations. This factor is commonly associated to lower output rate of aerosol generation, resulting in longer nebulization time. Viscosity-reducing excipients, such as lysine and arginine, can be added to the biologic formulation to increase output rate, which has been described as an effective way to improve patient adherence by reducing nebulization time.[6] Other frequently used excipients that have been found to stabilize biologic formulations are buffers containing sodium chloride, hydrochloric acid, citric acid, among others, by positively adjusting and maintaining the pH value of the formulations.

In a similar fashion, incorporation of polysorbates can decrease surface tension and at the same time stabilize biologic formulations by preventing aggregation. Nonetheless, it has been stated that lower surface tension results in lower output rate for mesh nebulizers, which can typically aerosolize solutions in the range of 35-75 mN/m (Figure 1).[7] Finally, the use of certain excipients has also been linked to causing coughing response in patients receiving their inhalation treatment due to stimulation of the transient receptors in the airway afferent nerves.[8]

FIGURE 1

Viscosity and surface tension are physicochemical properties that post great influence on the output rate of mesh nebulizers.

NEBULIZER CUSTOMIZATION & DRUG-DEVICE CO-DEVELOPMENT

In addition to the formulation tailoring alternatives to deliver biologics, mesh nebulizers also offer customization solutions that are increasingly becoming a new trend for the development of drug-device combination products. Adjustments in the hardware and software of the devices intend to satisfy the requirements to effectively deliver biologic drugs without affecting their properties. Accounting as one of the fundamental factors in the customization of these devices is the mesh membrane itself. Mesh membranes can vary based on different aspects of their composition, such as material, formation mechanism, pore size and structure, thickness of the membrane, and pitch. The combination of these aspects generates a vast number of alternatives to fit formulation characteristics. Similarly, modifications on the mesh driving power and frequency derived from the firmware can further support the delivery of highly viscous biologic drugs or those with lower surface tension induced by polysorbates.

Hence, co-development of a drug-nebulizer combination product may attain higher levels of success when knowledge from both formulation and device side are integrated to develop a combination product in which aspect of the two parts are adjusted to achieve the desired outcome (Figure 2). Then fluid communication between the teams becomes an essential aspect to address issues at an early stage of the feasibility studies, avoiding potential setbacks in the subsequent steps of the development process.

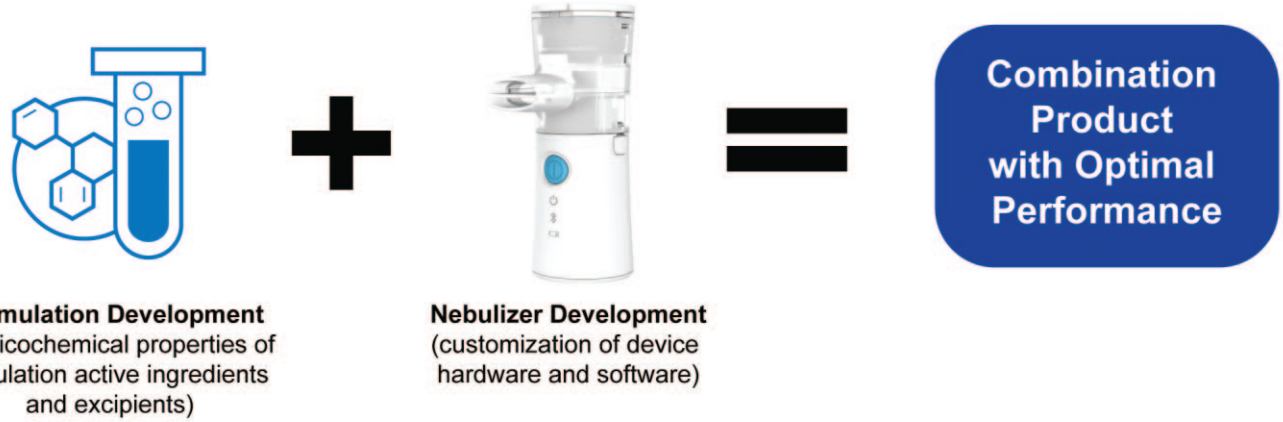
NEW FEATURES TO ENHANCE BIOLOGICS DELIVERY EFFICIENCY

Due to the higher cost of biologic drugs, one of the principal objectives when nebulizing these drugs is to reach elevated levels of active pharmaceutical ingredients being delivered to the respiratory airways. Most mesh nebulizers operate under a continuous-output mode; however, new technologies have been incorporated to these devices to switch to a mode in which aerosolization only takes place during a fraction of the inhalation cycle, thus reducing the amount of aerosol otherwise wasted during exhalation.[9] This mechanism called breath actuation is in many cases the preferable solution in the development of novel drug-nebulizer combination products.

Breath actuation can be incorporated to the nebulizer relying on different mechanisms, which can be either mechanical or electronic, with pressure sensors being one of the most widely applied technologies. Restricting aerosol formation during a specific fraction of the breathing cycle, does not only allow to increase the delivered dose, but also greatly reduces the amount of aerosol wasted in the environment during exhalation as well as the potential expulsion of aerosol that is not fully deposited into the lungs. This type of aerosol that is known as fugitive emission has been labelled as hazardous for people surrounding those receiving their inhalation treatment, resulting in an additional reason to prevent their excessive formation.[10]

Another feature with rapidly increasing demand in the inhalation field is connectivity. In recent years, connectivity has become the top choice for inhalers and

FIGURE 2



Co-development of drug-nebulizer combination products with biologic drugs requires close collaboration between pharmaceutical companies and device developers to tailor both formulation and device characteristics.

nebulizers, aiming to monitor and improve patient adherence.[11] Biologic drugs in combination products with nebulizers are also expected to move toward this trend as it will help better assess the efficacy of drugs either in clinical trials or later during commercialization. Creating a connected environment between physicians, nurses, caregivers, and patients would allow to closely follow the treatment of different diseases, monitor the patient's evolution, and improve the expected outcome even when the treatment is performed remotely from home. Due to the involvement of personal and private information, the development of these networks comes along with security risks that should be addressed under specific regulations to guarantee the protection of patients' private data at all times. Several regulations and guidelines are already in place, including the Health Insurance Portability and Accountability Act (HIPAA) and the General Data Protection Regulation (GDPR).[12]

SUMMARY

As novel therapies continue to be developed with the advancement of biologic treatments, new approaches in the inhalation therapy field, concerning to proteins, peptides, and nucleic acids, are also projected to continue to grow. At the current time, mesh nebulizers are positioned as one of the top systems to deliver these formulations. The final realization of these projects will ultimately depend on the integration for co-development between pharmaceutical companies and devices developers to bring together new treatment options for common and rare diseases. Moreover, the incorporation of new features, such as connectivity and breath actuation, will continue to add value to the development of biologic-nebulizer combination products by ensuring high levels of drug delivery and a well-structured and secure network to monitor and improve patient adherence. ◆

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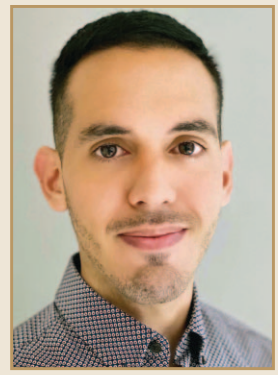

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TARGETED ONCOLOGY THERAPIES

Harnessing Nature's "Cues" to Selectively Activate the Immune System to Attack Cancer

By: Dan Passeri, MSc, JD

A PATH TOWARD MORE EFFECTIVE, TARGETED ONCOLOGY THERAPIES

Cancer research has advanced considerably throughout the past 3 decades in search of more targeted therapies designed to provide improved patient benefit with long-term efficacy and reduced toxicity.

A recent and important breakthrough in the fight against cancer has been the emergence of immunotherapies, a variety of approaches designed to engage and restore the heavy artillery of a patient's immune system to attack and destroy cancer cells.[1-3]

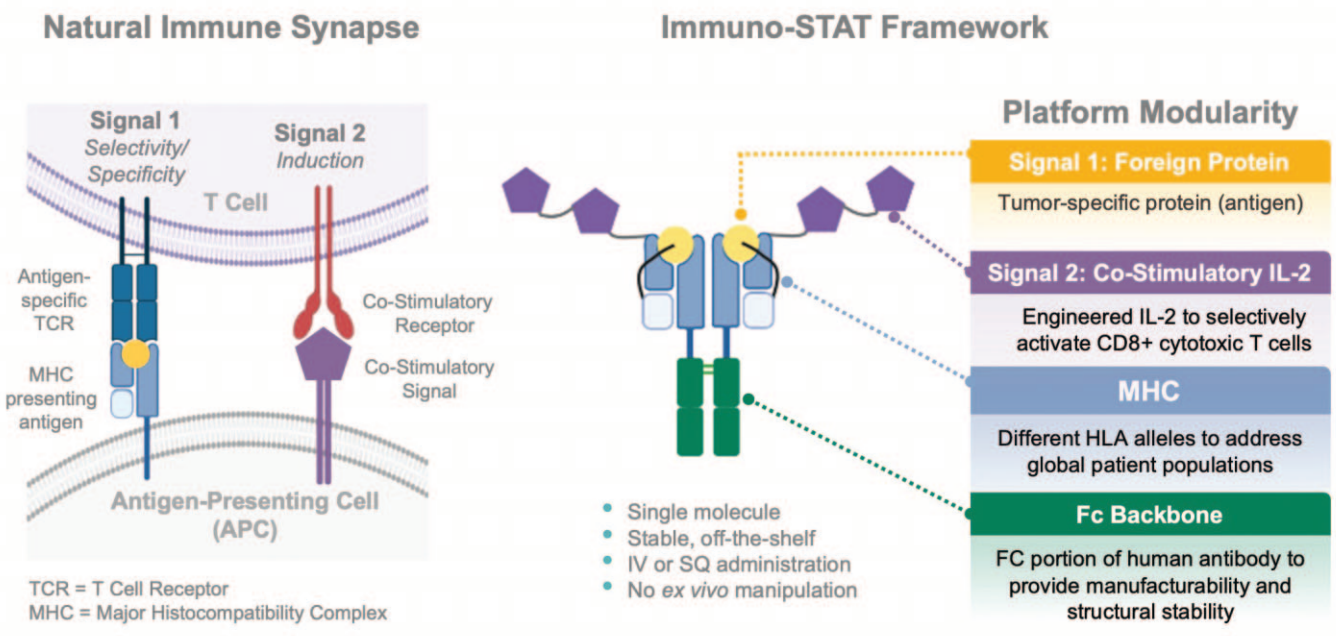
An early entrant and long-studied approach that has been in development for a few decades are the so-called immunotoxin therapies.[2,3] Immunotoxins are bispecific molecules with two anchoring moieties – one is a structure that binds to a protein present on cancer cells, and the other is a "toxin" delivered to the cancer cells to kill them.

One of the earliest examples of immunotoxin therapies is an antibody-drug conjugate (ADC) in which a cancer-targeting antibody is joined (conjugated) to a chemotherapy toxin.[3-5] With the ADC antibody helping direct the chemotherapy toxin to cancer cells, researchers found that it was possible to use more potent chemotherapy agents than with more traditional systemic delivery, and this often resulted in fewer side effects. In addition to ADCs, this promising bispecific strategy also has been used in other ways to help increase the effectiveness of a treatment while at the same time limiting its side effects.

Another example of such conjugated molecules includes interleukin-2 (IL-2) based bispecifics, designed to deliver this highly potent immunostimulant molecule to activate an immune response against cancer.[6-8] IL-2 is expressed throughout the body in a highly controlled and regulated manner and plays key roles modulating immune functions, including its ability to stimulate and activate T cells against cancer. Systemic IL-2 therapy was one of the earliest immunotherapy treatments that provided durable responses for cancer patients. However, delivery of systemic IL-2 has had very limited clinical success due to severe adverse effects and toxicity caused by the ubiquitous binding of IL-2 to receptors throughout the body, leading to death in some patients.[7,8] The bispecific approach has helped ameliorate some of the side effects of systemic IL-2 treatment by biasing the delivery of IL-2 directly to cancer cells.[6-8,10] Again, however, because IL-2 indiscriminately binds even at suboptimal therapeutic doses to any cell possessing an IL-2 receptor, these therapies have shown low tolerability and limited therapeutic responses to date. This brings a significant need for improved IL-2-based therapeutic options.

The two main limitations of IL-2 targeting therapies, which can in part explain low overall therapeutic response rates, are 1) they rely on the presence of tumor-specific T cells at the site of the tumor to be effective, and 2) there is a very small therapeutic window for natural IL-2 to have a desired clinical effect before treatment-limiting side effects emerge. There are on average 10-20 million unique T cell receptors, or unique immune system "addresses," in our body that can specifically respond to a particular pathogenic challenge or disease. Even in sufficient numbers, disease or cancer-specific T cells of interest are not always present in the area around a tumor (the "tumor microenvironment"). This

FIGURE 1



Cue Biopharma Molecules Mimic the Natural Interaction Between Immune Cells Against Cancer
(Left) Natural interaction between antigen-presenting cells (APCs) and T cells during an anti-tumor response. Tumor-specific proteins (antigens) are presented by the APCs through the major histocompatibility complex (MHC) to an antigen-specific receptor of the T cells (TCR receptor). Simultaneously, APCs present an immuno-stimulatory signal, such as IL-2, to T cells to activate them. **(Right)** Cue Biopharma Immuno-STAT™ IL-2-based molecules present two signals, stabilized by the Fc portion of a human antibody. Signal No. 1 - the tumor-specific antigen molecules are presented through MHCs; Signal No. 2 - Engineered IL-2 to selectively activate CD8+ cytotoxic T cells.

is particularly evident in "cold" tumors, where the amount of T cells in the tumor microenvironment is highly limited.[10]

One aim of the evolving field of immuno-oncology therapy is to amplify the immune response against cancer, but in a cancer-relevant and specific manner to marshal the patient's immune system to actively attack the cancer of interest. As a result, a new class of synthetic biologic drugs have been engineered by Cue Biopharma and designed to leverage the beneficial effect of IL-2 to selectively stimulate the proliferation and cytotoxic activity of disease-relevant T cells against cancer. These targeted therapeutics, which are infused directly in the patient's body, dynamically harness the patient's own immune system to fight cancer. In essence, Cue Biopharma's treatments mimic the natural process of immune recognition to activate T cells against specific disease targets such as cancer cells that can otherwise evade immune detection.

REVERSE-ENGINEERING THE NATURAL "CUES" OR SIGNALS TO HARNESS THE IMMUNE RESPONSE AGAINST CANCER

Cue Biopharma's approach has been to reverse engineer the process of how T cells become activated during an immune response. Similar to how immunotoxins have an anchoring or an "address" moiety that binds to a specific cancer to deliver the toxin to a specific tissue, Cue Biopharma's biologics are designed to preferentially engage tumor-specific T cells by taking advantage of the selectivity that already exists in nature, through targeting the specificity of T cell receptors for engagement of tumor-specific T cells.

Cue Biopharma's Immuno-STAT™ (Selective Targeting and Alteration of T cells) platform creates stable, off-the-shelf molecules, referred to as Immuno-STATs, which have been engineered to mimic the natural mechanism that antigen-presenting cells (APCs) use to engage T cells during an immune response. Immuno-STATs do this through simultaneous presentation of two different signals or "cues" that lead to selective T cell activation against the disease target of choice.[11-18]

Signal No. 1 – Targeting Cancer-Relevant T Cells for Selectivity & Specificity

In nature, when specialized immune cells called APCs encounter a foreign protein in the body (eg, a virus or bacteria), their role is to engulf it and break down the proteins into small peptide fragments. The APCs then present the peptide fragments on their cell surface through a com-

plex called the major histocompatibility complex (MHC). This MHC-peptide complex has a very specific three-dimensional configuration and will only bind to a T cell having a receptor (a "T cell receptor" or "TCR") that has a matching three-dimensional configuration. The TCRs of the human immune system have millions of different three-dimensional configurations, and this "specificity" is the key to the immune system engaging only the population of T cells that will respond to the specific foreign protein encountered by the APC.

This binding of an MHC-peptide complex to a matching TCR is the first signal (Signal No. 1) that is required in order to activate the population of target T cells within the human immune system.

Cue Biopharma scientists have been able to create a stable, synthetic MHC-peptide complex that presents a tumor peptide of interest in the correct three-dimensional configuration to matching, target TCRs. The target TCR specifically recognizes and binds to the MHC-peptide complex in Cue Biopharma's Immuno-STATs, thereby providing the same Signal No. 1 to the T cell. As in nature, this binding is the first step leading to T cell activation.

Signal No. 2 – Activating the Target T Cells to Amplify Anti-Cancer Activity

In nature, when an MHC-peptide complex binds to its matching TCR providing Signal No. 1, the T cell is primed to be activated through a second signal (Signal No. 2) referred to as a "co-stimulatory" signal. Co-stimulatory Signal No. 2 often consists of the key immune-regulatory signal, IL-2, which activates and amplifies the activity of the engaged T cell population and selectively converts these tumor-specific T cells into the CD8+ cytotoxic T cells that are the most relevant cells to promote destruction of cancer cells.

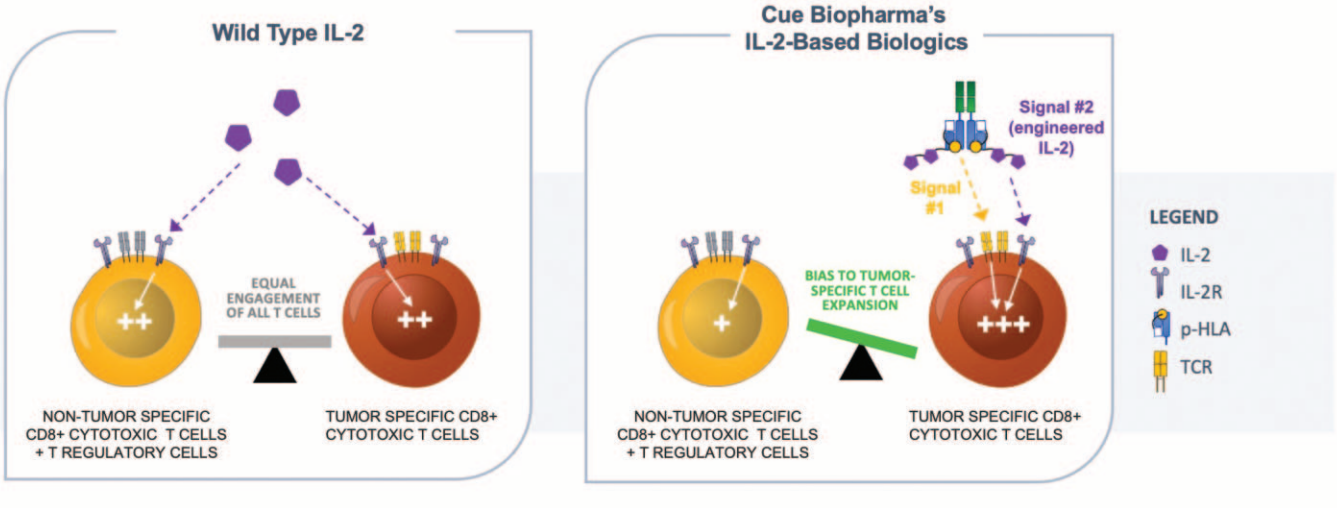
In essence, and as shown in Figure 1, the design of the Immuno-STAT molecule provides the targeting moiety through the MHC-peptide complex providing Signal No. 1, and also induces activation of targeted T cells through IL-2 providing Signal No. 2 . The Immuno-STAT is constructed upon a portion of a human antibody (the "Fc portion") that serves as the molecule's backbone and provides manufacturability and structural stability.

Through this combined signal approach, we believe Cue Biopharma has realized the promise of immunotherapy in cancer by targeting and activating cancer-relevant T cells directly in the patient's body without the unwanted side-effects associated with other immunotherapy approaches, including IL-2 therapy.

IL-2 ENGINEERING FOR PREFERENTIAL ACTIVATION OF TUMOR SPECIFIC CD8+ CYTOTOXIC T CELLS IN CUE BIOPHARMA'S IMMUNO-STAT BIOLOGICS

CD8+ T cells are a significant cellular subset for anti-cancer responses and as such, IL-2-based therapeutics in develop-

FIGURE 2



Ensuring Preferential Activation of Tumor-Specific Cytotoxic CD8+ T Cells
In order for Signal No. 1 to prevail over Signal No. 2 and warrant selectivity **(Right),** the binding affinity to the beta subunit of the IL-2 receptor in Cue Biopharma's Immuno-STAT™ molecules needs to be attenuated. If not attenuated, due to the potent activity of IL-2, the binding of Cue Biopharma's Immuno-STAT biologics and T cells would be primarily driven by the IL-2 signal, leading to activation of non-tumor specific CD8+ cytotoxic T cells **(Left)**

ment aim to activate the relevant members of this cell population to ensure effective cancer killing with an attractive tolerability profile. On the other hand, regulatory CD4+ T cells, also called Tregs, play more of a suppressive role in the immune response, and if activated, could dampen the benefit of CD8+ T cell activation.

IL-2 activates T cells, both CD8+ as well as CD4+, especially Tregs, through its interaction with different subunits of the IL-2 receptor in T cells (alpha, beta and gamma). IL-2 receptors have a wide natural range in binding affinities.[15-18] The high-affinity IL-2 receptor, highly expressed on Tregs, is composed of all three subunits. Conversely, most CD8+ effector cytotoxic T cells express intermediate affinity beta-gamma subunits of the IL-2 receptor. This means that wild-type, or natural, IL-2 is more likely to bind and activate Tregs over the cytotoxic CD8+ T cells that are best at destroying target cancer cells.

Cue Biopharma's IL-2 Molecules Are Engineered With Two Modifications That Maximize Activation of Tumor-Specific CD8+ T Cells & Minimize Off-Target Binding[14-15]

First, the IL-2 has been engineered to abrogate binding to the alpha subunit required for Treg engagement and activation, thereby minimizing the bias for regulatory T cell activation. Accordingly, the predominant effect of IL-2 binding by Immuno-STATs is the activation of cytotoxic CD8+ T cells.

Second, the IL-2 has been modified to attenuate, ie, lessen, the binding affinity to the beta subunit of the IL-2 receptor in order to ensure the activity of IL-2 is most favored to those T cells engaged with the Immuno-STAT molecule through Signal No. 1.

Both of these modifications to IL-2 enable the binding kinetics to be optimized for selective activation of only disease relevant T cells, harnessing the cooperative nature of T cell signaling (Figure 2). Therefore, Immuno-STAT therapeutics are both mimicking and improving the natural T cell activation response using a stable, synthetic off-the-shelf biologic drug.

OBSERVED INITIAL CLINICAL RESPONSE AS MONOTHERAPY

To date, Cue Biopharma's lead drug product candidate, CUE-101, has demonstrated promising clinical results as a monotherapy, without dose-limiting toxicities, in a Phase 1 dose escalation trial. The ongoing clinical trial is testing CUE-101 as a second line and beyond treatment for human papilloma virus positive recurrent/metastatic head and neck squamous cell carcinoma (HPV+ R/M HNSCC). In this highly pretreated and resistant patient population, clinical activity has been observed, including a confirmed partial response with an approximate 50% tumor reduction and six stable disease responses, as of June 2021– a rarity for the immuno-oncology space in which very few immunotherapies show single-agent clinical benefit.

CUE-101, which is designed to activate and expand tumor-specific T cells that target HPV16-driven malignancies, incorporates the HLA-A*0201 allele bound to an epitope from the HPV16+ E7 protein (E711-20) to provide Signal No. 1 (Figure 3).[11,14-18]

The observed clinical activity of CUE-101 as monotherapy establishes initial proof of concept for the clinical potential of Cue Biopharma's CUE-100 series of IL-2 based biologics for the treatment of cancer.

Given the targeted delivery of IL-2 and activation of tumor-specific T cells, Cue Biopharma's approach has the potential to dose higher concentrations of IL-2 than the systemic IL-2 therapies available today. Cue Biopharma's Immuno-STATs thus have the potential to engage tumor-specific T cells and provide anti-cancer efficacy without causing severe, systemic toxicity.

Additionally, the Company is advancing CUE-101 through a Phase 1 dose escalation trial in combination with the anti-PD-1 checkpoint inhibitor pembrolizumab (KEYTRUDA®), as first-line treatment in the same patient population.

Preclinical studies demonstrated the combination of CUE-101 and an anti-PD-1 checkpoint inhibitor appear synergistic by significantly extending survival in mouse models of HPV E7-driven cancers.

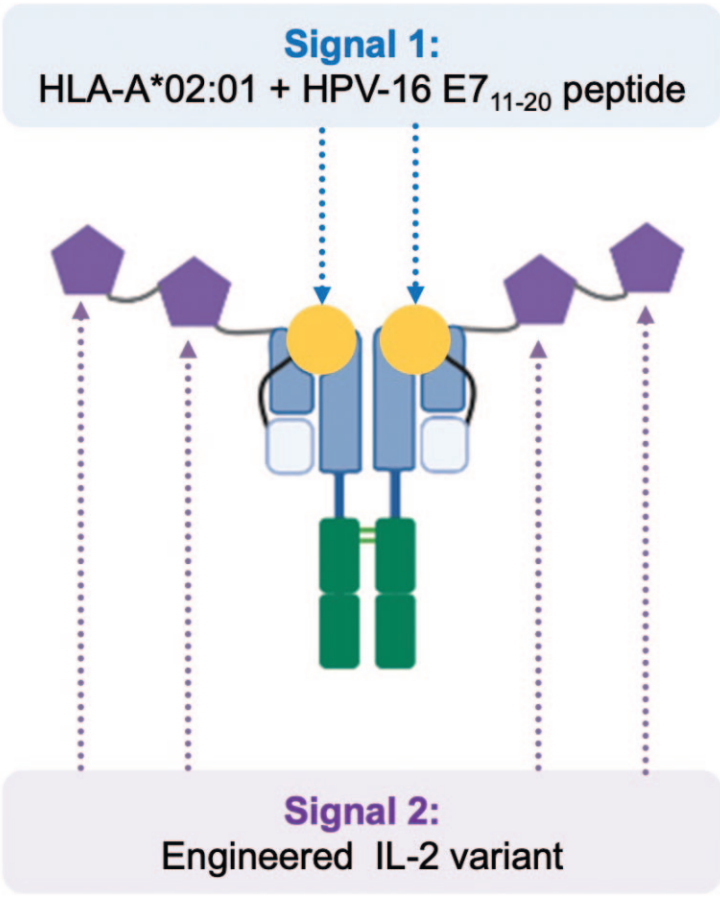
UNIQUE PLATFORM WITH PROMISING THERAPEUTIC POTENTIAL

In summary, the key differentiators of Cue Biopharma's Immuno-STAT biologics from other IL-2-based therapeutics in development include the following:

Tumor Specificity: Due to the unique engineered MHC component for the presentation of tumor specific peptides, Cue Biopharma's Immuno-STAT biologics can selectively activate cancer-specific T cells and turn them into cytotoxic T cells that can seek out and destroy cancer cells.

Selective Activation of CD8+ Cytotoxic T Cells: Due to the careful engineering of

FIGURE 3



CUE-101 is designed to selectively prime & expand HPV-Specific T cells using the HPV16+ E7 protein (E711-20) disease-specific epitope signal bound to the HLA-A*0201 allele.

the IL-2 molecule, Cue Biopharma's Immuno-STAT biologics are biased toward activation of effector cytotoxic T cells and avoid broad activation of Tregs.

Larger Therapeutic Window for IL-2 Effectiveness: Through additional modifications to the IL-2 molecules in Immuno-STATs, including lowering their binding efficiency for T cells, the Cue Biopharma team has greatly reduced the toxicities seen with other IL-2-based therapies. In clinical testing to date, CUE-101 has yet to show dose-limiting toxicities in dose escalation while already showing rare monotherapy clinical activity, suggesting these modifications are having their predicted effect.

As such, the key benefit of Cue Biopharma's Immuno-STAT biologics is that they do not only diminish the indiscriminate IL-2 binding that leads to high toxicity, but they also favor the activation of cancer-specific cytotoxic T cells, which should result in increased efficacy without known IL-2-related safety concerns. Immuno-STATs offer the promise of providing targeted therapies for cancers with the potential for higher efficacy while avoiding the negative side effects of global systemic approaches.

Cue Biopharma's molecules also present advantages over other tumor-specific immuno-therapies in development, such as CAR-T (chimeric antigen receptor T cells) or TCR-T therapies, because they do not require *ex vivo* manipulation.

Overall, given its unique mechanism of action by leveraging the natural immune response to exploit the specificity of T cells, its initial clinical efficacy as a monotherapy, and reduced toxicity, Cue Biopharma's therapies represent a true breakthrough in cancer immunotherapy treatment, with potential to provide new life-saving options for multiple cancers. ◆

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BIOGRAPHY

Dan Passeri is Chief Executive Officer of Cue Biopharma, and is a seasoned biotechnology executive with over 20 years of experience managing drug discovery and development programs as well as business development activities on behalf of publicly traded companies, with deep experience in both oncology and strategic partnership generation. Prior to joining Cue Biopharma, he served as President and Chief Executive Officer as well as Vice Chairman of the Board of Curis, Inc. Prior to joining Curis, he was employed by GeneLogic Inc., most recently as Senior Vice President, Corporate Development and Strategic Planning. Prior to his work at GeneLogic, he served as Director of Technology Management at Boehringer Mannheim. He earned his JD from the National Law Center at George Washington University, his MSc in Biotechnology from the Imperial College of Science, Technology, and Medicine at the University of London, and his BS in Biology from Northeastern University.

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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.

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

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

Future Growth is Our Priority

ABITEC is continuing to look at ways they can expand their capabilities to better serve the pharmaceutical market sectors. The acquisition of Larodan is already bringing new technologies and opportunities to the forefront, but in the coming year there will be even more exciting advancements to share!

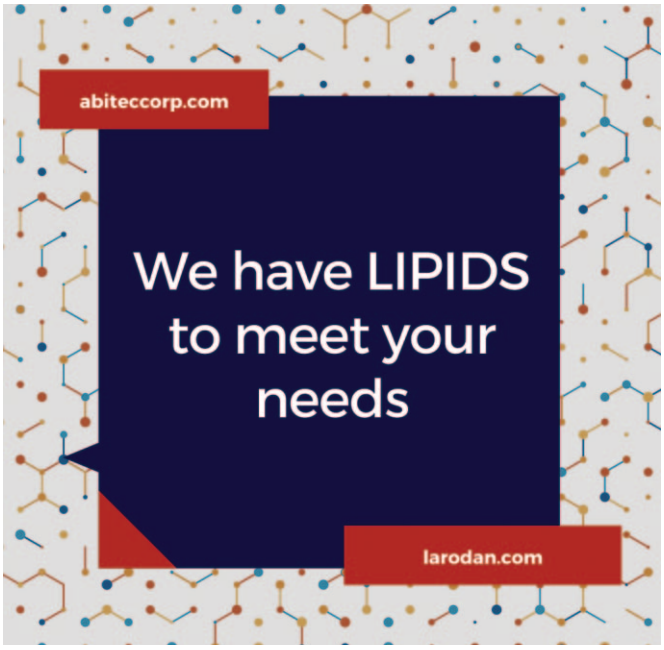
To Request a Sample – visit https://samples.abiteccorp.com/

Social Media Links:

LinkedIn - https://www.linkedin.com/company-beta/1454313/

Twitter - https://twitter.com/abiteccorp

YouTube - https://www.youtube.com/channel/UC9mfJCBOstRuc-i2Asgu4VQ




ABITEC
AN ABF INGREDIENTS COMPANY
Larodan
A part of ABITEC Corporation
Delivering Unique Lipids Today to Address the Research & Therapeutic Challenges of Tomorrow
CONNECT

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E : busdev@adareps.com
W: www.adarepharmasolutions.com

Adare Pharma Solutions is a global technology-driven CDMO providing product development through commercial manufacturing expertise focused on oral dosage forms for the Pharmaceutical industry. Adare's specialized technology platforms provide taste masking, controlled release, solubility enhancement, and patient-centric dosing 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, ANVISA for Brazil and PMDA for Japan.

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.

Our Commercial Manufacturing Capabilities include:

<u>Standard</u>

- Granulation and mixing
- Fluid bed processing
- Pan Coating
- Blending (Bin and Static)
- Tableting
- Capsule Filling
- Tech Transfer

<u>Specialized</u>

- Microencapsulation of solids and liquids
- Orally disintegrating tablet (ODT)
- Dry syrup/ Suspensions
- MMTS™ Minitabs
- Controlled substances: Manufacturing registration authorized for classes II-V, Analytical Labs authorized for I-V

A TECHNOLOGY-DRIVEN CDMO DELIVERING END-TO-END PATIENT-CENTRIC SOLUTIONS

TRANSFORMING DRUG DELIVERY. TRANSFORMING LIVES.

As a technology-driven CDMO, Adare Pharma Solutions provides analytical and formulation development through all clinical phases and manufactures at every scale—from clinical trial materials to full-scale commercial production. Our commitment to customers is reflected in a proven track record of exceptional quality and regulatory expertise. Let us put our knowledge and experience to work for your next project.

Connect with our experts today: BusDev@adareps.com

ADARE™
PHARMA SOLUTIONS

ADAREPHARMASOLUTIONS.COM

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LinkedIn: www.linkedin.com/company/ajibio-pharma-services/
Twitter: twitter.com/AjiBioPharma W: www.AjiBio-Pharma.com

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.

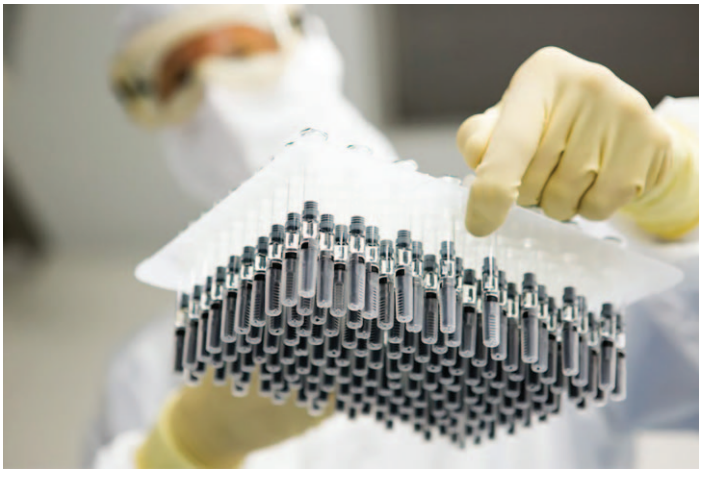
- Drug product aseptic fill finish
- Small molecule manufacturing
- Large molecule manufacturing
- Oligonucleotide and peptide synthesis
- ADC development and manufacturing

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.



LET'S MAKE A HEALTHY WORLD

WITH AJINOMOTO BIO-PHARMA SERVICES, YOU HAVE THE POWER TO MAKE.

To make your vision a reality. To make your program a sucess. To make a positive difference in the world.

Your programs deserve the most comprehensive suite of CDMO services available, and Ajinomoto Bio-Pharma Services has the Power to Make your therapeutic vision a reality - from preclinical through commerical production.

CDMO SERVICES:

- Small Molecules
- Large Molecules
- Process Development
- Oligos & Peptides
- High Potency & ADC
- Aseptic Fill Finish

WHAT DO YOU WANT TO MAKE?

www.AjiBio-Pharma.com

AJINOMOTO BIO•PHARMA SERVICES | THE POWER TO MAKE

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. 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. Alcami serves biologics and pharmaceutical companies of all sizes providing customizable and innovative solutions for development, clinical to commercial sterile and oral solid manufacturing, packaging, microbiology, and analytical services.

Quality & Compliance

- Experience supporting over 500 IND filings and over 30 NOA/ANDA approvals
- In-house quality team and regulatory support
- Successful regulatory inspection history
- Controlled substance capabilities at all facilities

Analytical Services

- Analytical development and validation for small and large molecules/biopharmaceuticals
- Environmental monitoring and cleanroom services
- Stability storage and testing
- Routine/compendial chemistry and microbiology testing
- Elemental impurities
- Abuse-deterrent studies, pediatric food studies, and other specially services

Oral Solid Dose Manufacturing

- Clinical formulation development and commercial dosage form design
- Low shear, high shear, spray granulation, roller compaction, and direct compression
- Powder in capsul/bottle, modified release, mini-tablets, sprinkle capsules, orally disintegrating, chewables, and other pediatric and specialty dosage forms
- Flex suites for novel manufacturing processes

Parenteral Manufacturing

- Formulation development of parenteral dosage forms and placebos
- Manufacturing of sterile solutions, suspensions, and emulsions
- Prefilled syringes and glass vials
- Fill-finish of large molecules/biopharmaceuticals
- Aseptic/sterile processing, terminal sterilization, and lyophilization

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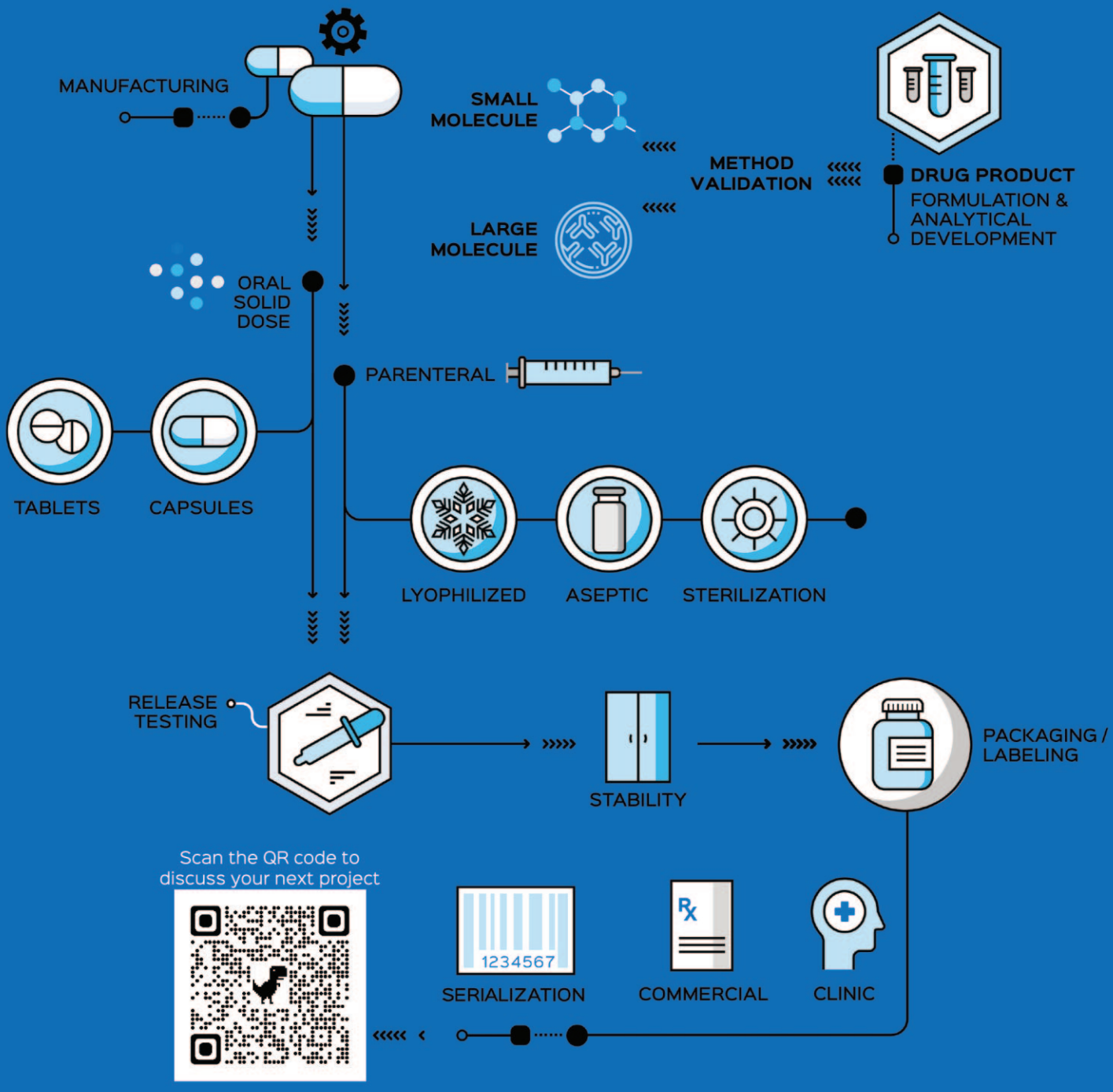
Secure your CDMO needs with US



alcami®

alcaminow.com

APTAR PHARMA
W: https://www.aptar.com/pharmaceutical/
E: info.pharma@aptar.com

With over 70 years of proven experience, **Aptar Pharma** is the go-to drug delivery expert for pharma customers worldwide, providing innovative drug delivery systems, components and active material science solutions across the widest range of therapeutic areas and delivery routes including nasal, pulmonary, ophthalmic, dermal and injectables.

End-to-End Support at Every Stage of Your Development Journey

From concepts to initial design, device and formulation development through the clinical trials phase, analytical testing, regulatory filings, and on to market launch, Aptar Pharma Services can support you at every stage of your product development pathway.

Unparalleled Expertise in Inhalation

Aptar Pharma is the global leader in pulmonary drug delivery solutions, delivering gold standard devices to manage asthma and COPD.

Market-Leading Solutions for Effective Nasal Drug Delivery

We are the global leader in nasal drug delivery solutions with over 280 market references.

Best-in-Class Complete Injectable Solutions

Our best-in-class injectable solutions for Vial, Lyophilization & Pre-Filled Syringes, including Aptar Pharma's PremiumCoat® ETFE-coated solutions, meet the highest quality standards to protect your drug and your patient.

Our pure formulations, state-of-the-art manufacturing process and Premium finishing derisk your drug development and accelerate your time to market.

Proven Know-How in Ophthalmic Drug Delivery Devices

Clearly the world leader in preservative-free multi-dose eye care devices, Aptar Pharma's proven OSD platform has over 300 market references worldwide for prescription medications and OTC products.

Aptar Pharma Services provide early stage to commercialization support to accelerate and derisk the drug development journey.

With a strong focus on innovation, Aptar Pharma is leading the way in developing connected devices to deliver digital healthcare solutions.

With a global manufacturing footprint of 14 GMP sites, Aptar Pharma provides security-of-supply and local support to customers.

Meeting the Growing Market Need in Dermal Drug Delivery

With its **Airless**+ range, Aptar Pharma offers a versatile solution platform for dermal drug delivery, serving the pharmaceutical market to enable brand differentiation and meet evolving regulatory needs.

Leading-Edge Connected Device Technology to Improve Patient Outcomes

Aptar Pharma offers a broad range of sophisticated digital healthcare solutions which are patient friendly, easy and intuitive to use. They are available for the prevention, diagnosis and treatment of diseases, as well as patient monitoring and health management. Available as fully integrated technologies or add-ons, we offer connected solutions for a wide range of drug delivery devices and routes of administration.

Working Towards a Sustainable Future

Our commitment to the environment and the health and safety of our people around the globe spans all levels of our organization and connects to all parts of our value chain.

Transforming bright ideas into brilliant opportunities for decades

Aptar Pharma – the go-to drug delivery expert

When pharmaceutical companies around the world want to develop safe, efficient and compliant medicines, they turn to Aptar Pharma for proven drug delivery solutions.

Leveraging our therapeutic insights, over 25+ years of regulatory expertise and the widest portfolio of solutions and services in the industry, we accelerate and derisk our customers' drug development process, helping them transform bright ideas into new market opportunities to improve and save patients' lives.

Let's partner together on your next bright idea. Visit **www.aptar.com/pharmaceutical** to get started.

Delivering solutions, shaping the future.

Aptar pharma

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Ascendia Pharmaceuticals is a specialty pharmaceutical CDMO that provides custom sterile and non-sterile enabling formulations and manufacturing, along with analytical methods for new chemical entities, complex dosage forms, and 505(B)(2) product development, as well as OTCs, nutraceuticals, and animal health.

Ascendia has invested heavily in drug delivery nanotechnologies that aid in large and small molecule formulations, as well as biologics. The specialty CDMO is expanding its talented people, capabilities, and facilities to exceed customer expectations from early to late stage development. Many clients have anointed Ascendia as a "Partner of Choice" because of the successes achieved for them.

Making *Insoluble Soluble*

Founded in 2012, Ascendia makes the *Insoluble Soluble* through a comprehensive suite of pre-formulation, formulation development, manufacturing, and stability services for parental, oral, opthalmic, and topical dosage forms. The company built its foundation of success on its customer-centric culture that exudes its **BEST** philosophy (**B**rilliant technology, **E**xcellent service, **S**uperior quality, and **T**rust).

Delivering Sophisticated Formulations

Ascendia delivers sophisticated formulations to enhance bioavailability and solubility using three proprietary nanotechnologies – NanoSol®, EmulSol®, and AmorSol®. These serve as the cornerstones to developing solutions for all dosage forms including small molecules and biologics that may not have been achieved otherwise.

Manufacture of Clinical Trial Materials

Headquartered in North Brunswick, NJ, Ascendia's facility has Class 10,000 (ISO 7) and Class 100 (ISO 5) cleanrooms, as well as Class 10,000 (ISO 7) manufacturing suites. Ascendia manufactures cGMP batches for orally administered dosage forms. It also provides cGMP manufacture of sterile, injectable dosage forms.

Its facility maintains stability chambers for conducting non-GMP and cGMP stability studies in accordance with ICH guidelines. Ascendia stability studies:

- determine robustness of formulation prototypes during early development
- ascertain chemical and physical integrity of lead formulations before advancement into animal/toxicology studies
- assure final formulations meet stability for clinical trials

Ascendia recognizes the challenge in developing parenteral dosage forms and specializes in early-stage development services for these projects. A major milestone in a pharmaceutical development project is the first-in-man study. This vital achievement is difficult for parenteral products due to the expense of producing clinical trial materials. By offering fast, flexible, and small-batch size services for conducting first-in-man study, Ascendia helps drug development teams stay on schedule and within budget.

Your Premier CMO for Specialized Sterile Injectables

Backed by over 90 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, 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.

BAXTER BIOPHARMA SOLUTIONS
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E: biopharmasolutions@baxter.com
Website: www.biopharmasolutions.baxter.com

Baxter

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 90 years of innovation, expertise and specialization in parenterals.

Learn more about us at **biopharmasolutions.baxter.com**

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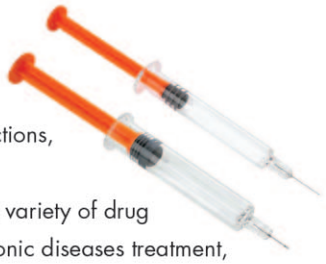
BD Medical - Pharmaceutical Systems

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

Bora Pharmaceuticals

Quality with flexibility. Your success is our promise.

Bora Pharmaceuticals is a premier international CGMP CDMO specializing in complex oral solid dosage (tablet & capsules), liquids (solutions, suspensions, & nasal sprays) and semi-solids (creams & gels) pharmaceutical Rx and OTC products for late-phase Clinical through Commercial manufacturing and packaging. Bora owns and operates three state-of-the-art CGMP manufacturing facilities (Taiwan and Canada) built to the highest international standards for manufacturing, packaging, R&D, and analytical testing.

We can handle high potency compounds, solvents, flammables, and IR/SR/ER release profile products.

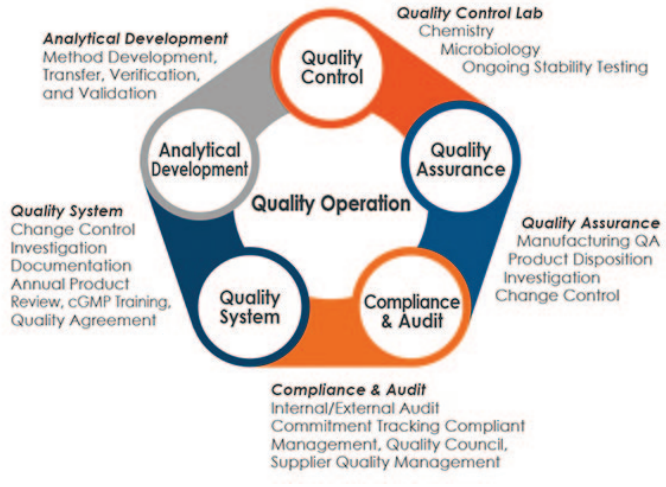
Our Taiwanese facilities are USFDA, MHRA, TFDA, Jordan FDA, and GCC (Gulf Cooperation Council) inspected. Our Mississauga, Our Canada site is approved by all major regulatory agencies including USFDA, Health Canada, ANVISA, EMA, PDMA, and the Japanese Ministry of Health. Our last USFDA audits have had no findings.

Our sites deliver to more than 100 markets around the world including the US/Canada, EU, Southeast Asia, Middle East, and South and Central Americas. All sites are TAA compliant. Our packaging lines are fully serialized. Our sites have over a 98% on-time delivery record!

Bora Pharmaceuticals has an extremely solid financial foundation and experienced management team, with over 20+ years working in the pharmaceutical industry.

Quality

Bora Pharmaceuticals has been dedicated to maintaining the world-class quality standard from its beginning. Advanced quality systems, including QMS, EDMS, and ERP, are effectively utilized to ensure the highest manufacturing quality. At Bora, it is our mission to provide our customers pharmaceuticals with an unparalleled quality they expect.



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Twitter: https://twitter.com/BoraPharma

Bora Pharmaceuticals

Searching for a better clinical to commercial manufacturing experience?

Partner with the right CDMO to scale your product with Bora's oral solid manufacturing/packaging capabilities.

Learn more at **www.boracorpcdmo.com**

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.

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.

Captisol, A Ligand Technology

3911 Sorrento Valley Road
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San Diego, CA 92121
877-575-5593

cdinfo@captisol.com

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

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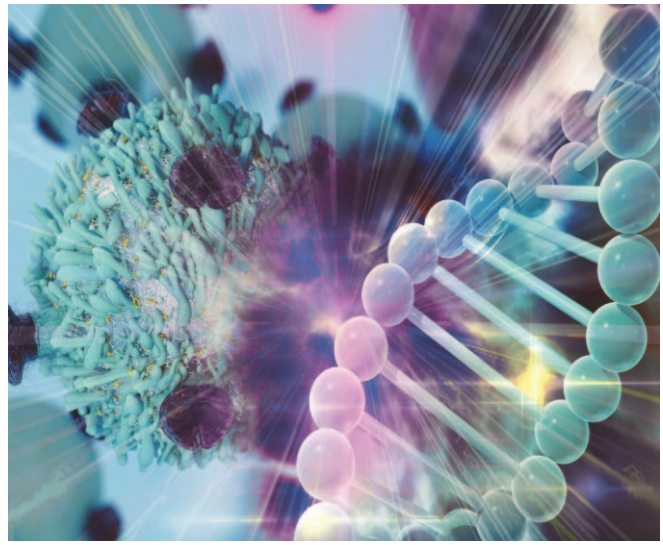
E: solutions@catalent.com W: www.catalent.com

Catalent is the global leader in enabling pharmaceutical, biotechnology, and consumer health partners to optimize product development, launch, and full life-cycle supply for patients globally. With broad scale and deep expertise in development sciences, delivery technologies, and multi-modality manufacturing, Catalent is a preferred industry partner for personalized medicines, consumer health brand extensions, and blockbuster drugs.

Helping to accelerate over 1,000 partner programs, and launch over 150 new products every year, Catalent's flexible manufacturing platforms, at over 50 global sites, supply over 70 billion doses of more than 7,000 products to over 1,000 customers annually. Catalent's expert workforce exceeds 17,000, including over 2,500 scientists.



Technology Highlights

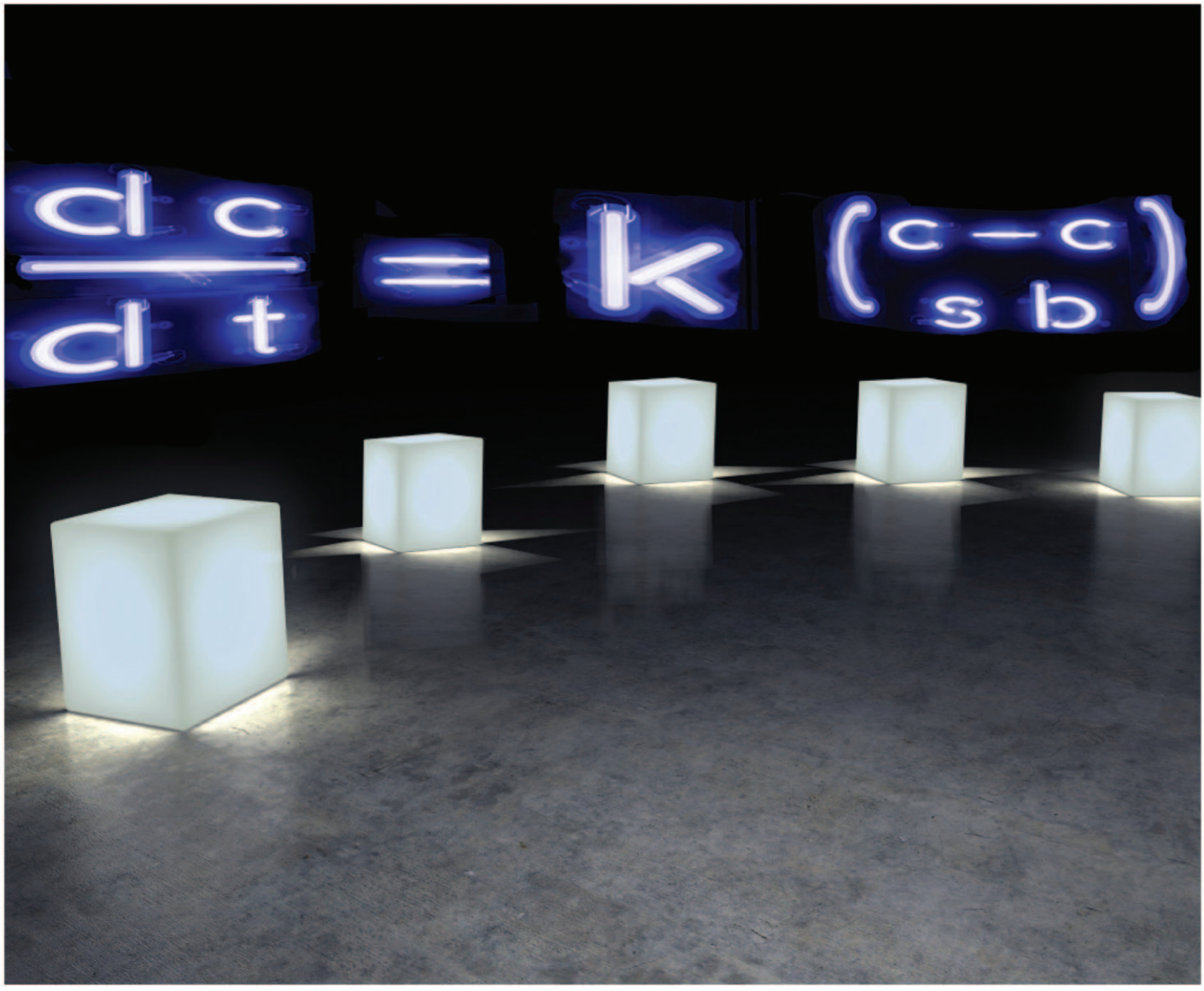
In both the U.S. and Europe, Catalent has recently announced extensive investments to enhance and expand its full range of development and commercial drug substance and drug product capabilities across biotherapeutics, vaccines, and plasmids, as well as cell and gene therapies.

- **Catalent Cell & Gene Therapy** is a full-service partner for adeno-associated virus (AAV) and lentiviral vectors, as well as plasmid DNA. Its comprehensive cell therapy portfolio includes expertise across multiple cell types including CAR-T, autologous and allogeneic cell therapy development and manufacturing, and human induced pluripotent stem cells (iPSCs);
- **Advanced GPEx®** cell line expression technology for 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 and bioavailability enhancement technologies;
- **Catalent R P Scherer®** softgel Rx and consumer health forms including oral and topical softgel technologies; gummies, soft-chews and lozenges;
- **Unique delivery technologies:** including OptiShell® gelatin-free capsule technology; Zydis® orally disintegrating tablets; oral controlled release including OptiGel® DR; FlexDose℠ stick pack; and injectable forms;
- **Comprehensive inhaled dose form development** capabilities for DPI, MDI and nasal spray delivery, including a commercial-scale spray dry dispersion facility in Boston, Massachusetts;
- **Integrated global clinical trial manufacturing and logistics network**, with new supply facilities in San Diego and Japan opened in 2021.

Integrated Solutions

Catalent offers integrated development and product supply solutions that can be combined or tailored, to enable customers to progress drugs, biologics, and consumer health products from laboratory to market, faster. Post-launch, Catalent provides comprehensive, integrated product supply, from sourcing bulk API through to manufacturing and packaging, release testing, and distribution. These flexible, scalable, and creative solutions meet the unique needs of both large and emerging biopharma and consumer health companies.

More products. Better treatments. Reliably supplied.™



FORMULATION DEVELOPMENT IS SCIENCE DELIVERING OPTIMAL CANDIDATE FASTER TO CLINIC IS ART.

Successful clinical candidates are built on the science of PBPK modeling, molecule characterization and advanced formulation technologies, and the art of accelerated technology selection and optimization.

OptiForm® Solution Suite (OFSS) is an integrated solution that utilizes above science to select, assess, formulate and deliver the right drug from candidate to clinic with minimal API, applying 5 advanced technologies in an accelerated optimization process. Coupled with comprehensive testing, optimal formulation technology and pk prototypes all in 12 weeks, OFSS can help turn your science into the optimal clinical candidate fast.

5 ADVANCED TECHNOLOGIES | PARALLEL SCREENING | PROTOTYPES IN 12 WEEKS | PBPK MODELING | DEDICATED SCIENCE ADVISOR

Catalent® | *WHERE SCIENCE MEETS ART.*

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

Celanese

The chemistry inside innovation™

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CUSTOMIZED SUPPORT FOR SUSTAINED RELEASE DRUG DELIVERY THERAPIES

From FEASIBILITY to DEVELOPMENT to COMMERCIALIZATION

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.

Our scientists and engineers are there from concept to commercialization, providing development services, material supply aligned with GMP principles and regulatory support through our state-of-the art development and feasibility lab. Our objective is to help our customers reduce R&D time and improve the likelihood of successful drug commercialization.

INTRODUCING THE VITALDOSE® PLATFORM

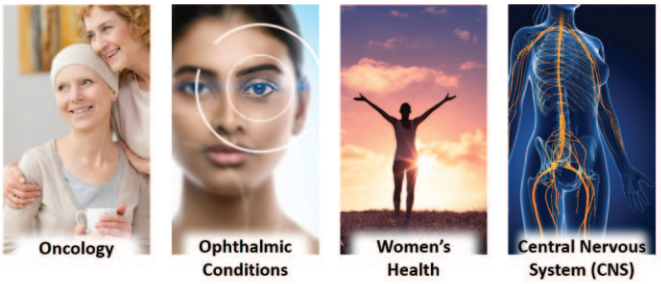
Our VitalDose® Ethylene-Vinyl Acetate (EVA) copolymer drug-delivery platform is an enabling technology for drug-eluting implants, inserts and transdermal films. The platform is flexible and customizable to address a variety of formulation challenges when it comes to tailoring the release rate of your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

- Compatible with biologics, peptides 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

Watch the on-demand webinar, **ENGINEERING DRUG DELIVERY TO IMPROVE THERAPEUTIC OUTCOMES: THE WHY AND HOW OF DRUG ELUTING IMPLANTS,** at https://healthcare.celanese.com/web-seminars.

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

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



ABOUT CELANESE

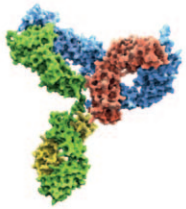
Celanese Corporation is a global technology leader in the production of differentiated chemistry solutions and specialty materials used in most major industries and consumer applications. We partner with our customers to solve their most critical business needs and strive to make a positive impact on our communities and the world through our commitment to sustainability and 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, expanding design possibilities with our customers. We're focused on developing new cutting-edge, chemistry-driven approaches to improve patient care. Our continuously expanding portfolio includes solutions and technologies across applications including drug delivery, medical devices, implantable devices, advanced surgical instruments and connected devices.

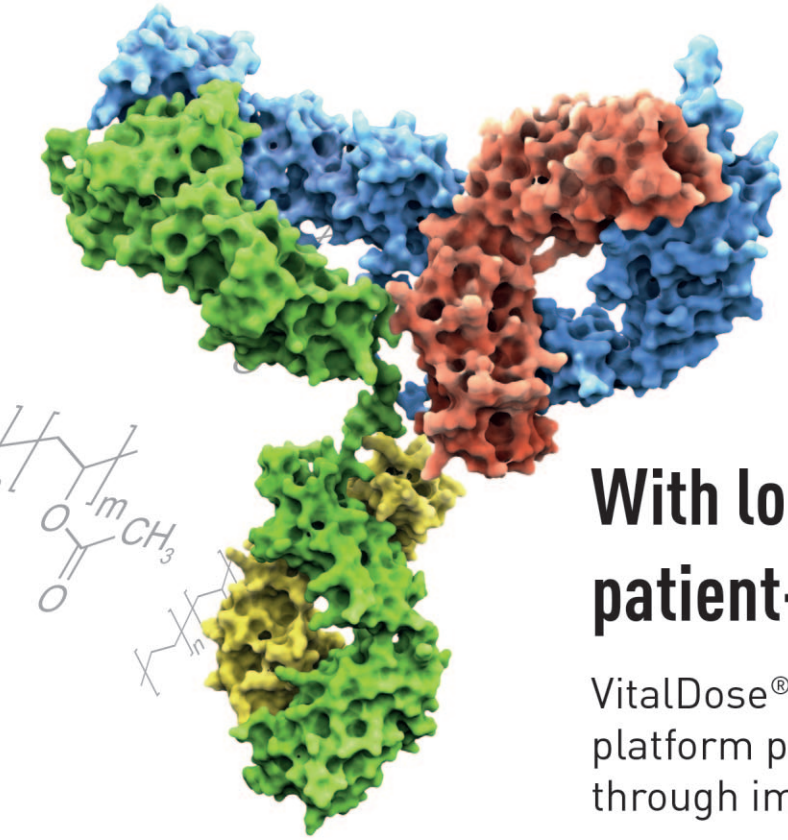
VITAL Dose®

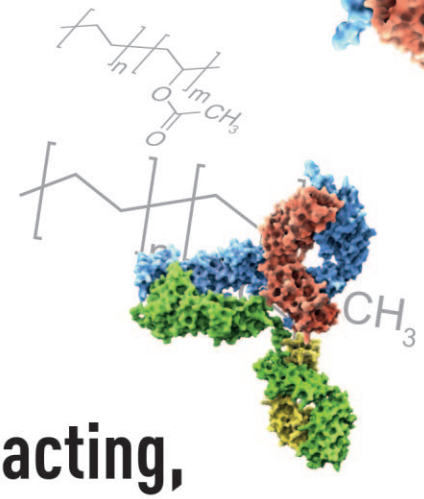
Celanese
The chemistry inside innovation™

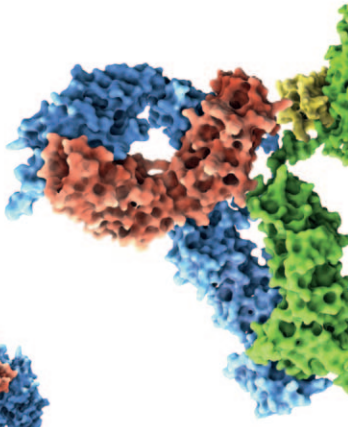
VITAL Dose®



Sustained Drug Delivery







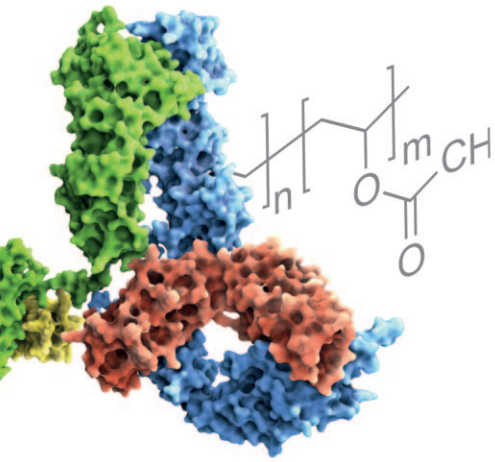
With long-acting, patient-centric therapeutics

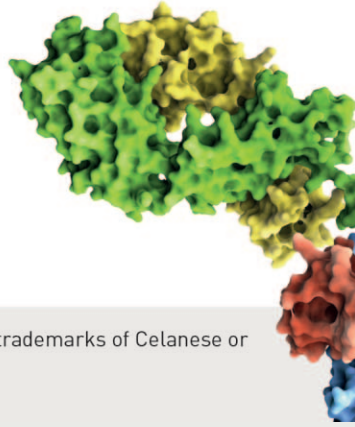
VitalDose® EVA is a copolymer drug-delivery platform providing controlled release through implant and insert dosage forms.

The VitalDose® platform is flexible and customizable with high drug loading capacity (≤ 75%).

Our scientists and engineers will partner with you to create novel delivery systems for:

- Monoclonal antibodies
- Small molecules
- RNA





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

Testing experts.
Service specialists.

DDL Minnesota
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F: (952) 941-9318
E: ddlinforequests@ddltesting.com
W: https://www.ddltesting.com

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DDL – New Jersey
551 Raritan Center Parkway
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F: (732) 346-0295

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.

CREDENCE MEDSYSTEMS, INC.
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W: www.CredenceMed.com

Credence MedSystems, Inc.

Credence MedSystems is setting a new standard in drug delivery, helping you differentiate your products through innovative delivery systems while preserving your trusted processes.

Credence MedSystems is an innovator of drug delivery systems that solve unmet market needs for the pharmaceutical industry. Credence's philosophy of Innovation Without Change allows pharma manufacturers to impress and protect their end users while preserving their existing processes, sourcing strategies and preferred primary package components.

The Companion® family of syringe systems includes proprietary needle retraction technology, syringe reuse prevention and other critical safety and usability features. The Dual Chamber Reconstitution platform offers single-step mixing and injection for medicines that require reconstitution at the time of delivery. The Credence Connect™ brings digital connectivity to any syringe and has the potential to impact chronic disease management and clinical trial compliance. Metered dose systems and other novel devices address the needs of specific therapeutic markets such as ocular therapies and cosmetic applications.

IMPRESS. PRESERVE. PROTECT

IMPRESS. Provide a better experience for users, consistently, across our entire platform of products.
Simple, safe, and intuitive usability creates a better, safer experience for patients and healthcare professionals. Innovative designs provide safety activation clicks, end-of-dose feedback cues, and automatic needle retraction — without changes to familiar injection procedures.

PRESERVE. Differentiate without disruption.
Our unique product innovations coexist with your existing processes, avoiding disruption to your filling lines and simplifying your secondary packaging operations. Use the primary container and components of your choice. Maintain your preferred sourcing strategy and manufacturing processes.

PROTECT. Safeguard healthcare professionals and patients.
Protect your end users from needlestick and prevent reuse — the needle retracts into the plunger rod after use and is secured inside the barrel. Eliminate glue from your combination products, maintaining your drug integrity and enhancing patient safety.

STAND OUT AMONG THE COMPETITION

Differentiating through drug delivery has never been safer, more achievable, and less disruptive. Change the value you provide without changing your processes.

Note: This product has not been evaluated by FDA.

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Twitter: https://twitter.com/CuriaCDMO
LinkedIn: https://www.linkedin.com/company/curia-cdmo/

Curia, formerly AMRI, is a leading contract research, development and manufacturing organization providing products and services from R&D through commercial manufacturing of large and small molecules to pharmaceutical and biopharmaceutical customers. Curia's 3,700 employees at 30 locations across the U.S., Europe and Asia help its customers advance from curiosity to cure. Learn more at curiaglobal.com.

RESEARCH & DEVELOPMENT

Discovery: Identify, refine and secure breakthrough compounds. Curia is an extension of your team, applying deep scientific expertise to help you accelerate progress and meet critical milestones.

Drug Substance & Process Development: Advance the development of your compound. Leverage our unmatched experience and flexibility to navigate toward product launch.

Drug Product Formulation & Process Development: Maximize the potential of your formulation. Trust our practical experience, rigorous quality standards, and risk assessment expertise to guide the development of your injectable product.

COMMERCIAL MANUFACTURING

Drug Substance Manufacturing: Securely move your complex compound from development to commercial manufacture. Our scale-up and tech transfer expertise brings your product to market quickly and safely.

Drug Product Manufacturing: Maximize the impact of your product. Curia delivers high-quality, flexible sterile contract manufacturing services customized to meet your needs.

LAB TESTING SERVICES

Accelerate and validate your compound. We provide the expertise and partnership you need to ensure product efficacy and patient safety, ultimately reducing time-to-market.

The journey to breakthrough medicine is never simple. But the right CDMO partner can ease your path with scientific excellence, relentless curiosity and expert, reliable delivery. For decades, Curia—formerly AMRI—has accelerated our partners' work, from research and development through commercial manufacturing. Together, we can turn life-changing potential into life-changing progress.

Learn more at **curiaglobal.com/curiosity**.

RESEARCH & DEVELOPMENT COMMERCIAL MANUFACTURING LAB TESTING SERVICES CONSULTATIVE SERVICES

curia

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T: +1 240 631 3200 (outside US)
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LinkedIn: https://www.linkedin.com/showcase/emergent-biosolutions-cdmo

Perfecting Your Formula

Emergent CDMO is dedicated to helping pharma and biotech innovators bring life-saving, life-extending therapies to patients throughout the world. Our development and manufacturing facilities in North America and Europe can support preclinical to commercial production of therapeutics and vaccines. Whether you're looking for initial process development support, small volumes of material for clinical trials, or large-scale production for a global commercial therapy, our experienced CDMO team is ready to serve as your trusted guide from molecule to market.

Making Your Impossible

Emergent BioSolutions' mission is to protect and enhance life through innovation. Over the last few decades, Emergent has developed, manufactured, and delivered therapeutics and vaccines throughout the world to tackle the most serious health threats.

Emergent's CDMO business draws on this experience and has supported the development and manufacture of over 40 commercial and more than 200 clinical programs for their clients. As a dedicated and experienced CDMO solutions partner, clients can leverage Emergent CDMO's diverse technology platforms, customizable solutions, infrastructure, and capabilities to support the clinical and commercial successes of their molecules.

Technologies & Platforms for Every Strategy

Our CDMO teams have extensive experience and expertise to support biopharma innovators' needs for a wide range of platforms and technologies including mammalian, microbial, viral, plasma protein-based biotherapeutics and vaccines. Additionally, we can provide process and viral vector development services for gene therapies.

Development Services

- Process Development
- Analytical Development
- Formulation Development
- Lyophilization Development
- Non-GMP Lab-Scale Manufacturing

Drug Substance Manufacturing

- Upstream & Downstream Processing
- Single-Use Platforms (up to 4000L)

Drug Product Manufacturing

- Vials and Prefilled Syringes
- Lyophilization Services
- High Containment Filling (viral and non-viral)
- Packaging & Labeling

Wherever you are in your journey, whatever challenges you face, our team of experts and resources are ready to go to work for you.

Let's get started with your next clinical or commercial candidate. Your new formula for success awaits.

emergent biosolutions®

CDMO

Let's Do Your Impossible

If the distance left to travel between "right now" and "product to patients" seems daunting, we can help.

From clinical trials to large-scale production, you'll find Emergent a committed, experienced CDMO partner to help make your biotherapeutic or vaccine a reality. Our development services, drug substance platforms, and drug product manufacturing capabilities are primed to help advance your program through every mile marker and beyond.

Let's solve your impossible together at
emergentCDMO.com/possible

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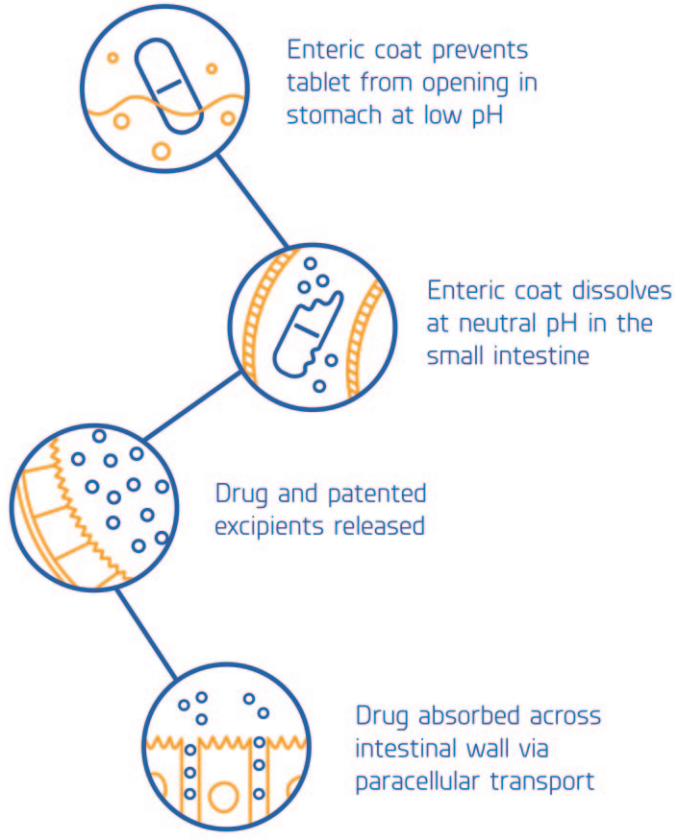
E: info@enterisbiopharma.com - W: www.enterisbiopharma.com
LinkedIn: https://www.linkedin.com/company/3194623/
Contact: Joshua Stephens, Sales Manager, Pharmaceutical Drug Delivery

Custom Solutions: From Bench to Market™ - The Preferred Partner for the Development & Manufacture of Oral BCS III & IV Drug Products

Enteris BioPharma Inc., a wholly owned subsidiary of SWK Holdings Corp. (Nasdaq: SWKH), is a fully integrated development and manufacturing organization offering innovative oral drug delivery solutions. Since its founding in 2013, Enteris has adapted its oral drug delivery technology to advance multiple internal and client programs into the clinic. More recently, Enteris has completed a renovation of its 32,000 square-foot GMP facility, including HPAPI containment and handling, in Boonton, New Jersey, enabling long-term partnerships for challenging solid oral drug product development from preclinical through commercial cGMP manufacturing.



Unlike other technologies, Peptelligence® and ProPerma® uniquely address issues with both solubility and permeability in a solid oral dosage form, enabling new and highly scalable treatment opportunities for peptides, peptidomimetics, and small molecules that typically need to be injected. Peptelligence® and ProPerma® utilize an enteric coating surrounding a tablet core containing the API with a synergistic combination of pH-lowering and solubilizing agents that are known to have permeation-enhancing properties.

Enteris' oral drug delivery technologies have been proven safe and effective in over 15 clinical studies, showing exceptional results in enhancing oral bioavailability of various peptide modalities, including but not limited to GLP-1, GnRH, PTH, DACRA, and KORA analogs. For certain small molecules, the technology has been shown to provide over 20-fold improvement in oral bioavailability. As a true full-service provider of choice, Enteris is uniquely qualified to provide total integrated oral drug product development for the most challenging compounds.

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

Curiosity is the spark for medical breakthrough. The right CDMO partner can nurture that spark with scientific excellence and expert, reliable delivery. For decades, Curia—*formerly AMRI*—has accelerated our partners' work, from research and development through commercial manufacturing. Together, we'll work to turn your idea into a life-changing **cure.**

CURIAGLOBAL.COM/CURIOSITY

RESEARCH & DEVELOPMENT
COMMERCIAL MANUFACTURING
LAB TESTING SERVICES
CONSULTATIVE SERVICES

curia

eurofins | BioPharma Product Testing

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E: pha@eurofinsUS.com
W: www.Eurofins.com/BPT
LinkedIn: www.linkedin.com/company/eurofins-biopharma-product-testing-usa

Experience Our Expertise

Eurofins BioPharma Product Testing offers complete CMC Testing Services for the Bio/Pharmaceutical industry, including all starting materials, process intermediates, drug substances, drug product, packaging, and manufacturing support through our broad technical expertise in Biochemistry, Molecular & Cell Biology, Virology, Chemistry and Microbiology.

In Our World, Global Is Local

With a global capacity of more than 2,000,000 square feet of facilities and 37 locations worldwide, our network of GMP laboratories and vast experience allow us to support projects of any size from conception to market.

Our local presence with four key sites in the US, including Lancaster, PA; Portage, MI; Columbia, MO; and San Diego, CA, ensures personal service backed by a unique global breadth of harmonized capabilities that supports all functional areas of bio/pharmaceutical drug development.

Collaboration Drives Cost-Effectiveness

Our fundamental philosophy is to help clients efficiently allocate their research and manufacturing expenditures by strategically engaging them to meet their unique outsourcing needs.

We offer the ability to manage your testing programs more efficiently through your choice of three unique service models, including our award-winning PSS Insourcing Solutions® (PSS), Full Time Equivalent (FTE) or traditional fee-for-service. You can choose the best, most cost-effective service solution for your project goals.

Comprehensive Services

- Sterile Fill/Finish Manufacturing
- Rapid Sterility Testing
- Method Establishment (Development, Feasibility, Optimization, Verification, Qualification, Validation, Transfer)
- Characterization
- Raw Material Testing
- Critical Reagents/Reference Standard Management
- Residual Impurities Testing
- Release Testing (Strength/Content, Identity, Purity, Product/Process Related Impurities, Safety)
- Stability Testing and Storage
- Sterile (Compendial and Rapid) and Non-sterile Microbiology Testing
- Cell Bank Manufacturing and Characterization
- Viral Clearance & Viral Safety Testing
- Bioassay & Potency Testing
- Extractables & Leachables Testing
- Container, Packaging & Closure Integrity Testing
- Functional Testing and Failure Analysis
- Shipping Studies
- Disinfectant Efficacy/Cleaning Validation Studies
- Environmental Monitoring
- Facility and Process Validation
- Organism Identification
- Formulation Development/Testing
- Custom Synthesis & Radiolabeling
- Clinical Trial Material Support
- Scientific Consulting

One CTO. One comprehensive suite of services. One Project Management team eager to make outsourcing simple. Access the leader in consultative problem-solving and world-class testing capabilities.

eurofins | BioPharma Product Testing

www.eurofins.com/BPT

From Starting Materials through Finished Product Testing, Eurofins BioPharma Product Testing's 37 facilities in 19 countries deliver the world's most comprehensive scope of harmonized GMP testing services and seamless regulatory acceptance.

As we have grown to become the world's largest network of GMP product testing labs, we continue to uphold our founding promise of personal service and impeccable quality.

When the world awaits your product, choose the lab that provides complete capabilities and rigorous quality systems you can trust.

Comprehensive GMP Testing Services

Method Development & Validation • Release Testing • Stability Testing & Storage
Cell Banking Services • Virology Services • Facility & Process Validation
Chemistry • Biochemistry • Molecular & Cell Biology • Microbiology
Raw Materials Testing • Primary & Secondary Package Testing

Flexible Service Models

Fee For Service (FFS)
Full-Time-Equivalent (FTE)
Professional Scientific Services® (PSS)

Global Facilities

Australia	Denmark	Ireland	New Zealand	Switzerland
Austria	France	Italy	Spain	UK
Belgium	Germany	Japan	Slovakia	US
Canada	India	Netherlands	Sweden	

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LinkedIn: https://www.linkedin.com/showcase/flex-health-solutions
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 Product 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, optics, sensors and actuators, miniaturization, and connectivity, and human machine interface.

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. Precision tool making and 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

Drug delivery platforms, 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.

flex

WE HELP YOU GET FROM WHERE YOU ARE TO WHERE YOU WANT TO BE.

As a leading provider of design and manufacturing services for the medtech and pharmaceutical industries, we work with you to provide innovative medical products cost effectively. At the same time, our eye is on elevating manufacturing efficiencies, shortening the timeline from production to patient, backed by a highly resilient global supply chain.

Whether your focus is on personal diagnostics, drug delivery devices, clinical imaging and diagnostic systems, or hospital equipment, let's partner together to help improve people's lives.

Visit flex.com/health or email us at healthsolutions@flex.com

- Human Factors & Industrial Design
- Full Product & Process Development
- Design For Manufacturing
- IP Protection
- New Product Introduction
- Global Manufacturing
- Total Supply Chain Management
- World Class Quality System
- Digital Health & Medical Mobile Apps

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.

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www.gattefosse.com

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GATTEFOSSÉ USA Regional Office
Tel: +1 201 265 4800 - info@gattefossecorp.com

GATTEFOSSÉ

A Winning Strategy
Lipid-Based Formulations
for Oral Bioavailability Challenges

A unique combination of benefits

Experiencing limited absorption due to poor solubility, poor permeability, or pre-systemic elimination?

Lipid excipients have the capability to overcome these hurdles and enhance oral bioavailability.

Oily vehicles	Maisine® CC Peceol™ Labrafac™ Lipophile WL 1349
Surfactants (HLB > 10)	Gelucire® 44/14 Gelucire® 48/16 Gelucire® 50/13 Labrasol® ALF
Co-Surfactants (HLB ≤ 9)	Capryol® 90 Labrafil® M 1944 CS Labrafil® M 2125 CS Lauroglycol™ 90 Plurol® Oleique CC 497
Solvent	Transcutol® HP

Advantages *in vivo*

- \+ Increase drug solubility
- \+ Maintain drug solubilization throughout digestion
- \+ Increase intestinal permeability
- \+ Target lymphatic transport
- \+ Mitigate food effect

Scan me!

▸ Visit our website for more information

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LinkedIn: https://www.linkedin.com/company/genezen-laboratories/
Twitter: @GenezenLabs https://twitter.com/GenezenLabs

Specializing in lentiviral and retroviral vectors, **Genezen** offers early-phase process development, GMP vector production, analytical testing services and assay development. Leveraging the expansive knowledge and experience of its team, Genezen accelerates cell and gene therapies to commercialization and helps deliver life-changing therapeutics to patients.

Founded in 2014, the company strives to make viral vector production accessible to early-stage, growth-oriented companies and established industry leaders.

Genezen officially opened its 25,000-square-foot, state-of-the-art, cGMP-compliant process development lab in late 2021. Situated in the fast-growing life sciences hub of Indianapolis, the laboratory is the first phase of a larger cGMP-compliant lentiviral and retroviral vector production facility which will house multiple cGMP production suites with capabilities for host cell expansion and banking and viral vector production.

SERVICES

Process Development

- Transient transfection and plasmid system options
- Producer cell line development
- Plasmid design
- Selection of viral vector platform and cell line for vector production
- Reproducible process design with commercialization approach

Process Optimization

- Upstream and downstream processing
- Proof of concept evaluation runs
- Research cell banks
- Engineering runs at variable scales for further optimization in the process development lab
- Optimized cGMP runs
- cGMP master and working cell bank productions

GMP Vector Production

- Aseptic processing using single-use closed systems from upstream processing to fill and finish
- Adherent cell capability for up to 140L production
- Roller bottles, cell stacks and fixed-bed bioreactor
- Proprietary suspension 293T cell line for up to 200L production
- Single-use/closed systems for virus harvest, purification and concentration
- Access to cGMP compliant master cell banks for common cell lines including HEK293T

Testing

- **Potency:** Biological titers, physical titers (p24), Empty vs Full particle ratio, transduction efficiency
- **Safety:** RCL testing (co-culture and qPCR based), RCR (GALV, ecotropic and direct), endotoxin, mycoplasma, sterility, in-vitro viral assay, PERT
- **Identity:** Vector Copy Number by qPCR, vector insert identity & stability, insertional site analysis, ADA Isoenzyme analysis
- **Stability:** Cell line, viral vector and transgene studies
- **Residual testing:** Benzonase, host cell proteins, host cell DNA, plasmid DNA, E1A qPCR, SV40 qPCR

Cell Manufacturing

- Capabilities across,
  - CAR T, NK, T lymphocytes and other immune cells
  - Hematopoietic progenitors and stem cells, including MSCs
  - Embryonic and induced pluripotent stem cells (iPSCs)
- Enrichment or depletion of specific cell subsets
- Genetic modification (transduction)
- Expansion and differentiation
- Cryopreservation
- Cellular stability studies
- Suspension cell line development
- Producer cell lines

Genezen

Your lentivirus and retrovirus partner

Genezen offers contract process development, GMP viral vector production, transduced cell manufacturing and testing services.

Why Genezen?

Production Capacity

New state-of-the-art, cGMP-compliant multi-vector production facility in Indiana

GMP Vector Manufacturing

Unique expertise in lentivirus and retrovirus production

Process Development

Robust, efficient and scalable processes with in-house assay development

Cell Manufacturing

World-class partnerships to streamline production

Testing

Minimize your time to trial through rapid testing

Solutions to propel your therapies forward.

genezen.com | info@genezen.com

Connect with us:

HASELMEIER™

A medmix Brand

High-Quality Self-Injection Systems

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 2021, Haselmeier represents the Drug Delivery business unit of medmix, Haag, Switzerland (www.medmix.swiss).

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 and auto-injectors from Haselmeier can help reduce risk and shorten time-to-market.

HASELMEIER, INC.
126 JOHN STREET, SUITE 11
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W: www.haselmeier.com

HASELMEIER™

A medmix 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
www.haselmeier.com

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Terry.Ohagan@medmix.com

HERMES PHARMA

Get the dose right®

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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 is the leading expert in developing and manufacturing user-friendly oral dosage forms. As a CDMO, we offer customized services along the entire pharmaceutical value chain, from new product development and formulation to manufacturing and regulatory support. For more than 40 years, healthcare companies around the globe have worked with HERMES PHARMA to expand their product lines and grow their brands.

Our sister company HERMES Arzneimittel has a rich portfolio of OTC brands and a long history in pharmaceutical excellence. So, we truly understand the challenges of our customers and can support them on their way to market success.

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.

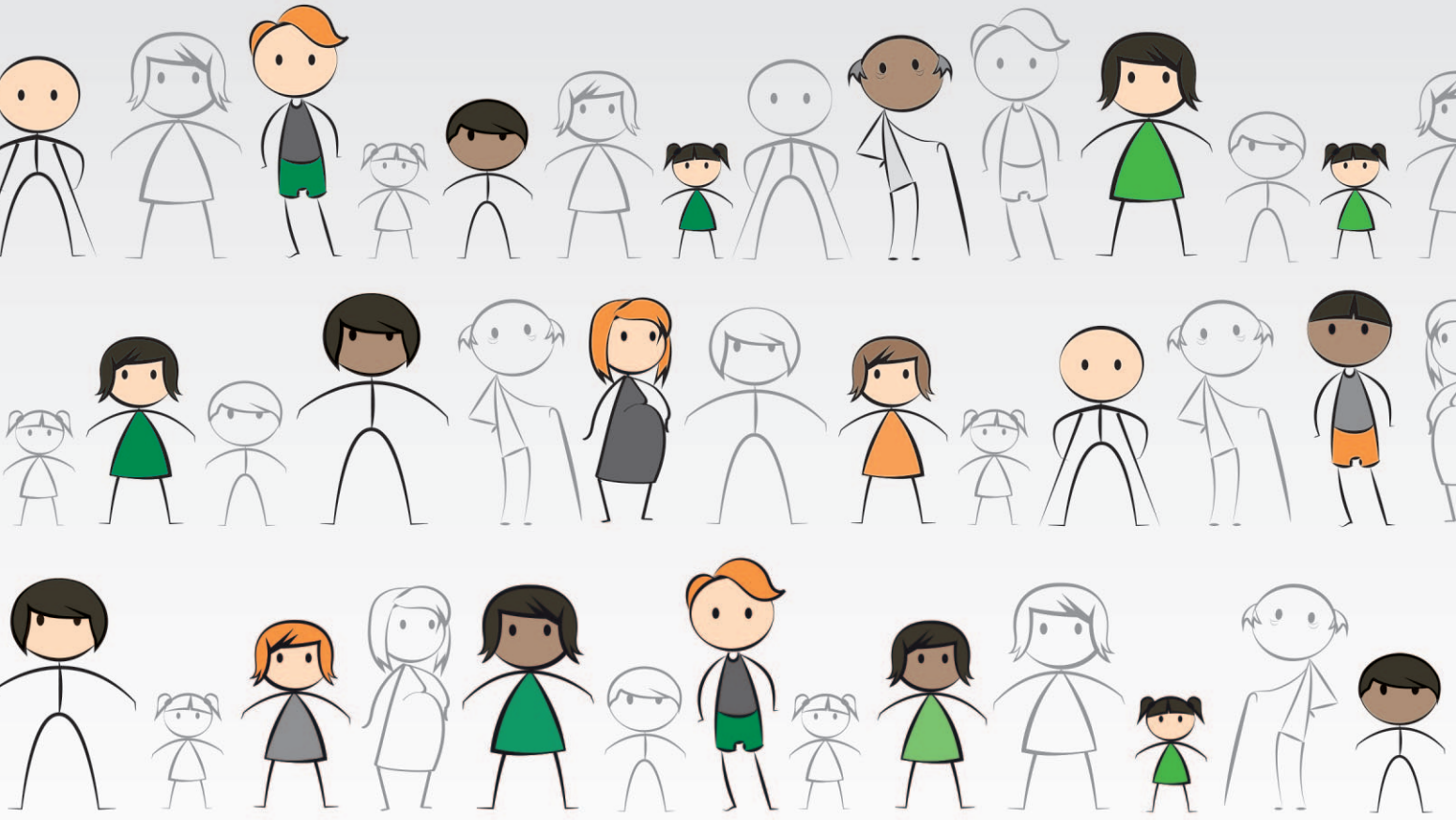
Our effervescent and chewable tablets, lozenges, instant drinks, orally disintegrating granules and HERMES NutriCaps are user-friendly alternatives to conventional tablets and capsules. They provide an added value to patients and consumers as they:

- 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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E: Kahle@Kahle.it
W: www.KahleAutomation.com

If you're looking for an automation partner who understands the precision and care required to manufacture the world's finest drug delivery devices, consider Kahle Automation, Engineering Perfection since 1920.

Engineering Perfection requires an automation partner who truly understands the process of manufacturing medical devices.

CELEBRATING OUR 100-YEAR ANNIVERSARY. Kahle is the only large-scale automation company in the world that focuses exclusively on custom automated assembly equipment for medical and pharmaceutical devices. For nearly a century, Kahle has shaped the industry through the use of innovative technologies and we bring this experience to your project. Today, we create systems that handle, assemble, inspect, test and package every medical device imaginable – from syringes, tubing sets and catheters and needle products to diagnostic, pre-filled and combination pharmaceutical devices.

Safety and quality go hand-in-hand with a successful automation project. All of our work is guided by GAMP 5 and ISO 9001 quality standards and we work with our customers to help them meet FDA 21 CFR Part 820 and Part 11 regulations.

Engineering Perfection requires an automation partner who brings the best technology to your project.

Regardless of whether you're looking for a system that assembles thousands of devices per minute, improves the quality and consistency of your manufacturing process or whether you're simply trying to maximize the space in your clean room, Kahle has the technical solutions to meet your goals.

Every year, Kahle dedicates over 182,500 man-hours to designing automation systems that manufacture medical devices. This effort has resulted in the largest portfolio of proprietary automation technology in the entire industry. From this portfolio, you can choose from continuous, indexing and asynchronous motion assembly platforms that feature the latest innovations in mechanical, pneumatic and robotic assembly with premium inspection and process control operations. This flexibility allows us to create cost efficient, effective systems for projects of every size.

Engineering perfection requires an automation partner that guarantees performance.

Beyond creating the ideal assembly system for your project, your Kahle team is also focused on getting your machine validated promptly and transitioned efficiently into production. Further, we want to make it easy for your employees to be trained to operate and maintain the equipment. To these ends, your Kahle machine arrives with the best quality and validation documentation in the industry.

Celebrating 100 Years
100
KAHLE
Automation Excellence

Pointed in the right direction.

Automation machinery solutions to keep you ahead of your competition.

Kahle® is dedicated to providing custom automation machinery solutions for the Medical Device, Pharmaceutical, and Healthcare Industries.

KAHLE®
Manufacturer of Automation Equipment

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Kymanox
Your Life Science Solutions Partner

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E: info@kymanox.com - W: www.kymanox.com

Corporate Description

Kymanox is a life science professional services organization that offers engineering, scientific, and compliance support to companies exclusively in the biotechnology, pharmaceutical, medical device, and combination product industries. With its diverse team, Kymanox helps clients navigate commercialization challenges that arise throughout a product's lifecycle – from early development to post-market commercialization – with optimized safety, quality, efficacy, and accessibility.

Kymanox engineers and scientists, in conjunction with engineers from Neuma by Kymanox, provide end-to-end, integrated support to clients. The combined team helps resolve product design and development challenges, thus more effectively bringing specialized drug delivery and medical device solutions to patients in need.

- Kymanox understands the interaction between devices and drug products. The company's experience with combination products includes, but is not limited to, injectables, nasal, respiratory, kits, and wearable devices.
- Kymanox transforms innovative and valuable technologies into drug delivery and medical solutions, getting you one step (or many steps) closer to commercial launch.
- Kymanox understands why "the product is the process" and how to implement solutions to unique challenges.
- With drug development constantly evolving with new regulations and technology, Kymanox stays up to date to maintain compliance.

Kymanox serves clients globally from their headquarters in Raleigh (RTP), NC and its offices across the United States. The team consists of more than 200 employees, including over 75 engineers and a well-credentialed contractor network. Kymanox is 100% focused on the life sciences industry with extensive experience across facility, process, and product development. Kymanox offers a number of life science solutions including the following:

Quality, Regulatory, and Compliance Solutions:

- Quality Assurance and Compliance
- Global Quality Auditing
- Quality Engineering
- Quality Control
- Regulatory Affairs
- Clinical & Medical Affairs
- CGxP Microbiology and Environmental Monitoring

Strategy, Planning, and Execution Solutions:

- Program and Project Management
- Technology Transfer
- Staffing Solutions
- Due Diligence
- Innovation Solutions
- Enterprise Resource Planning

Development and Operations Solutions:

- Process Engineering
- MS&T and Supply Chain
- Product and Process Development
- CMC Services and Analytical Sciences
- Packaging Technology and Engineering
- Human Factors Regulatory and Strategy

Commissioning, Qualification, and Validation (CQV) Solutions:

- Process Validation
- Facilities and Utilities CQV
- Cleaning Validation
- Lab and Equipment CQV
- Computer System Validation
- Validation Master Planning

Kymanox partners with you to makes it easier for your life science team to Get More [DONE].

SOLVE THE PUZZLING COMPLEXITIES OF COMBINATION PRODUCTS WITH KYMANOX

Kymanox Provides Comprehensive Engineering and Development Solutions from Concept and throughout Commercialization

- PRODUCT STRATEGY & ENGINEERING
- DEVICE DEVELOPMENT
- REGULATORY AFFAIRS
- PROCESS ENGINEERING & QUALIFICATION
- TECHNICAL PROGRAM MANAGEMENT
- QUALITY ASSURANCE
- PACKAGING ENGINEERING
- HUMAN FACTORS REGULATORY STRATEGY & MANAGEMENT
- POST-MARKET SUPPORT
- CMO & SUPPLIER SELECTION AND MANAGEMENT

Connect the pieces and fill the gaps in your combination product development with Kymanox — your premier, one-stop, engineering solutions provider for Right First Time development, scale-up, and approval.

Kymanox
Your Life Science Solutions Partner

Learn more at kymanox.com/combination-products
+1 919 246-4896 | sales@kymanox.com

LUBRIZOL LIFE SCIENCE HEALTH
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The Health business of **Lubrizol Life Science (LLS Health)**, in partnership with customers, advances solutions inspiring a healthier life. We specialize in helping clients from idea to execution by offering innovative polymers and excipients, as well as best-in-class contract development and manufacturing services. Our long history of polymer expertise and continued investment in research and manufacturing means we offer you and your customers a smooth and streamlined approach to innovative healthcare solutions.

Excipients

Our pharmaceutical grade Carbopol® polymers, Noveon® polycarbophil, and Pemulen™ polymers are used in a wide range of applications, including:

- Sustained release oral solids
- Topical semisolids and liquids
- Transdermal patches
- Oral liquids
- Drug-eluting devices (Pathway™ thermoplastic polyurethane)

These excipients have been used in both Rx and OTC products for decades to impart critical functionalities, such as mucoadhesion, rheology modification, and controlled drug release. Additionally, our Apinovex™ and Apisolex™ polymers function as solubility and bioavailability enhancers in oral solid and injectable applications, respectively.

CDMO

We offer end-to-end contract development and manufacturing (CDMO) services. For over 20 years, we've partnered with clients to overcome formulation challenges and help get their products to market. Our FDA-inspected facility in Bethlehem, PA features clinical and commercial manufacturing suites to accommodate vials, bottles, syringes, and non-traditional dosage forms. Our focus areas include:

- Solubility and Bioavailability Enhancement
- Long-Acting Injectables and Implantables
- Aseptic Manufacturing/Sterile Fill-Finish
- Biologics
- Highly Potent APIs and Controlled Substances

LUBRIZOL
LIFE SCIENCE

DRIVEN BY INNOVATION, POWERED BY PARTNERSHIP.

Lubrizol Life Science Health is advancing solutions aimed at improving patient outcomes. We offer best-in-class polymers and excipients, along with drug product and medical device design, development, and manufacturing services.

Learn more at
Lubrizol.com/Health

HEALTH

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Cleveland, OH 44141-3201 USA

21-1804

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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.

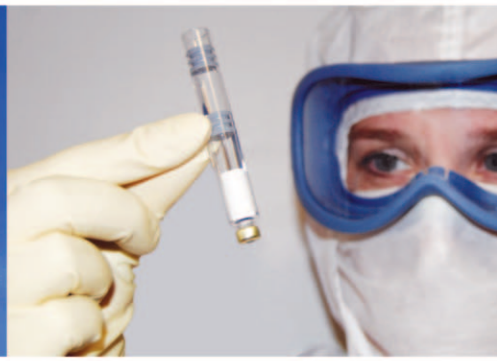
- Customized Training
- Consulting on equipment specifications
- Process requirements
- Guidance on CMC submission
- Support on IQ/OQ and process validation
- Technology transfer
- Process excursions
- Product and process troubleshooting
- Batch record review
- Compliance auditing

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

30 INDIAN DRIVE • IVYLAND, PA 18974 USA • +1 (215) 396-8373

Medical Engineering Technologies delivers excellence in combination device testing, globally.

Services include: biocompatibility and chemical characterization, dose delivery accuracy, extractable and leachable studies, formulation stability, mechanical performance, RLD comparisons, sterile barrier verification, human factors studies, and lots of good advice.

Medical Engineering Technologies is the destination for combination device batch release and design validation testing. Clients from across the globe have found our laboratory services to be rapid, precise, and very effective. MET has successfully delivered testing to medical device and pharmaceutical companies in over 20 countries across: Africa, Asia, Australasia, Europe, and the USA. We knowledgeably, reliably, and effectively deliver medical device and packaging validation, and we are a world-leading CRO for combination devices and prefilled syringes testing.

With accreditation to ISO 17025 for validation testing, and GMP for batch release testing, you can have complete confidence in the quality and accuracy of our results.

We only test medical devices, and we know about medical devices. Our technicians start with a product review and risk analysis. Then they can draw up a protocol. This may be for some quick verification testing or for a complete stability program. Project plans are also submitted to clients. We will feel like an extension for your team with our communication channels always open. Reporting may be at the end of a short project or at each stage of a longer study.

Physical performance and dose accuracy studies - A full suite of equipment along with knowledgeable technicians is available to meet your needs.

Extractables and leachables/ISO 10993-18 chemical characterization - With an ISO 10993-18 committee member on our team, we will always be up to date with all your testing needs.

Drug container compatibility, formulation stability - Our analytical chemistry laboratories work with combination devices at all stages of validation.

Design validation - Just check out our design validation guidebooks (available on request from our website) to confirm that we are leaders in developing validation/verification programs.

Batch release and importation testing - Fast turnaround work to previously agreed protocols reported with a certificate of analysis.

Human factors/Usability - Available for all delivery devices across multiple countries (summative or formative).

Find out why Medical Engineering Technologies is becoming the world-leading laboratory for combination device testing and why we are the best partner for supporting your product claims and regulatory submissions.

MEDICAL ENGINEERING TECHNOLOGIES LTD (MET)
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Dover, UK
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E: sales@met.uk.com
W: www.met.uk.com

MEDICAL ENGINEERING TECHNOLOGIES

Combination Device Testing

Medical Engineering Technologies is the destination for combination device batch release and design validation testing. Clients from across the globe have found our laboratory services to be rapid, precise and very effective.

- Consulting
- Device Performance
- Materials Analysis
- Package Validation
- Stability Testing

Global Excellence in Medical Device Testing

Medical Engineering Technologies
Unit 16, Holmestone Road,
Dover, Kent,
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UKAS TESTING
7848

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Greenville, NC 27834
T: (252) 752-3800
E: thomas.salus@maynepharma.com
W: www.metricscontractservices.com

VITAL STATISTICS

Year Founded: 1994
Number of Employees: approx. 450
Contact: Britton Jimenez, VP, Business Development

WHO WE ARE

Metrics Contract Services is a science-led, full-service global contract development and manufacturing organization (CDMO) specializing in novel oral solid 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. Metrics Contract Services — Harnessing complexity to deliver confidence.

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, hard wall 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

ILC Dover
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Newark, DE 19713
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Toll Free: (800) 631-9567
W: ilcdover.com

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 on cost, and maximize productivity so that operators can work uninterrupted at peak performance.

- **EZ BioPac®** is the industry's most efficient and effective single-use powder containment and transfer system that speeds fill time and makes it easy to adjust contents to precise target weight.

- **DoverPac® SF** is a global premier product for disposable pharmaceutical and biopharmaceutical processes. It's the premier product for disposable process and powder containment systems and the global standard for containment, reliability, and service.

- **ArmorFlex® Films** are the premier film for pharmaceutical and biopharmaceutical powder handling and containment that provide unmatched performance characteristics while increasing handling speed and safety. Unlike other films on the market, only components that meet the materials-of-contact test protocol requirements are used to produce ArmorFlex® films. They're regulatory friendly, slip-agent free, and custom-formulated to deliver superior elongation performance (nearly 500%) for ruggedness and high strength.

- **Continuous Liners** are effective and easy-to-use systems for containing APIs and other hazardous compounds. Continuous Liner System assures a safe and effective transfer of powders, giving operators the ability to fill multiple drums without breaking containment.

- **Flexible Isolators**, such as the soloPURE™ Aseptic Isolator, are based on more than twenty years of designing and building custom isolators for powder containment and sterile manufacturing. Standardized, modular designs allow quick delivery of isolators for many contained pharmaceutical powder handling processes.

- **Sentinel XT™ Clear System** is an innovative PAPR specifically designed for pharmaceutical applications. It offers a full 320-degree field of view, allows the wearer to have facial hair or a head covering, and reduces feelings of claustrophobia.

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Morrisville, NC 27560
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W: www.microporetech.com
Twitter: @microporetech
LinkedIn: linkedin.com/company/micropore-technologies-ltd/

COMPANY DESCRIPTION

Micropore Technologies is a global process technology and service provider to the pharmaceutical industry featuring patented crossflow mixing equipment for the commercially scalable development of microspheres, nanoparticles, and emulsions used in a wide range of controlled release, topical, and sterile injectable drug products. Originally spun-out of Loughborough University's internationally renowned chemical engineering department, the company's global headquarters and technical center is located in the Wilton Center, UK with offices and operations in the USA, India, South Korea & Japan supporting over a hundred clients and strategic partners.

OUR TECHNOLOGY & SERVICES

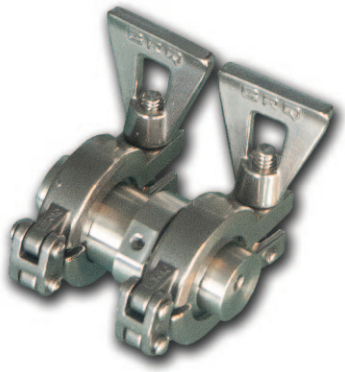
Micropore's award-winning technology allows our customers to engineer mono-disperse microspheres, nanoparticles & emulsions, with the precision of microfluidics while producing them at the scale of conventional processes such as homogenization. We offer best in class formulation consultation and lab-scale preclinical feasibility trials supporting our developmental and commercial production equipment.

Proven benefits of our approach include:

- Less set-up time, reduced raw materials, and maintenance cost
- Unform microspheres require less stabilizer and downstream processing
- Vast chemical versatility including biodegradable polymers, complex coacervates, lipid nanoparticles, and hydrogels
- Minimal shear forces to protect sensitive biologics
- Aseptic cGMP compliant design

Capabilities

- Early-stage formulation development
- cGMP process consultation and scale-up from lab to commercial
- Pre-clinical batch production
- Particle sizing, shape, and encapsulation efficiency analysis
- Tech transfer of production hardware
- Global technical support and troubleshooting
- Higher product yields through less wastage
- No degradation of biologics or primary emulsions
- Reduced use of expensive production additives
- Extremely energy efficient "green" production at all scales



Micropore AXF-mini crossflow device

MilliporeSigma
400 Summit Drive
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T: (800)-645-5476
W: www.emdmillipore.com
Twitter: @MilliporeSigma
Facebook: @MilliporeSigma
LinkedIn: www.linkedin.com/company/milliporesigma/

An Industry-Leading Portfolio of Formulation Products

Our portfolio of formulation products includes excipients for solid, semi-solid and liquid dosage forms for small and large molecules, allowing you to formulate APIs to your exact specifications and requirements. We offer both customized manufacturing and a standard portfolio of synthetic lipids and functionalized PEGs, biodegradable polymers for sustained release of small and large molecules and functional excipients for excellent performance in tableting processes, solubility enhancement and controlled release.

Drug Delivery

Our portfolio of GMP biodegradable polymers, synthetic lipids and functionalized polyethylene glycols enables you to create small and large molecule drug formulations with the optimized release kinetics and targeted drug delivery characteristics needed to maximize product efficacy. We provide high quality portfolio products as well as customized solutions to meet your specific drug delivery and formulation needs. At every phase of clinical development and commercialization, we have the resources and expertise to support your critical development milestones. We offer regulatory expertise and support to help you meet today's complex regulatory challenges.

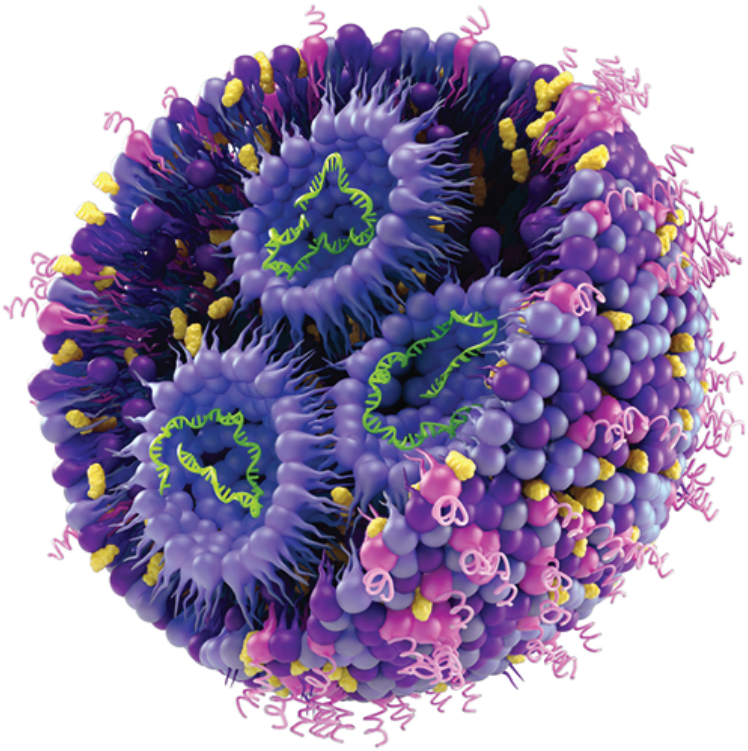
Liquid Formulation

Our broad portfolio of high-quality excipients for both small molecule and large molecule formulations allows you to target different administration routes such as ophthalmics, nasal, parenteral, oral, and otic preparations. Specifically developed for high-risk biopharmaceutical applications, we offer a wide range of buffers, salts and stabilizers low in bioburden and endotoxins. And to help you minimize regulatory and quality-associated risks, all of our excipients are supported by extensive documentation via the industry-leading Emprove® Program. Explore our portfolio of excipients for liquid formulation on our website.

Solid Formulation

Our high-quality raw materials and functionalized excipients form a comprehensive portfolio that addresses all your most pressing challenges in solid formulation manufacturing, with products that include: antioxidants and preservatives, binders and fillers, coatings and supporting material, disintegrants, lubricants and glidants, pH adjusters, surfactants and stabilizers, and taste modifiers.

Our particle optimized Parteck® functional excipients, for example, are specifically developed to address formulation challenges in solid dose, featuring unique particle properties and outstanding individual functionalities. The result is excellent tableting behavior and simplified formulation design, so you can speed your product to market. In addition, you can rely on our industry-leading Emprove® Program to meet today's complex regulatory challenges with a superior combination of comprehensive documentation and transparency. Our high-quality raw materials, regulatory expertise, and dedicated support provide everything you need to simplify supplier qualification, speed up processes, and reduce your total cost of ownership.



MilliporeSigma

Unique Solutions for Complex Formulation Challenges

POWER UP YOUR FORMULATION GAME

Novel modalities, preferred routes of administration to ensure patient compliance, and improved release kinetics are changing the playing field. And these new challenges call for new formulation solutions.

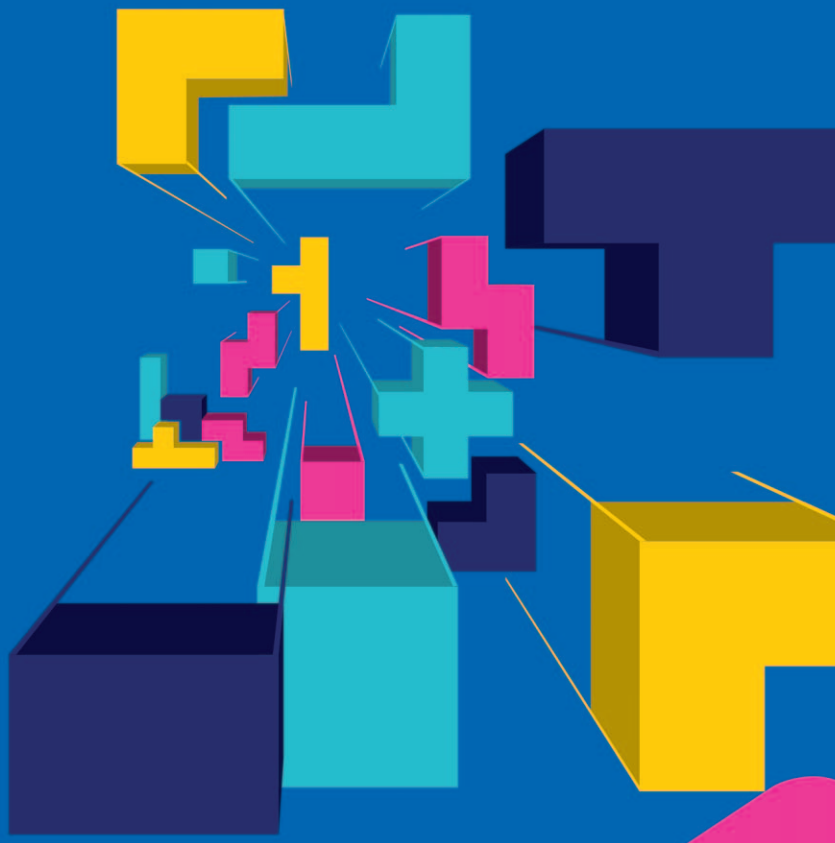
With a proactive excipient partner, you are not alone on your journey, and you will know which variables to change and which to keep the same.

Gain greater control in your formulation game:

- Global application labs and consultative services
- Specialized excipients for controlled release and solubility enhancement
- Customized solutions for advanced drug delivery

Excipients for Pharma & Biopharma | Lipids | aPEGs | Polymers for Drug Delivery

To find out more, visit:
emdmillipore.com/control-in-formulations



The Life Science Business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the US and Canada.

SAFC®
Pharma & Biopharma Raw Material Solutions

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 New Business Development Department for tackling a variety of today's problems, and the department 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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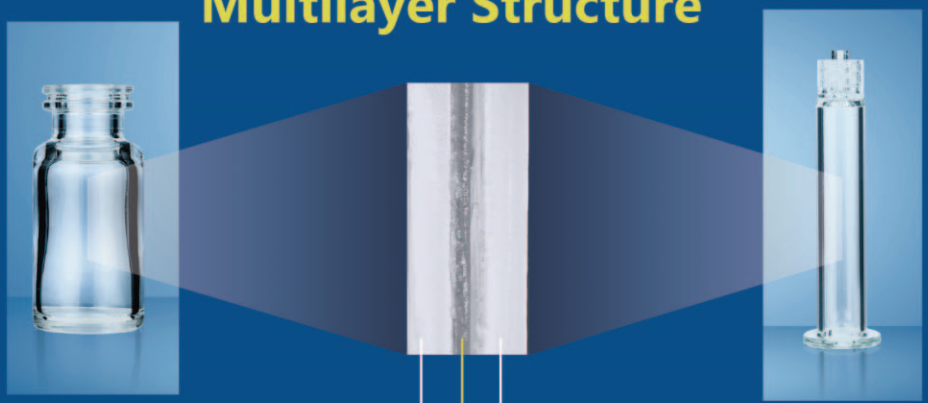
E: nb3.pharmapackage@mgc.co.jp W: https://www.mgc.co.jp/eng/products/abd/oxycapt.html

OXYCAPT™ Plastic Vial & Syringe

Multilayer Structure



Water Vapor Barrier Layer (COP)

Oxygen Barrier Layer (New Polymer)

Drug Contact Layer (COP)

- 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 & Gene/Cell Therapy

2, 6, 10, 20mL Vial

Nest & Tub for Vial

1, 2.25mL Syringe

Nest & Tub for Syringe

MITSUBISHI GAS CHEMICAL

Mitsubishi Gas Chemical Company, Inc.
https://www.mgc.co.jp/eng/products/abd/oxycapt.html
Mitsubishi Gas Chemical America, Inc.
http://www.mgc-a.com
Mitsubishi Gas Chemical Europe GmbH
https://www.mgc-europe.de

NEMERA
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As a world-leading drug delivery device solutions provider, Nemera's goal of putting patients first enables it to design and manufacture devices that maximize treatment efficacy. **Nemera** is a holistic partner and helps its customers succeed in the sprint to market with its combination products. From early device strategy to state-of-the-art manufacturing, Nemera is committed to the highest quality standards. Agile and open-minded, the company works with its customers as colleagues. Together, they go the extra mile to fulfil its mission.

NEMERA IS YOUR HOLISTIC PARTNER FOR THE COMBINATION PRODUCT JOURNEY

From device selection through product lifecycle management, Nemera is your single partner for the whole of the combination product journey. By focusing on solutions that make patients' lives easier and safer, Nemera has built a strong portfolio of innovative products and technologies. To complement the products portfolio, **Nemera also offers end-to-end services and expertise in device development, device consulting, and contract manufacturing** to help you through every step of the journey. Nemera applies this know-how and its singular focus on healthcare to realize its vision of becoming the most patient centric drug – device company in partnership with our customers.

OPHTHALMIC: A CLEAR VISION FOR EYE CARE

One of the main criticalities of self-administered eye care treatments today is poor patient adherence, especially with chronic diseases. We strive to improve patient experience by providing safe and effective multidose eyedroppers for preservative-free solutions, used all over the world: **Novelia®** is a preservative-free multidose eye dropper delivering consistent drops for better patient compliance.

NASAL, BUCCAL, AURICULAR: MAKE EVERY SPRAY COUNT

The number of drugs delivered through the ear, nose and throat is expanding. We provide a comprehensive range of pumps, compatible with a wide choice of actuators for each delivery route (ear, nose and throat), suitable for regulated and low regulated markets: **multidose pump systems (SP270+, SP370+, SP27, SP37, In-vitro Bioequivalence for nasal sprays, Child-resistant solutions), unidose systems (UniSpray), Retronose®, and electronic technologies (Safe'n'Spray™ and Electronic Nasal device)**. We guarantee precision and dose consistency to maximize treatment efficacy and improve patients' outcomes.

DERMAL: CONVENIENT FOR PATIENTS, PROTECTIVE FOR FORMULATIONS

The dermal application is a convenient non-invasive way to administer liquid sprays, lotions, gels, or creams to the skin for dermatological, anti-inflammatory or systemic treatments. Our airless and atmospheric delivery devices are suitable for RX and OTC formulations and have all the documentation needed to be registered on regulated markets: Sof'Bag®+, Sof'Airless, Spray pumps for vicous formulations and Child Resistant Closure systems.

PARENTERAL: COMPLEX DEVICES, SIMPLE PATIENT CARE

The growing prevalence of chronic diseases, along with the evolution of self-administration at home, is driving new ways of administrating parenteral drugs. As injecting a drug means increased risks of use errors and needlestick injuries, self-administration at home translates into a need for safer, easy-to-use and ergonomic devices. We are committed to ensure adherence and user well-being for patients and healthcare professionals providing a comprehensive parenteral product range that matches their need: **Passive Safety Systems (Safe'n'Sound® 1ml and 2.25ml), Reusable and Disposable Pen platforms, Implanters, and Body injectors (Symbioze)**.

INHALATION: A BREATH OF EXPERTISE

From the concept idea to large scale manufacturing, we're the utmost holistic partner to develop your inhalers. We help our customers succeed in the sprint to market with their formulations targeting the inhalation treatments. We also are an active contributor to the scientific community and we strive to consider in our research evolving trends in inhalation and in patient needs, as well as increasing interest to digital and sustainability related factors.

Nemera
we put patients first

From design to manufacturing, we partner in your device strategy

NEMERA: YOUR COMBINATION PRODUCT PARTNER

Patients first. Always.

Partnering in drug delivery devices. Holistically.

Going the extra-mile. Together.

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OX20 1TU, United Kingdom
W: https://www.ompharmaservices.com/

With almost 70 years of experience in medical devices, **Owen Mumford Pharmaceutical Services** is a division of Owen Mumford, with the Head Office located in Woodstock, UK. Our global presence spans from manufacturing facilities in the UK and Malaysia to subsidiaries in the US, Germany, and France.

Owen Mumford Pharmaceutical Services specializes in the design, development, and manufacture of injectable drug delivery systems for the pharmaceutical, biotech, and generics industries. Our trusted devices are used daily in the delivery of various medications for a multitude of conditions across the globe.

Our Products

Our offering includes single- and multi-dose reusable and disposable auto-injectors, pens, and syringes for subcutaneous and intramuscular administration. These innovative products are designed to meet the needs of both our pharmaceutical partners and their patients through simplicity, ease of use, and improved safety and patient compliance. Our products are supported by our services, and we work with our partners every step of the way, supporting and guiding their combination product development all the way through to taking it to market.

UniSafe® Platform: With an established history of developing world-leading custom devices, we have now extended our capabilities to produce platform products, which includes our flagship UniSafe platform, a spring-free safety device for pre-filled syringes. For further information about UniSafe, please visit https://www.ompharmaservices.com/unisafe-platform/.

Aidaptus®: Our latest innovation is Aidaptus®, a platform disposable auto-injector offering next-generation benefits of flexibility and versatility. Aidaptus® is compatible with either a 1-mL or 2.25-mL prefilled syringe in the same base device, with only a minimal number of change parts, whilst maintaining its small, discreet size (162 mm x 18 mm). In addition, the novel self-adjusting plunger allows the use of a range of syringe fill volume options with no change to the device. For more information on Aidaptus and to explore its key benefits, please visit our Aidaptus virtual experience at https://www.ompharmaservices.com/explore-aidaptus/.

Aidaptus®

2-step single-use auto-injector platform

Versatile design

intuitive delivery

Fill Volume Flexibility

Aidaptus® readily adapts to a range of different drug fill volumes with no changed parts, using a self-adjusting plunger.

* In addition to an air bubble & overfill

No change parts required for fill volume changes

Want to know more?

Find out more about our new innovative Aidaptus® auto-injector by scanning the QR code or visiting **ompharmaservices.com/explore-aidaptus**

Available now

Owen Mumford

Pharmaceutical Services

OMPS/dd&d/ad/ob/1221/7

PACE LIFE SCIENCES – PEOPLE ADVANCING SCIENCE
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T: (651) 738-2728 W: www.pacelifesciences.com

Additional CDMO/CRO network site locations:
Boston, MA - Salem, NH - San Diego, CA
Norristown, PA - Ann Arbor, MI
South New Berlin, NY - San German, PR

PHARMACEUTICAL CMC DEVELOPMENT (CDMO)
PHARMACEUTICAL GMP LABORATORY TESTING (CRO)

SUPPORTING PHARMA-BIOLOGICS INNOVATION WORLDWIDE

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, Salem, NH, San Diego, CA, Philadelphia, PA, and Ann Arbor, MI, 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 and packaging services.

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:

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

Pharmaceutical Development

- Characterization of Novel Molecules & Biologics
- Solid State and API Characterization
- Formulation Development
  - Long-Acting injectables
  - Lyophilization
  - Hot-Melt Extrusion
  - Spray Drying
- Clinical Supplies Manufacture (Sterile & Non-Sterile capabilities)
  - Sterile Aqueous products
  - Ophthalmic
  - Tablets/Capsules
  - Solutions, Suspensions, Ointments, Creams Clinical Packaging
- Analytical Method Development

GMP Laboratory Testing

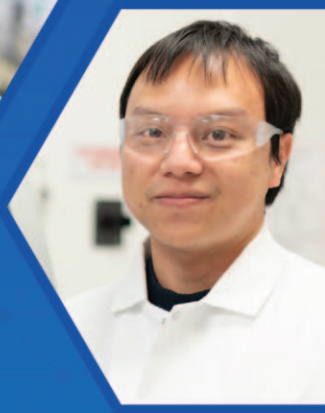
- Raw Materials Clearance Programs
- Methods Development & Validation
- In-process & Finished Product Testing
- ICH Stability Programs
- Reference Standards Programs
- Extractables/Leachables
- Elemental Impurities
- Physical-functional Testing
- Microbiology Testing Services
- Commercial Product Support

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
3001 Red Lion Rd. Philadelphia, PA 19114
T: USA (815) 484-8913 - T: UK/EU +44 1495 713 633
F: + 1 215 613 3601
LinkedIn: https://www.linkedin.com/company/pciservices/
E: talkfuture@pciservices.com - W: www.pci.com

PCI Pharma Services

PCI is as a leading global CDMO, providing clients with integrated end-to-end drug development, packaging and manufacturing capabilities that increase their products' speed to market and opportunities for commercial success. PCI brings the proven experience that comes with more than 50 successful product launches each year and over five decades in the healthcare services business. Leading technology and continued investment enable us to address global development needs throughout the product life cycle – from manufacturing capabilities in complex and high potent formulations, to Phase I clinical trials and commercialization. Our clients view us as an extension of their business and a collaborative partner, with the shared goal of improving patients' lives. For more information, please visit pci.com.

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

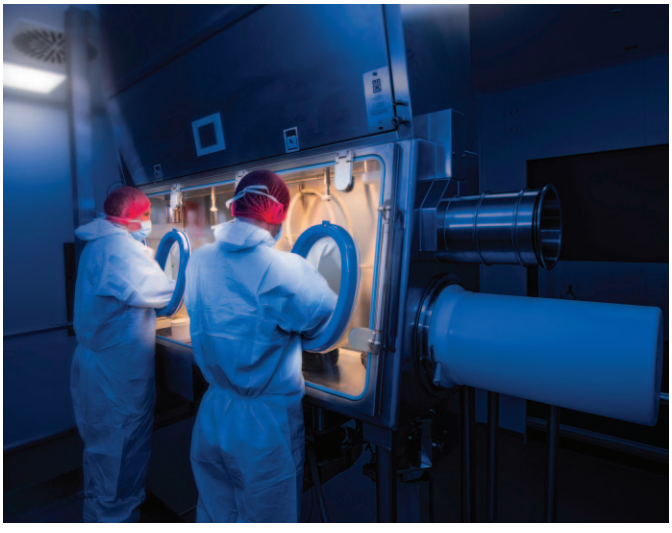
PCI offers full service Formulation Development including Analytical Development/Characterization and Xcelodose® product-in-capsule delivery for early phase clinical trials, as well as an extensive array of sterile and nonsterile delivery forms for early phase studies.

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.



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.

pci | DRUG DEVELOPMENT & MANUFACTURING

pci | CLINICAL TRIAL SERVICES

pci | COMMERCIAL PACKAGING TECHNOLOGY

www.pci.com

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PFIZER CENTREONE®
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W: www.pfizercentreone.com

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

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 U.S. under Pfizer quality standards:

- Steroids
- Hormones
- Antibiotics
- Prostaglandins

DELIVERING PFIZER EXPERTISE & EXCELLENCE THROUGH INTELLIGENT COLLABORATION

Pfizer CentreOne combines its scientific knowledge with open dialogue to solve challenges and help customers bring their innovations to market. For our customers, our collaborative approach means more efficient routes to market and high-quality APIs and drug products.

Pfizer CentreOne Development Services

We conquer complexity with imagination and intelligence. Our years of experience mean there are few challenges we haven't faced. We have problem-solving down to a fine art.

Collaborative. Creative. Considered.

We are backed by the scientific power and regulatory expertise of Pfizer:

- Over 90 new products in Pfizer's drug development pipeline
- More than 400 tech transfers in various stages a year
- Regulatory experience supporting 60+ countries

Draw upon the scientific power of Pfizer to shape your development masterpiece

Experience the art of science with Pfizer CentreOne

IMAGE

Two polymorphs of cholesteryl acetate recrystallised from the melt
Gary Nichols, Materials Characterisation, Sandwich, UK.

Pfizer CentreOne

www.pfizercentreone.com/art-of-science

PFANSTIEHL, INC.
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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

Keeping you connected to your target audience is now more important than ever.

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.

For more than 20 years, Drug Development & Delivery has successfully connected technology and service providers with R&D scientists, business development professionals and corporate managers working at pharmaceutical and biotechnology companies.

So, while we work through these challenging times, Drug Development & Delivery keeps you in front of your key audience.

Call us today or visit us at drug-dev.com and let us show you how

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PHARMACIRCLE™

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 8,000 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
- Epidemiology Data

To learn more about how PharmaCircle can help your company, please visit our website www.pharmacircle.com.

PHARMACIRCLE LLC
323 Sunny Isles Blvd., Suite 700
Sunny Isles Beach, FL 33160 USA
E: contact@pharmacircle.com T: 1-800-439-5130 www.pharmacircle.com

- 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

PHARMACEUTICS INTERNATIONAL, INC. (PII)
10819 Gilroy Road
Hunt Valley, MD 21031
T: (410) 584-0001
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

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:

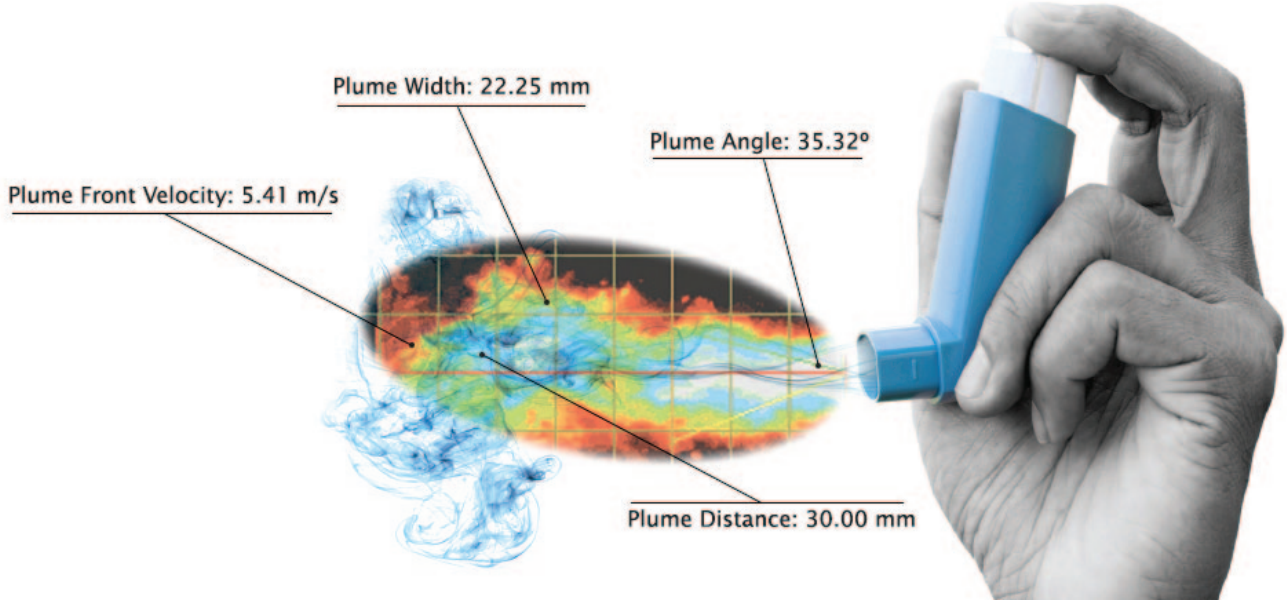
- accelerate successful product development and prevent late-stage development failures
- realize significant savings in time and resources by streamlining testing workflows
- evaluate the suitability of various OINDP delivery devices and optimize device parameters for maximum efficacy
- optimize testing 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

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RECIPHARM
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SE-101 32 Stockholm
T: + 46 8 602 52 00
E: info@recipharm.com - W: https://www.recipharm.com/

Recipharm is a leading contract development and manufacturing organisation (CDMO) in the pharmaceutical industry employing almost 9,000 employees. Recipharm offers manufacturing services of pharmaceuticals in various dosage forms, production of clinical trial material and APIs, pharmaceutical product development and development and manufacturing of medical devices. Recipharm manufactures several hundred different products for customers ranging from big pharma to smaller research and development companies. The company operates development and manufacturing facilities in France, Germany, India, Israel, Italy, Portugal, Spain, Sweden, the UK and the US and is headquartered in Stockholm, Sweden.

DRUG SUBSTANCE

Recipharm has more than 20 years' experience in drug substance development and manufacturing. We are able to deliver a wide range of drug substance services from our dedicated development facilities all around the world.

DRUG PRODUCT

At Recipharm, we offer drug product development services for all common dosage forms. Our team can manage the complexity of your project and help you to find the best solution, whether you are looking for development support to take your product to first-in-human (FIH) studies or to advance your product to market.

DRUG DELIVERY DEVICES

Together with Bespak by Recipharm, we deliver market leading design, development and manufacture of drug delivery devices to the global pharmaceutical market. This includes inhalers, nasal technologies and auto-injectors, as well as development and manufacturing services.

Recipharm has the competence, flexibility and facilities to take on challenging projects that require custom tailored processes. With a broad range of expertise and technologies available, we can offer our support and services, ranging from development and procurement to full-scale manufacturing. Covering a range of dosage forms, including: solids, semi-solids, liquids, inhalation, steriles and ophthalmics, Recipharm can provide integrated services tailored to meet your product.

Whether you are a big pharma company outsourcing a key stage of your production or a small to medium sized specialty firm seeking support in the development, transfer and production of a product; we're a reliable option.

By helping to manage the complexity of processes and projects, we reduce the risk for our clients.

Recipharm

Recipharm has the competence, flexibility and facilities to take on even the most challenging projects.

With a broad range of expertise and technologies available, Recipharm offers support and services ranging from development and procurement to full-scale manufacturing, distribution, tech-transfer, stability studies, and life cycle management.

Proven and responsible manufacturing capabilities for the global market. Find out more about our flexible capabilities at recipharm.com

OPHTHALMICS

STERILES

SEMI-SOLIDS

LIQUIDS

SOLIDS

INHALATION

SALUBRENT PHARMA SOLUTIONS
150 N Research Campus Dr., Suite 3700
Kannapolis, NC 28081
T: (704) 250-2110
W: https://salubrent.com/
Number of employees: 5
Date Founded: 11/2020

Salubrent is a technology-focused CDMO currently offering comprehensive analytical services to clinical and commercial stage pharma and biotech companies. Salubrent has assembled a quaity-driven team of industry veterans with more than 200 years of combined experience in the pharmaceutical, biotech and CDMO industries. This experience has been leveraged to establish the analytical services business in the North Carolina Research Campus in Kannapolis.

TECHNICAL SERVICES

- Stability testing for all clinical phases and commercial product
- HPLC method development & testing
- Gas chromatography
- Dissolution method & testing
- Particle size distribution evaluation
- Reference standard qualification & program management
- Drug substance & reference standard material characterization
- ELISA testing

FACILITIES

Salubrent operates in over 5,000 square feet of cGMP lab space located at the North Carolina Research Center in Kannapolis, NC.

MARKETS SERVED

Currently, Salubrent serves the US market

COMPREHENSIVE ANALYTICAL AND STABILITY SERVICES BACKED BY A GREATER OVER ALL CUSTOMER EXPERIENCE

Meet Salubrent, a company focused on *you* and the success of *your products*.
Our GMP-compliant laboratory is purpose-designed and outfitted to provide best-in-class analytical services. Our scientists are experts in the development of analytical methods for testing the safety, efficacy, and stability of your API or drug product. We also have the capacity to handle very large stability studies at a variety of temperatures, as well as the capability to perform special testing services that can be hard to find at other analytical labs. And most importantly, we're using the latest technologies to deliver a better customer experience—one that's more personalized and responsive to your needs. Contact us today to speak with one of our experts about your next project: **bd@salubrent.com**

Salubrent™
PHARMA SOLUTIONS

WWW.SALUBRENT.COM

SGS Health Science
E: Us.pharmaqc@sgs.com
W: https://sgs.com/healthscience

Locations

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+1 973 244 2435

Lincolnshire, IL
+1 847 821 8900

West Chester, PA
+1 610 696 8210

Mississauga, Ontario
+1 905 364 3757

Markham, Ontario
+1 905 305 0998

SGS offers high quality analytical testing for pharmaceutical and biopharmaceutical products through all phases of drug development – from discovery through early development and commercialization. With five conveniently located North American locations that offer a wide range of testing capabilities, SGS can help you ensure product and patient safety, as well as compliance with current regulations.

COMPANY OVERVIEW

SGS Health Science 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

- Quality control testing of raw materials, APIs, and finished products
- Nitrosamine testing
- 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

Health Science

Health Inspired, Quality Driven.

Get to market quickly, safely & efficiently

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

Services include:

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

Learn more:

healthscience@sgs.com sgs.com/healthscience sgs.com/healthcommunity

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WHEN YOU NEED TO BE SURE

SGS

SINGOTA SOLUTIONS
4320 W. Zenith Drive
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

Founded in 1949, Stevanato Group is a leading global provider of drug containment, drug delivery and diagnostic solutions to the pharmaceutical, biotechnology and life sciences industries. The Group delivers an integrated, end-to-end portfolio of products, processes and services that address customer needs across the entire drug life cycle at each of the development, clinical and commercial stages. Stevanato Group's core capabilities in scientific research and development, its commitment to technical innovation and its engineering excellence are central to its ability to offer value added solutions to clients.

Global Presence, Local Capabilities

Today, Stevanato Group counts over 4,300 people in 16 sites in 9 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 Drug Container Solutions & 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 enhancing the integrity of medicines

Stevanato Group

stevanatogroup.com

TERUMO PHARMACEUTICAL SOLUTIONS

Terumo Pharmaceutical Solutions develops patient-oriented parenteral delivery solutions for therapeutic performance and safety

Globally trusted for quality and precision, Terumo Pharmaceutical Solutions offers pharmaceutical and medical device manufacturers around the world comprehensive product design and development services as well as a portfolio of injection, infusion, and primary packaging solutions.

With decades of experience collaborating with pharmaceutical companies from the earliest phases of drug development to the latest stages of product commercialization, we help optimize critical aspects of parenteral drug delivery.

Comprehensive parenteral delivery product portfolio

Our broad portfolio of injection, infusion, and primary packaging solutions offer innovative drug delivery technologies ready for today's most demanding applications.

Injection

Pioneering hypodermic needle innovation designed for patient comfort. Terumo offers a comprehensive range of precision-engineered needle and needle stick prevention technologies for most applications.

Infusion

More confident, comfortable infusions. Integrating the best of Terumo Pharmaceutical Solutions' needle technology with interlocking color-coded wings, our Surflo™ Winged Infusion sets with (Filter) and Needle Protection offer an improved overall experience for both patients and caregivers.

Primary packaging

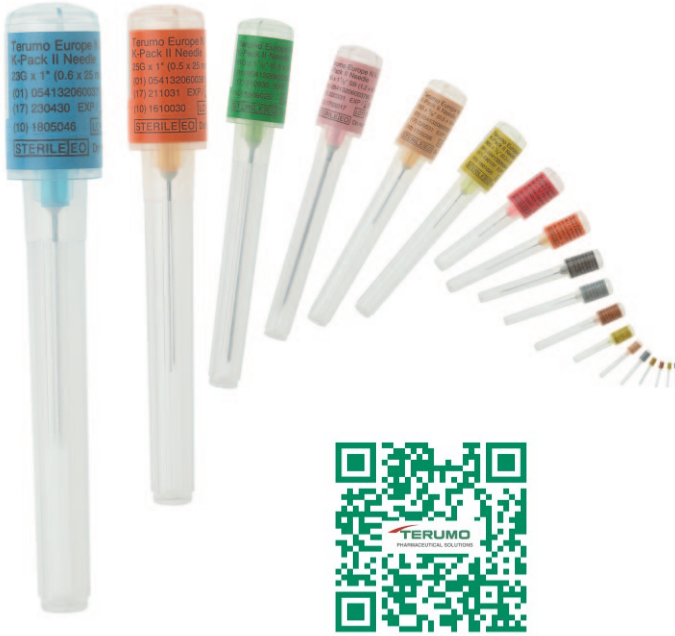
Ready to fill polymer syringes, ready for breakthrough formulations and demanding fill & finish processing environments. Terumo PLAJEX™ primary packaging solutions offer the functionality and compatibility to deliver today's most challenging biologics and parenteral drug products.

TERUMO PHARMACEUTICAL SOLUTIONS
T: +32 16 38 12 11
E: Info@terumo-ps.com
W: www.terumopharmaceuticalsolutions.com

Terumo Pharmaceutical Solutions is part of the Terumo Group. Based in Tokyo, Japan, and a global healthcare technology leader since 1921, Terumo (TSE:4543) employs over 25,000 associates across key international markets, delivering a full portfolio of medical and parenteral delivery solutions to more than 160 countries worldwide.

In keeping with our founding principles and 100 years of innovation, Terumo Pharmaceutical Solutions remains dedicated to delivering outstanding technology.

We listen. We question. We deliver.



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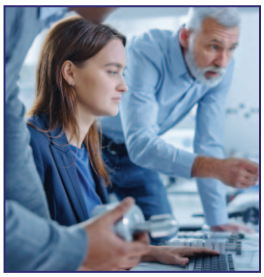




YOUR PARTNER IN ASEPTIC FILLING AND PACKAGING

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 and Rankweil, Austria
- Sales offices for Asia Pacific in Singapore, Japan, South Korea and China
- Approximately 5,500 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.**

Primary Packaging & Closure Solutions

With the global rise of chronic diseases and the COVID19 outbreak, increasingly complex drug products are being tested and launched on the market. Choosing the right primary packaging and closure solution is essential to facilitating regulatory approval and fast time-to-market. Building on 70 years' experience in the development and manufacturing of drug packaging solutions, **Aptar Pharma** offers end-to-end services, accelerating and de-risking the choice of closure component. Our PremiumCoat® Service packages address key customer challenges at different stages of their drug development. Leveraging our state-of-the-art PremiumCoat® technology, internal capabilities, expertise, and knowledge of the drug development journey, Aptar Pharma offers three packages to support the validation of PremiumCoat® with your glass container (Platform Package) or your specific drug (E&L Package). The Development Package accompanies our customers through their validation process, to ensure their success. For more information, visit Aptar Pharma at **www.aptar.com/pharmaceutical/.**

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 90 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, powder-filled vials and sterile crystallization. For more information, visit Baxter BioPharma Solutions at **www.biopharmasolutions.baxter.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.**

cGMP CDMO

Bora Pharmaceuticals is a premier international cGMP CDMO specializing in complex oral solid dosage (tablet & capsules), liquids (solutions, suspensions, & nasal sprays), and semi-solids (creams & gels) pharmaceutical Rx and OTC products for late-phase Clinical through Commercial manufacturing and packaging. Bora owns and operates three state-of-the-art cGMP manufacturing facilities (Taiwan and Canada) built to the highest international standards for manufacturing, packaging, R&D, and analytical testing. We can handle high potency compounds, solvents, flammables, and IR/SR/ER release profile products. Our sites deliver to more than 100 markets around the world, including the US/Canada, EU, Southeast Asia, Middle East, and South and Central Americas. All sites are TAA compliant. Our packaging lines are fully serialized. Our sites have over a 98% on-time delivery record! For more information, visit Bora Pharmaceuticals at **www.boracorpcdmo.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.**

Oral Dose Design & Development

Catalent is the global leader in drug development and delivery, and offers partners end-to-end solutions in formulation, development, and dose design. Its tools, experience, and expertise ensure the right decisions are made at each stage of development, creating oral dose forms that can improve a drug's clinical efficacy and commercial success: including softgels, fast-dissolving tablets, modified-release capsules, and stick packs. Catalent's Better Treatments by Design™ service aims to combine the needs of innovators, prescribers, and patients to create superior products. Using the widest array of drug delivery technologies to overcome each product's unique challenges and requirements, solutions can be matched to molecules to maximize the potential of a drug, from Phase 2 through to commercial supply. For more information, contact Catalent Pharma Solutions at (888) SOLUTION or visit **www.catalent.com**.

Drug Delivery Platform

Celanese

The chemistry inside innovation™

Celanese Corporation is a global chemical leader in the production of differentiated chemistry solutions and specialty materials used in most major industries and consumer applications. Our VitalDose® EVA drug delivery platform offers the flexibility for formulators to design patient-centric dosage forms for effective long-acting, controlled release of both small and macro molecules. We work closely with you as a strategic partner from concept to commercialization providing development services, material supply aligned with GMP principles, and regulatory support. For more information, visit **healthcare.celanese.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.**

CDMO

curia

Introducing Curia! Discover the end-to-end expertise of the CDMO formerly known as AMRI. What happens when the science of impact meets the art of possibility? A new era begins. The journey to breakthrough medicine is never simple. But the right CDMO partner can ease your path with scientific excellence, relentless curiosity, and expert, reliable delivery. For decades, Curia — formerly AMRI — has accelerated our partners' work, from research and development through commercial manufacturing. Together, we can turn life-changing potential into life-changing progress. For more information, visit Curia at **curiaglobal.com/curiosity.**

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.**

Perfecting Your Formula

emergent CDMO

Emergent is dedicated to helping pharma and biotech innovators bring lifesaving therapies to patients from around the world. Our nine development and manufacturing sites in North America and Europe can support early to late stage production of biotherapeutics and vaccines. Whether you're looking for initial process development support, small volumes of material for clinical trials, or large-scale production for a global commercial therapy, our experienced CDMO team is ready to serve as your trusted guide from molecule to market. We support a broad portfolio of preclinical through commercial programs with experience in a wide range of platforms and technologies including mammalian, microbial, viral, plasma, and gene therapies. For more information, visit Emergent CDMO at **www.emergentcdmo.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.**

Eurofins Testing

Eurofins BioPharma Product Testing is a global leader in bio/pharmaceutical laboratory services, providing complete CMC Testing Services for the Bio/Pharmaceutical industry, including all starting materials, process intermediates, drug substances, drug product, packaging, and manufacturing support through our broad technical expertise in Biochemistry, Molecular & Cell Biology, Virology, Chemistry and Microbiology. With 60 years of analytical expertise, Eurofins BioPharma Product Testing's Lancaster site has vast experience working with virtually every type of molecule, formulation, therapeutic area and comparator product to support the needs of more than 1,000 biopharmaceutical companies from virtual to large pharma and biopharma. For more information, visit Eurofins BioPharma Product Testing at **www.Eurofins.com/BPT.**

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.**

Hands-On Formulation Support

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 stand to assist with your projects at all stages of development, from solubility screening 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.**

Lentiviral & Retroviral Vectors

We're specialists in lentiviral and retroviral vectors, accelerating your therapy to commercialization and helping you deliver life-changing therapeutics to patients. Whether you have a defined process or need guidance to identify the best path forward, our experts have the flexibility to support you wherever you are in your journey. **Genezen** offers contract process development, GMP viral vector production, transduced cell manufacturing, testing services and assay development. Keeping growth front of mind, we tailor our solutions to your needs and ensure your therapy progresses as quickly and safely as possible. Our new state-of-the-art, cGMP-compliant facility has recently opened in the fast-growing life sciences hub of Indianapolis, providing our partners with the capacity and technologies for the aseptic manufacture of lentiviral and retroviral vectors. For more information, visit Genezen at **https://genezen.com/.**

On-Body Drug Delivery

SensAIR is a platform for on-body drug delivery that can deliver drugs of higher viscosity, such as monoclonal antibodies. The aim is to provide patients with the best possible support in the subcutaneous delivery of large-volume biologics. The ready-to-use SensAIR On-Body Delivery Device is easy to use and enables patients to start medication in a self-determined manner in familiar surroundings. The SensAIR On-Body Delivery Device can be adapted to medications of different viscosities and with different requirements. This applies to the size of the medical device as well as to the needle used, variable cartridge sizes and possible connectivity, for example to the patient's smartphone. Together with Gerresheimer's One-Stop-Shop quality promise, which includes a solution from the cartridge to the drug delivery device from a single source, SensAIR enables optimized delivery of biologics. For more information, visit Gerresheimer at **www.gerresheimer.com.**

High-Quality Self-Injection Systems

HASELMEIER™
A medmix Brand

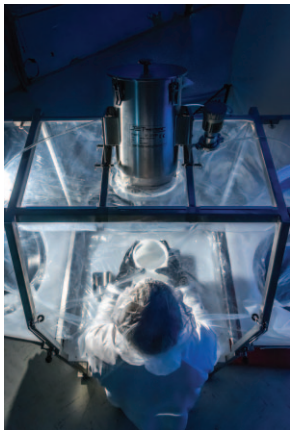
Experts in subcutaneous drug delivery systems for self-administration, Haselmeier provides innovative and award-winning individual system solutions to support patients for a successful therapy. Representing the Drug Delivery segment of medmix, Haselmeier covers all steps – from design to planning to industrialization – in the creation of high-quality self-injection systems. In 2020, this well-established company was 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 Oral Dosage Forms

HERMES PHARMA
Get the dose right®

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 the newly developed HERMES NutriCaps. As a CDMO, we offer customized services along the entire pharmaceutical 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 worked with HERMES PHARMA to extend their pharmaceutical and nutraceutical product lines as well as to grow their brands. Our sister company HERMES ARZNEIMITTEL has a rich portfolio of successful OTC brands and a history of more than a hundred years in pharmaceutical excellence. This heritage makes HERMES PHARMA a reliable and experienced partner who truly understands the challenges of its customers. For more information, visit HERMES PHARMA at **www.hermes-pharma.com.**

Atmospheric Control Module



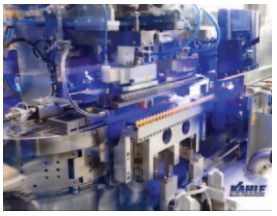
JetVent™, ILC Dover's atmospheric control module, provides safe, automatic, and pressurized containment for higher-potency active pharmaceutical ingredients (HPAPIs) within manufacturing-area isolators, lab areas, and for GMP chambers where airflow, temperature, humidity, and pressure differentials exist 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.**

Integrated Products & Services

JUBILANT PHARMA

Jubilant Pharma Limited (JPL), a company incorporated under the laws of Singapore and a wholly owned subsidiary of Jubilant Pharmova Limited, is an integrated global pharmaceutical company engaged in manufacturing and supply of Radiopharmaceuticals, Allergy Therapy Products, Contract Manufacturing of Sterile Injectables and Non Sterile products, APIs, and Generics, through six US FDA- approved manufacturing facilities in the US, Canada, and India and a network of 49 radiopharmacies in the US. The company has a team of around 5,200 multicultural people across the globe. It is well recognized as a Partner of Choice by leading pharmaceutical companies globally. For more information, visit Jubilant Pharma at **www.jubilantpharma.com.**

Medical Manufacturing



Kahle Automation idesigns and builds machines for the assembly and inspection of all types of medical devices and drug delivery products. Kahle's services include custom equipment design, system integration, parts feeding, material and package handling, and equipment validation, along with the documentation to meet the unique requirements of all types of manufacturing applications. Kahle' staff is dedicated to designing solutions for only one industry, allowing us the opportunity to develop the expertise required to build turnkey production systems with a complete understanding of the challenges that face the Medical Manufacturing community. For more information, visit Kahle Automation at **www.KahleAutomation.com.**

Device Development Services

Neuma by **Kymanox** is an engineering services company focused on the development of robust, verifiable, reliable, and manufacturable drug delivery devices. Neuma turns developing and innovative drug delivery technologies into commercially successful devices. Neuma has extensive experience with novel, custom, and platform device adaptations across prefillable syringes, autoinjectors, reconstitution devices, and wearable injectors. Neuma provides Design for Production (DFP) services, addressing the Design for Testing, Design for Sterilization, Design for Manufacturability, and Design for Assembly requirements that are often overlooked or neglected in the development process. Neuma's device experts are ready to transform your technology into a medical solution. For more information, visit Kymanox at neumaengineering.com and **www.kymanox.com**.

Innovative Polymers & Excipients

LUBRIZOL LIFE SCIENCE

The Health business of **Lubrizol Life Science (LLS Health),** in partnership with customers, advances solutions inspiring a healthier life. We specialize in helping clients from idea to execution by offering innovative polymers and excipients, as well as best-in-class contract development and manufacturing services. Our long history of polymer expertise and continued investment in research and manufacturing means we offer you and your customers a smooth and streamlined approach to innovative healthcare solutions. For more information, visit LLS Health at **www.Lubrizol.com/Health.**

Lyophilization Services & Solutions

Lyophilization TECHNOLOGY Inc.

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.

Combination Device Testing

MEDICAL ENGINEERING TECHNOLOGIES
GLOBAL EXCELLENCE IN DEVICE TESTING

Getting your delivery device approved by regulators is important, right? Then come to **Medical Engineering Technologies** for your validation and stability testing. We only test medical devices, and we know about medical devices. We will understand your needs and efficiently deliver testing and advice from the start of your project right through to your submission. Services include: biocompatibility and chemical characterization, dose delivery accuracy, e and l studies, formulation stability, mechanical performance, RLD comparisons, sterile barrier verification, human factors studies, and lots of good advice. We will make sure that your project moves rapidly forward. For more information, visit Medical Engineering Technologies at **www.met.uk.com.**

The Right Equipment for Your Project

metrics contract services

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.**

Improved Formulation

Micropore Technologies

From lab experiments through to aseptic/cGMP manufacturing, Micropore's award-winning membrane-based, formulation equipment offers the precision of microfluidics (CV of less than 10%) and a more efficient output than homogenization for microsphere, nanoparticle, and emulsion production. The low-shear processing prevents damage to protein-based therapies and other sensitive active ingredients in controlled-release, sterile injectable drug products and allows the replacement of undesirable emulsifying agents. Suitable for PLGA, PLA, PCL encapsulation and simplified liposome and lipid nanoparticle construction, the technology delivers higher product yields through less wastage and reduced degradation. We offer early stage formulation development; cGMP process consultation, and scale-up from lab to commercial; preclinical small batch production; particle sizing, shape, and encapsulation efficiency analysis; tech transfer of production hardware; and global technical support and troubleshooting. For more information, visit **www.micropore.co.uk/.**

Life-Saving Therapies

MilliporeSigma is a leading science and technology company in healthcare, life science, and performance materials. MilliporeSigma offers more than 400 pharmaceutical formulation raw materials for solid, liquid, and semi-solid dosage forms, a wide range of active pharmaceutical ingredients and drug delivery compounds that include activated PEGs, lipids, and PEG lipids for bioavailability enhancement. In addition, MilliporeSigma provides extensive documentation and support to ensure regulatory compliance and to help advance the promise of life-saving therapies. For more information, visit MilliporeSigma at **www.embmillipore.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

As a world-leading drug delivery device solutions provider, **Nemera's** goal of putting patients first enables it to design and manufacture devices that maximize treatment efficacy. Nemera is a holistic partner and helps its customers succeed in the sprint to market with its combination products. From early device strategy to state-of-the-art manufacturing, Nemera is committed to the highest quality standards. Agile and open-minded, the company works with its customers as colleagues. Together, they go the extra mile to fulfil its mission. For more information, visit Nemera at **www.nemera.net.**

Injectable Drug Delivery

Owen Mumford Pharmaceutical Services is a specialist in the design, development, and manufacture of injectable drug delivery systems for the pharmaceutical, biotech, and generics industries. These include single-dose and multi-dose reusable and disposable auto-injectors, pens, and syringes for subcutaneous and intramuscular administration. Our innovative products are designed to meet both the need of our pharmaceutical partners and their patients by facilitating ease of use and improving safety and patient compliance. Our devices are also designed with the aim of reducing complexity and risk for the pharmaceutical and biotech industry in the development of their combination products. Our products are supported by our services, and we work with our partners every step of the way, supporting and guiding from initial concept stage through to taking the solution to market. For more information, visit Owen Mumford Pharmaceutical Services at **www.ompharmaservices.com.**

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

Integrated CDMO Services

Recipharm is a leading contract development and manufacturing organiZation (CDMO) with the competence, flexibility, and facilities to take on challenging projects that require custom tailored processes. With a broad range of expertise and technologies available, we can offer our support and services, ranging from development and procurement to full-scale manufacturing. Covering a range of dosage forms, including: solids, semi-solids, liquids, inhalation, steriles, and ophthalmics, Recipharm can provide integrated services tailored to meet your product. Whether you are a big pharma company outsourcing a key stage of your production or a small to medium-sized specialty firm seeking support in the development, transfer, and production of a product; we're a reliable option. For more information, visit Recipharm at **www.recipharm.com.**

Technology-Focused CDMO

Founded in 2020 by industry veterans from the Pharma and Biotech industries, **Salubrent** is building a specialized CDMO focused exclusively on flexible batch, aseptic fill & finish drug delivery solutions. Salubrent is a technology-focused CDMO currently offering comprehensive analytical services to clinical- and commercial-stage pharma and biotech companies. Salubrent has assembled a quaity-driven team of industry veterans with more than 200 years of combined experience in the pharmaceutical, biotech- and CDMO industries. This experience has been leveraged to establish the analytical services business in the North Carolina Research Campus in Kannapolis. For more information, visit Salubrent at **https://salubrent.com/.**

Contract Service Organization

SGS Health Science is a leading contract service organization providing analytical development, biologics characterization, biosafety and quality control testing. With a wholly-owned network of 22 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 Health Science at healthscience@sgs.com or visit **www.sgs.com/healthscience.**

Agile CDMO

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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.**

Parenteral Delivery Solutions

Terumo Pharmaceutical Solutions develops patient-oriented parenteral delivery solutions for therapeutic performance and safety. Globally trusted for quality and precision, Terumo offers pharmaceutical and medical device manufacturers around the world comprehensive product design and development services as well as a portfolio of injection, infusion, and primary packaging solutions. Decades of experience collaborating with pharmaceutical companies from the earliest phases of drug development to the latest stages of product commercialization to optimize critical aspects of parenteral drug delivery. Our comprehensive parenteral delivery product portfolio of injection, infusion, and primary packaging solutions offer innovative drug delivery technologies ready for today's most demanding applications. For more information, visit Terumo Pharmaceutical Solutions at **www.terumopharmaceuticalsolutions.com.**

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Nov/Dec 2021 Advertiser Index

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