Drug Development & Delivery

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Company Profiles & Capabilities

The science & business of drug development in specialty pharma, biotechnology, and drug delivery

IN THIS ISSUE

INTERVIEW WITH
BD MEDICAL – PHARMACEUTICAL SYSTEMS' DIRECTOR, TECHNICAL SERVICES GROUP
THERESA BANKSTON, PHD

THE DIFFERENCE OF ONE DRUG DELIVERED

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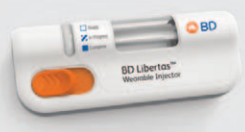

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Importance of Cell Cycle & Cellular Senescence in the Placenta Discovered

Working with researchers from Stanford University and St. Anna Children's Cancer Research, researchers from Jürgen Pollheimer's laboratory at the Medical University of Vienna's Department of Obstetrics and Gynecology have now, for the first time, identified basic relationships of the cell cycle and cellular senescence in the human placenta.

The main finding of the study: During pregnancy, the cycle of cell division of placental trophoblasts stops after duplication of the whole genome to prevent uncontrolled growth. "Genome duplication acts like an automatic stop sign," explains study author Philipp Velicky, who conducted the study at MedUni Vienna and is currently working at IST Austria (Institute of Science and Technology – Austria).

"We were therefore able to demonstrate for the first time that trophoblasts duplicate their entire genome during their development, thus becoming polyploid, and then go into a sort of cellular retirement, known as senescence, to protect themselves. They stop dividing but continue to send out certain messenger substances,"explains molecular biologist Velicky.

At the same time, the results of the study indicate that cellular senescence is an important mechanism for preventing uncontrolled trophoblastic cell division and proliferation. The study also enabled researchers to establish that this important control mechanism is absent in so-called anembryonic pregnancies. Gestational trophoblastic disease affects approximately one in every 1,000 women worldwide. An empty egg is fertilized in the uterus so that, even though a placenta develops, no embryo is formed. Nor do the other processes of a normal pregnancy start. This means that there is no natural molecular "stop sign.""

The result: the placenta proliferates wildly; the trophoblasts don't age. Instead they rapidly become polyploid, carry hundreds of copies of their genome and divide in a completely uncontrolled manner. The system gets into a complete muddle and affected women subsequently have a significantly higher risk of developing particularly aggressive chorionic carcinoma (a highly malignant tumor of the trophoblastic tissue). The tumor tends toward rapid metastasis.

The better understanding of cells and their functions in the placenta could lead to the development of a therapeutic response to over-proliferating cells in future and also provides a better general understanding of carcinogenic processes and how to prevent them.

Medical University Vienna (MedUni Vienna) is one of the most traditional medical education and research facilities in Europe. With around 8,000 students, it is currently the largest medical training center in the German-speaking countries. With 5,500 employees, 26 university hospitals and three clinical institutes, 12 medical theory centers and numerous highly specialized laboratories, it is also one of Europe's leading research establishments in the biomedical sector.

Athenex Announces FDA Allowance of Investigational New Drug Application

Athenex, Inc. recently announced the FDA has allowed the Investigational New Drug (IND) application for Athenex's oral version of Eribulin currently named Eribulin ORA.

This FDA action allows Athenex to commence its clinical trial program, currently planned for first half of 2019. Eribulin, an effective treatment for metastatic breast cancer and liposarcoma, is currently limited to intravenous administration.

Utilizing Athenex's proprietary Orascovery platform with Eribulin, we were able to demonstrate that good oral absorption of Eribulin is possible, based on preclinical studies. In addition, the Eribulin active pharmaceutical ingredient (API) has been developed internally using a novel synthetic approach. We believe these developments demonstrate the broad utility of the Orascovery platform and commitment of Athenex to becoming a major global oncology biopharmaceutical company.

Dr. Michael Smolinski, Athenex's Head of Preclinical Research, said "Athenex is delighted that the FDA has allowed the IND of Eribulin ORA. The demonstration of a favorable pharmacokinetic profile, with lowered peak plasma concentration and longer duration of the drug within the desired plasma concentration range, provides the potential for a better efficacy and an improved safety profile for Eribulin, similar to what we have observed with Oraxol (oral form of paclitaxel) and others. We have also developed a novel and efficient synthetic process for Eribulin with an excellent purity profile. This is the eighth US IND allowance that Athenex has obtained, reflecting the passion and dedication of the company to bringing new therapies to cancer patients."

Eribulin is an anticancer drug marketed by Eisai Company under the trade name Halaven. It is used to treat certain patients with breast cancer and liposarcoma. Eribulin is a synthetic derivative of the natural product Halichondrin B. The potent anticancer effects of this agent come primarily from its unique means of targeting microtubule dynamics, a process critical to cell proliferation.

Dr. Rudolf Kwan, Athenex's Chief Medical Officer, said "Eribulin is approved for the treatment of metastatic breast cancer patients who have received at least two prior chemotherapy regimens for late-stage disease, including both anthracycline- and taxane-based chemotherapies. It is important to note that Eribulin is active in paclitaxel-resistant tumors. This profile is expected to create a number of synergistic opportunities with the other drug candidates in our Orascovery clinical pipeline. We look forward to initiating the Phase I clinical studies soon."

The lead compound in Athenex's Orascovery program, Oraxol, is currently in a pivotal Phase III study. The Orascovery platform was developed by Hanmi Pharmaceuticals and licensed exclusively to Athenex for all major worldwide territories except Korea, which is retained by Hanmi.

Founded in 2003, Athenex, Inc. is a global clinical stage biopharmaceutical company dedicated to becoming a leader in the discovery and development of next generation drugs for the treatment of cancer. Athenex is organized around three platforms, including an Oncology Innovation Platform, a Commercial Platform and a Global Supply Chain Platform.

The company's current clinical pipeline is derived from four different platform technologies: (1) Orascovery, based on non-absorbed P-glycoprotein inhibitor, (2) Src kinase inhibition, (3) T-cell receptor-engineered T-cells (TCR-T), and (4) Arginine deprivation therapy. Athenex's employees worldwide are dedicated to improving the lives of cancer patients by creating more active and tolerable treatments. Athenex has offices in Buffalo and Clarence, NY; Cranford, NJ; Houston, TX; Chicago, IL; Hong Kong; Taipei, Taiwan and multiple locations in Chongqing, China. For more information, visit www.athenex.com.

Wave Life Sciences to Develop Programs in Rare, Genetic Eye Diseases

Wave Life Sciences Ltd. recently announced plans to design and advance stereopure oligonucleotide therapeutics for the potential treatment of rare, inherited eye diseases.

Wave's research in ophthalmology will initially focus on the following four inherited retinal diseases which commonly lead to progressive vision loss typically starting in childhood or adolescence: retinitis pigmentosa due to a P23H mutation in the RHO gene, Stargardt disease, Usher syndrome type 2A and Leber congenital amaurosis 10. The company expects to announce its first ophthalmology development candidate in the second half of 2019.

"We have long believed that oligonucleotides have the potential to be particularly effective and durable in the eye and are energized by our latest research that provides additional validation of our precisely designed stereopure oligonucleotides," said Paul Bolno, MD, MBA, President and Chief Executive Officer of Wave Life Sciences. "Our aim is to move quickly to develop long-acting, intravitreally injected, disease-modifying therapies to address the enormous need across a spectrum of rare, genetically defined eye diseases."

Wave's decision to expand its therapeutic pipeline into ophthalmology is supported by its data presented at the 14th Annual Meeting of the Oligonucleotide Therapeutics Society on October 1, 2018, in Seattle, WA. The data demonstrate that a single intravitreal injection of stereopure oligonucleotide in the eye of non-human primates resulted in greater than 95% knockdown of a target RNA in the retina for at least four months. Based on these data, the company is working to design development candidates that could achieve a therapeutic effect with only two doses per year.

Inherited retinal dystrophies are a wide range of heterogeneous, rare eye disorders characterized by progressive loss of vision and/or eventual blindness caused by inherited genetic mutations. These conditions affect approximately 200,000 people in the US.

There are currently no cures or treatments for this category of diseases, except for one approved disease-modifying therapeutic in the US for patients with biallelic RPE65 mutation-associated retinal dystrophy.

Wave's research will assess four genetic targets, RHO P23H, USH2A, ABCA4 and CEP290 to address four rare, inherited retinal diseases. The company estimates that approximately 10,000 U.S. patients could potentially be treated by

Wave Life Sciences is a biotechnology company focused on delivering transformational therapies for patients with serious, genetically defined diseases. Its chemistry platform enables the creation of highly specific, well-characterized oligonucleotides designed to deliver superior efficacy and safety across multiple therapeutic modalities. The company's pipeline is initially focused on neurological disorders and extends across several other therapeutic areas. For more information, visit www.wavelifesciences.com

Acer Therapeutics Submits NDA for EDSIVO; Requests Priority Review

Acer Therapeutics Inc. recently announced it has submitted a New Drug Application (NDA) to the US FDA for EDSIVO for the treatment of vascular Ehlers-Danlos syndrome (vEDS). Pursuant to the Prescription Drug User Fee Act (PDUFA), the FDA has 60 days to determine whether to accept the submission for review. Along with the NDA submission, Acer has requested Priority Review, which if granted, could result in a six-month review period. Priority Review is a designation given to drugs that offer a significant improvement in treatment or provide treatment where no satisfactory alternative therapy exists.

"Our NDA submission represents the culmination of extensive efforts of our employees, investigators, clinical trial sites, contract research organizations, caregivers, and patients," said William Andrews, MD, FACP, Chief Medical Officer of Acer. "We now look forward to continuing to work with the FDA as they review our NDA, with hopes to make EDSIVO available as quickly as possible in the US. We are grateful to the vEDS patient and advocacy community for their continued involvement, support and feedback as we work together to advance EDSIVO™, which has the potential to be a significant step forward in the care of patients with this devastating disease."

Ehlers-Danlos Syndrome (EDS) is a group of hereditary disorders of connective tissue. vEDS is the most severe subtype where patients suffer from life threatening arterial dissections and ruptures, as well as intestinal and uterine ruptures. The average mortality is 51 years of age. An Acer-commissioned patient-finder study phenotypically identified 4,169 vEDS patients in the US from an analysis of a commercially available patient claims database with data of approximately 190 million unique patient lives.

Based on that information, Acer estimates the prevalence of phenotypically defined vEDS in the US could be greater than 1 in 45,000. Currently, there are no FDA-approved therapies for vEDS. Acer is advancing EDSIVO (celiprolol), a new chemical entity (NCE), for the treatment of vEDS based on a randomized controlled clinical study of celiprolol and submitted an NDA to the FDA in October 2018. Acer requested priority review for EDSIVO which, if granted at the time of potential acceptance of NDA for filing, could result in a Prescription Drug User Free Act (PDUFA) action date of late second quarter 2019. EDSIVO received FDA Orphan Drug Designation for the potential treatment of vEDS in 2015.

Acer, headquartered in Newton, MA, is a pharmaceutical company focused on the acquisition, development and commercialization of therapies for patients with serious rare and ultra-rare diseases with critical unmet medical need. Acer's late-stage clinical pipeline includes two candidates for severe genetic disorders: EDSIVO (celiprolol) for vascular Ehlers-Danlos syndrome (vEDS), and ACER-001 (a fully taste-masked, immediate release formulation of sodium phenylbutyrate) for urea cycle disorders (UCD) and Maple Syrup Urine Disease (MSUD). There are no FDA-approved drugs for vEDS and MSUD and limited options for UCD, which collectively impact approximately 7,000 patients in the US.

Amicus Therapeutics Enters Research & Development Collaboration

Amicus Therapeutics recently announced a major collaboration with the Gene Therapy Program in the Perelman School of Medicine at the University of Pennsylvania (Penn) to pursue research and development of novel gene therapies for Pompe disease, Fabry disease, CDKL5 deficiency and one additional undisclosed rare metabolic disorder. This relationship will combine Amicus' protein engineering and glycobiology expertise with Penn's adeno associated virus (AAV) gene transfer technologies to develop AAV gene therapies designed for optimal cellular uptake, targeting, dosing, safety and manufacturability.

"This groundbreaking collaboration with Penn offers a new opportunity to potentially transform the lives of people living with these severe genetic disorders," said John F. Crowley, Chairman and Chief Executive Officer of Amicus. "For people living with Fabry, it is a fulfillment of our pledge to advance science toward a cure for Fabry disease. We are partners now with the Fabry community for life. For Pompe, this is another important step on a lifelong journey toward the ultimate answer to finally cure Pompe. If we are to do so, we must have a gene therapy that addresses the many technical challenges in Pompe disease and that employs state of the art science in both protein and gene therapy engineering. For CDKL5 and other rare metabolic disorders, this collaboration is the foundation for advancing new therapies for these devastating genetic disorders."

Penn's AAV vector technology is designed to improve targeting, tropism, safety, immunogenicity, and gene delivery, while Amicus' protein engineering capabilities may optimize protein expression, secretion, targeting and uptake of the target protein. The agreement between Amicus and Penn is a Research, Collaboration and License Agreement, with funding provided to Penn to advance the preclinical research programs in the Wilson Lab and to license certain technologies invented under the funded Research Collaboration. The collaboration program will focus on developing innovative new AAV gene therapies for Pompe disease, Fabry disease, CDKL5 deficiency and one additional undisclosed rare metabolic disorder.

"Amicus has developed unique abilities in drug development in the lysosomal storage disorders, particularly in Pompe and Fabry diseases," said James M. Wilson, MD PhD, Professor of Medicine and Pediatrics at the Perelman School of Medicine. "There are multiple and unique challenges in developing optimal gene therapy products for patients living with Pompe and Fabry diseases. I believe that we can combine the technologies and capabilities from my research laboratory at Penn with the Amicus expertise in protein engineering, glycobiology and disease biology understanding to rapidly advance novel gene therapies to the clinic. Because of their unique capabilities and their commitment to great science and to patients, we are excited about our new partnership with Amicus to develop AAV gene therapies for patients with urgent unmet needs."

Principia Achieves $10 Million in Additional Milestones

Principia Biopharma Inc. recently announced the achievement of $10 million in additional milestones related to successful development activities conducted by Principia as part of the clinical development of PRN2246. PRN2246, also known as SAR442168, is a Bruton's tyrosine kinase (BTK) inhibitor that crosses the human blood-brain barrier and modulates immune cell function in the brain for the potential treatment of central nervous system (CNS) diseases. PRN2246 is being developed under a collaboration agreement with Sanofi, a company committed to discovering and developing new treatment options for people living with multiple sclerosis (MS).

"Principia is pleased that, with the achievement of these additional milestones, we have now earned, in the aggregate, $25 million in milestones in 2018 related to our successful development efforts for PRN2246," said Martin Babler, Chief Executive Officer of Principia. "We intend to present the results of our Phase 1 clinical trial at a future scientific conference and we look forward to Sanofi commencing Phase 2 development in MS following Principia's completion of our remaining Phase 1 activities."

The Phase 1 clinical trial, PRN2246 was considered generally safe and well-tolerated following both single and multiple dose administration to healthy human volunteers for 10 days. There were no serious adverse events or deaths reported in the trial, and all drug-related adverse events were classified as mild. Importantly, in a dedicated arm of the trial, pharmacologically-relevant cerebral spinal fluid (CSF) exposure to PRN2246 was confirmed, highlighting the potential for PRN2246 to impact B-cell driven inflammation in both the periphery and the CNS.

PRN2246 is being developed to potentially treat MS and other CNS diseases, in part by penetrating the blood-brain barrier and modulating B cells and other immune cells in the CNS. During neuro-inflammation, the number of B cells in the brain increases, which is thought to play a central role in the pathology of MS and other CNS diseases. In late 2017, Principia formed a collaboration with Sanofi under which Principia granted Sanofi an exclusive, worldwide license to develop and commercialize PRN2246. Principia is responsible for completion of Phase 1 activities.

Principia's proprietary Tailored Covalency platform enables Principia to design and develop reversible and irreversible covalent, small molecule inhibitors with potencies and selectivities that have the potential to rival those of injectable biologics, yet maintain the convenience of a pill. PRN1008, a reversible covalent BTK inhibitor, is being evaluated in a Phase 2 clinical trial in patients with pemphigus, an orphan autoimmune disease, and in a Phase 2 clinical trial in patients with immune thrombocytopenic purpura, a rare hematological disease. PRN2246, a covalent BTK inhibitor which crosses the blood-brain barrier, has completed a Phase 1 clinical trial in healthy volunteers, and has been partnered with Sanofi for development in multiple sclerosis and, potentially, for other diseases of the CNS. PRN1371, a covalent inhibitor of Fibroblast Growth Factor Receptor (FGFR), is being evaluated in a Phase 1 trial in patients with solid tumors.

ContraVir Pharmaceuticals Announces Completion of Phase 1 With CRV431

ContraVir Pharmaceuticals, Inc. recently announced that the primary endpoints of safety and tolerability were met in a single ascending dose (SAD) study of CRV431 conducted in the United States.

Subjects in the study were treated with escalating doses of CRV431 administered as a single dose. In addition to a favorable safety and tolerability profile, pharmacokinetic (PK) profiling demonstrated CRV431 exposure levels that are anticipated to be efficacious in future HBV patient studies.

"We are extremely pleased with the PK results in this study indicating good exposure to CRV431," said James Sapirstein, Chief Executive Officer of ContraVir. "The positive results from this trial support the continued development of CRV431 in a Phase 2 clinical efficacy study. Continued progress of our CRV431 clinical program allows ContraVir to drive toward its goal of participating in a curative regimen for Hepatitis B in a streamlined development program as announced earlier this year."

As a first-in-class host targeting candidate medicine, CRV431 is expected to complement other anti-HBV viral agents. CRV431 is a non-immunosuppressive analog of cyclosporine A (CsA) whose primary biochemical action is inhibition of cyclophilin isomerase activity, playing a key role in protein folding. Other viruses such as HIV-1 and HCV, similarly use cyclophilin for their replication. In pre-clinical studies, CRV431 has shown potential in experimental models to complement current hepatitis B treatments by reducing multiple markers of infection including HBV DNA, HBsAg, HBx, HBeAg, and HBV uptake by cells. Studies have also demonstrated that CRV431 reduces the progression of fibrosis in an animal model and also reduces both the number and size of liver tumors in a hepatocellular carcinoma (HCC) model.

ContraVir is a biopharmaceutical company focused on the development and commercialization of targeted antiviral therapies with a specific focus on developing a potentially curative oral therapy for hepatitis B virus (HBV). The company is developing two novel anti-HBV compounds with complementary mechanisms of action.

TXL, a direct acting antiviral (DAA) nucleotide analog lipid prodrug of tenofovir (TFV), is designed to deliver higher hepatic intracellular concentrations of the active tenofovir species (tenofovir diphosphate) while reducing concentrations of tenofovir outside the liver, causing fewer off-target toxicities and side-effects. CRV431, the other anti-HBV compound, is a host-targeting antiviral (HTA) next-generation cyclophilin inhibitor with a novel chemical structure that optimizes the selective index against HBV.

In vitro and in vivo studies have thus far demonstrated that CRV431 reduces HBV DNA and other viral proteins, including surface antigen (HBsAg), while offering additional benefits to mitigate liver disease. For more information, visit www.contravir.com.

Inovio Develops Novel Vaccine; Generates Cross-Reactive Responses & Provides Complete Protection Against Lethal Preclinical Challenges

Inovio Pharmaceuticals, Inc. recently announced its SynCon vaccine approach using a collection of DNA antigens generated broadly protective antibody responses against the most deadly strains of the H3N2 influenza viruses from the past 50 years and provided complete protection against heterologous lethal challenge in a preclinical study.

Study results were published online in the journal, Human Gene Therapy, in an article by Inovio and its collaborators entitled, A Synthetic Micro-Consensus DNA Vaccine Generates Comprehensive Influenza-A H3N2 Immunity and Protects Mice Against Lethal Challenge by Multiple H3N2 Viruses. This work was supported by a grant from the US National Institutes of Health. Inovio is currently in discussions with third-party funders to support further development of the company's technology with its advantages in promoting global human health.

Throughout the 2017-18 flu season the commercially available H3N2 vaccine efficacy was reported low due to the mismatch between the vaccine and circulating H3N2 viruses. In some populations the vaccine showed only 13% effectiveness, which contributed to a much greater rate of pneumonia and flu-related deaths. In a pursuit of overcoming the antigenic diversity of H3N2 viruses, Inovio developed a collection of H3HA DNA antigens and demonstrated broad, functional antibody responses against H3 viruses in mice. Vaccination was also capable of inducing robust CD4 and CD8 T cell responses, which are reported to be critical for prevention of disease in the elderly population. Additionally, all (100%) vaccinated mice survived when infected with 10 times of the lethal viral doses from two of the H3N2 virus which circulated during the 1968 and 1982 outbreaks, highlighting the strong protection afforded by Inovio's H3HA vaccine.

Earlier this year Inovio reported that its synthetic vaccine approach using a collection of synthetic DNA antigens generated broad protective antibody responses against all major deadly strains of H1 influenza viruses from the last 100 years including the virus that caused "Spanish Flu" in 1918 in multiple animal models including mice, guinea pigs and non-human primates. According to CDC, H3N2 hits people harder than other seasonal flu strains and can be especially deadly among vulnerable groups like the elderly and children. Researchers still aren't sure why, but they've found that a flu season involving the H3 virus is generally more virulent — with more hospitalizations and flu-related deaths — than seasons involving mostly H1N1 or influenza B viruses. Furthermore, the H3 part of the commercially available vaccine doesn't just work poorly in older adults. Last year adults aged 18 to 49 got very little protection—13%—from the H3 component.

Inovio is a late-stage biotechnology company focused on the discovery, development, and commercialization of DNA immunotherapies that transform the treatment of cancer and infectious diseases. Inovio's proprietary platform technology applies next-generation antigen sequencing and DNA delivery to activate potent immune responses to targeted diseases.

REGENERATIVE MEDICINE

Cell Therapy - The Quest for Finding the Cure

By: Aarti Chitale, MBA

INTRODUCTION

Regenerative Medicine[1] is the science of replacing damaged, diseased tissue or organ with a healthy cell using advanced tools, such as cellular therapies, tissue engineering, and gene therapies. Globally, there is a paradigm shift from chemical drugs to a large-scale adoption of biologic therapies. These biologic therapies are emerging as an alternative solution to some of the previously untreated health issues, such as late-stage cancer, juvenile diabetes, and heart failure.

Up until the early 2000s, the market was dominated by chemical drugs, such as chemotherapeutic agents for cancer, biguanides for diabetes, and many more that were manufactured in bulk volumes, catering to the needs of large populations at a go. The market players traditionally followed the bulk manufacturing pattern for these drugs, which suited the market demands. However, with the changing times, and advancements in the field of biotechnology, applied sciences replaced the traditional drug development patterns giving rise to novel biologic drugs.

While technological advancements have made the daily lives of human beings easier with improved spending capacities, it has unknowingly given rise to a major issue of sedentary lifestyles with minimal physical exercise. These have in turn led to a rise in lifestyle-related disorders. Conditions such as diabetes, hypertension, and high cholesterol, which were earlier, associated with age, are now found in most the middle-aged population. As per the World Health Organization, diabetes is one of the leading lifestyle disorders in the modern world with 422 million[2] cases in 2014 and hypertension surpassing diabetes with more than a billion[3] cases worldwide.

On the other hand, a surging geriatric population that is set to reach 1 billion[4] in the next 10 to 15 years is worsened by growing cancer cases amounting to 15 million[5] by 2020. In this situation, the available chemical drugs are not fulfilling the changing therapeutic demands. Especially in case of cancer, in which cases of relapse are primarily treated with chemotherapy, there is an ardent requirement of cutting-edge therapies that not just treat the symptoms but cure it.

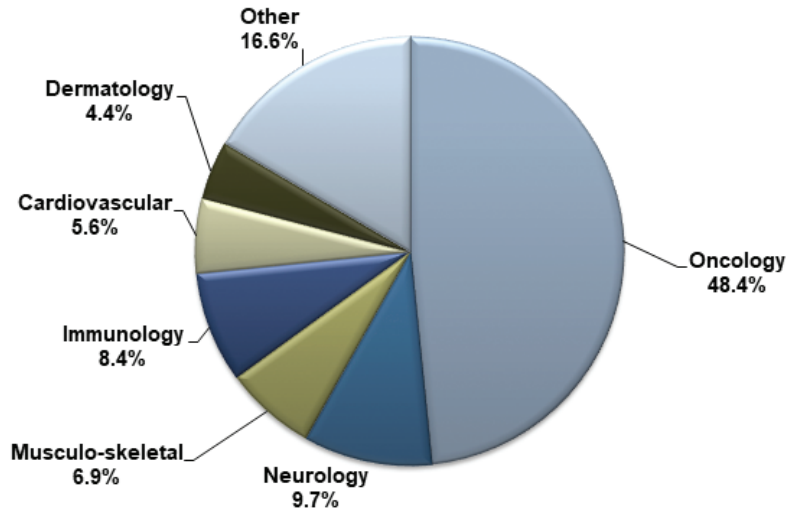
This growing need has given rise to advancements in biologics and in turn regenerative medicine. Cellular and gene therapies and tissue engineering are the major segments constituting the entire regenerative medicine arena. Successful studies and clinical trials are generating new hopes in the form of cutting-edge cell and gene therapies. More so, these are the ones making the news.

ADVENT OF CAR-T CELL THERAPIES – A SILVER LINING

Globally, cell therapy is witnessing a surge in R&D activities with tremendous efforts from small- to mid-segment companies with targeted therapeutic focus. Whilst the market is loaded with dermatological (especially anti-aging) and musculoskeletal therapies, the approval of Kymriah by Novartis and Yescarta by Gilead have indeed brought in a fresh lease of life for previously unresolved cancer cases. In August 2018, Novartis received marketing authorization for Kymriah from the European Commission becoming the first and only company with an approved CAR-T cell therapy for two distinct indications in the United States and the European Union. Following Novartis' and Gilead's footsteps, BlueBird Bio[6], in July 2018, received an accelerated assessment by the Committee for Medicinal Products for Human Use (CHMP) and the European Medicines Agency (EMA) for their cutting-edge

gene therapy LentiGlobin™, a severe sickle cell disease therapy, further strengthening the case for life-saving therapies. Likewise, companies, such as Juno Therapeutics, Celgene, and Tigenix, are moving in the same direction with either their in-house pipeline of novel cell therapies or through the acquisition of niche players. For instance, in June 2018, Celgene acquired Juno for a whopping $9 billion, gaining access to Juno's upcoming CAR-T cell therapy. This was following the $11.9-billion acquisition of Kite Pharma by Gilead, gaining access to their now marketed CAR-T cell therapy Yescarta.

FIGURE 1



Percentage Breakdown of Pipeline Products, Global

THE FUTURE – WHAT TO EXPECT?

Strong Pipeline Spanning Therapeutic Areas

The very purpose of these huge acquisitions is to support the development of novel therapies not just across oncology, but also in other areas, including neurology, cardiology, and musculoskeletal therapies. Renova Therapeutics, Mesoblast, Japan Regenerative Medicine, and Viacyte Inc., are amongst the key players focusing on cardiovascular and metabolic therapies. Viacyte's lead product PEC-Direct™ is a stem cell therapy based on pancreatic progenitor cells for type 1 diabetes. Most of these small- to mid-segment players focus on specific therapy areas and develop novel cell and gene therapies either on their own through private funding or in collaboration with bigger firms.

As highlighted in Figure 1, although oncology[7] has been leading the charts in terms of R&D activities, significant investments have been made in neurology, musculoskeletal diseases, and immunology. Histogenics, a US-based cell therapy player is developing NeoCart®, a fortified 3D scaffold designed to accelerate healing and reducing pain in patients receiving treatment with functional cartilage.

Furthermore, in terms of geographic spread, the Figure 2 suggests that, alongside North America[7], APAC is emerging as a key region supporting cell therapy research with several local companies such as Mesoblast, Pharmicell, and Kangstem Biotech, having potential product launches in the next five to seven years.

Prominent Partnership Models

In order to support a large number of trials, most market players resort to a collaborative approach toward drug development. The most prominent partnership models that persist across the cell therapy market include:

Acquisition: Bigger pharma players acquiring small- to mid-segment players with an aim of gaining technology

FIGURE 2

Product	Company	Indication	Phase	Region
Tab-cel™	Atara Biotherapeutics	Immunotherapy	Phase III	NA
Alofisel	TiGenix	Immunology	Approved	EU
ImmuniCell	TC Biopharm	Oncology	Phase III	EU
NiCord	Gamida Cell	Oncology	Phase III	Global
Furestem	KangStem	Dermatology	Phase III	APAC
autologous chondrocyte tissue implant	Histogenics	Musculoskeletal	Phase III	NA
Revascor	Mesoblast	Cardiovascular	Phase III	APAC
JRM-001	Japan Regenerative Medicine	Cardiovascular	Phase III	APAC
HLCM-051	Athersys	Neurology	Phase III	APAC
PREOB	Bone Therapeutics	Neurology	Phase III	EU
Lenti-D	Bluebird Bio	Neurology	Phase III	NA
Cerecellgram-Spine	Pharmicell	Neurology	Phase III	APAC
ALS therapy	BrainStorm Cell Therapeutics	Neurology	Phase III	NA
PLX-PAD	Pluristem	Other	Phase III	EU

Note: NA: North America; EU – Europe; APAC – Asia Pacific

Potential Market Launches Across Cell Therapy Market

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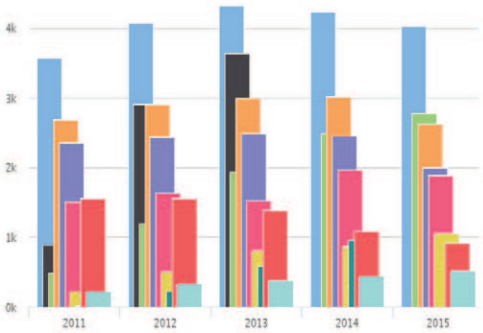
BUSINESS APPLICATIONS

- Research new therapeutic areas, and identify market gaps
- Uncover emerging science and evaluate new and promising technologies
- Target potential partners in a specific country or region, and screen potential licensing and investment opportunities
- Review comparable deals, acquisitions and financings
- Find and compare contract manufacturers and other outsourced services
- Assess competitive landscapes around an indication and research competitor pipelines
- Track generics and biosimilars, and identify Rx to OTC switch opportunities



Dynamic, customizable data display

Easy to Use Apps

Prospector
Search on industry sector, indication, route, most advanced phase and molecule/API type. Find companies within the search criteria in any region of the world by drawing a circle around the location of interest. Click for detailed information on companies within the selected search parameters and geographic area.

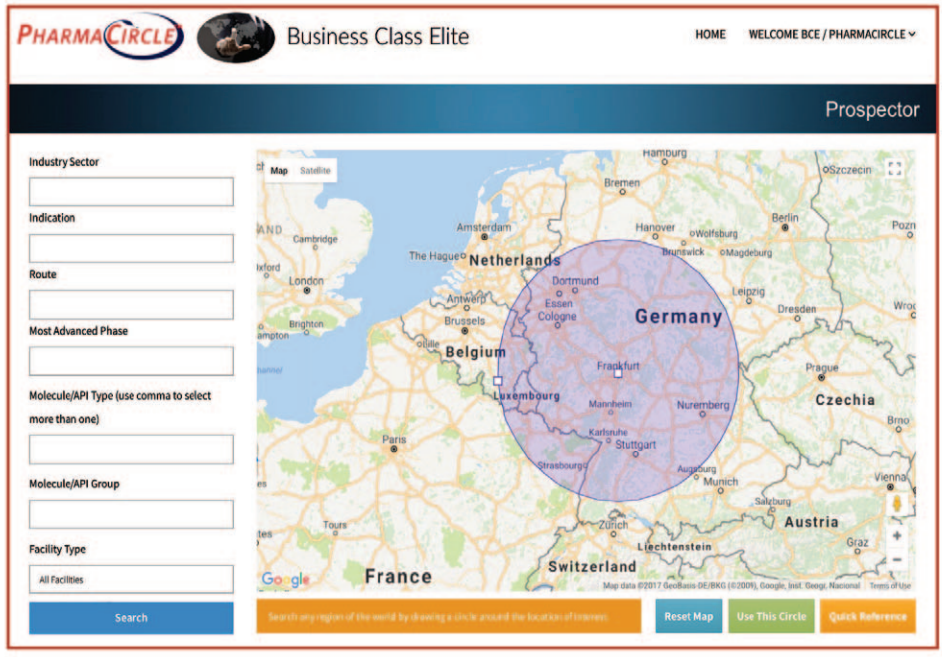
Spyglass
Create your personal watch list and track up to 30 indications, companies and products. Receive latest industry news with daily updates on your selections.

Timescape
View development timeline. Chart phase dates by region/country. Export chart as an image file and underlying data to an Excel spreadsheet.

Label Comparison
Compare current and previous versions of the label for the same product with changes highlighted, and view labels for different products side-by-side. Export comparisons to Excel and PDF.

Reconnaissance
Quick view and instant analytics on the competitive landscape around an indication, competitive intensity within an indication, and competitor pipelines across indications. Chart drugs and biologics by owner companies, highest development status within the indication, mechanism type, NME/ Generic/OTC, route, and dosage form. Programs/products are linked to development summaries.

Merge Simulator
Create a virtual company incorporating global assets of two business entities. Overlay and analyze pipeline/product, technology, operations, and financial details to assist with initial due diligence on prospective acquisitions and mergers.



Be the first to recognize new opportunities and seize the competitive advantage.

Content & Capabilities	Professional	Elite
Keyword Search Across All Datasets	✓	✓
Company Capabilities Profiles	✓	✓
Products & Pipeline Intelligence	✓	✓
Trial Landscape Explorer	✓	✓
Key Product Sales & Forecasts	✓	✓
Strategic Deals Analyzer	✓	✓
Venture Capital Investment Tracker	✓	✓
News & Insights	✓	✓
Prospector - Business Prospecting Application	✓	✓
Spyglass - Watch List Application	✓	✓
Drug Delivery Technology Analyzer		✓
Patent Exclusivity Trackers		✓
Paragraph IV Filings & Case Tracker		✓
API & Finished Dosage Form Manufacturer Finder		✓
Drug Label Comparison Tools		✓
Timescape - Development Timeline Application		✓
Reconnaissance - Competitive Landscape Analysis		✓
Merge Simulator - Acquistion & Merger Simulation		✓
Management Details & Contact Information		✓

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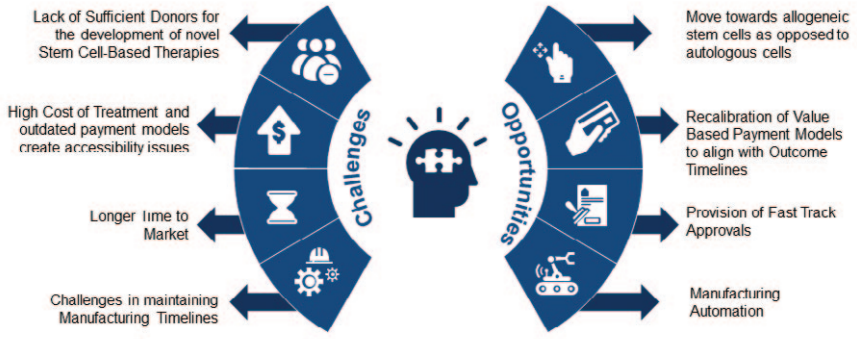
FIGURE 3



New Market Opportunities Across Global Cell Therapy Market

and therapeutic expertise. In May 2018, Novartis invested a total sum of $8.7 billion for the acquisition of Avexis gaining access to the latter's cutting-edge gene therapy for spinal muscular atrophy.

Co-Development: This type of partnership acts as a risk-sharing model, by dividing the cost of development as well as the associated risks in case of product failure. Celgene collaborated with BlueBird Bio for the co-development and commercialization of BlueBird Bio's CAR-T cell therapy bb2121.

Outsourcing: This is the most convenient way of achieving drug development and manufacturing milestones. Outsourcing reduces the cost of development manifolds as well as reduces the crucial time to market especially in the case of T-Cell Therapies and CAR-T Cell therapies' manufacturing, which is highly time sensitive. Zelluna collaborated with MasTherCell in March 2018 for the development for the development of their TCR therapy.

BUSINESS & REGULATORY ADVANCEMENTS TRANSFORMING THE CELL THERAPY LANDSCAPE

Challenge 1: Lack of Sufficient Donors for the Development of Novel Stem Cell-Based Therapies

- Potential game-changing strategy – Move toward allogeneic stem cells as opposed to autologous cells

Stem cell therapies are the major contributor to the growing cell therapy arena. Whilst the trend is shifting from traditional cord cell banking to utilizing these stem cells for creating novel therapies, companies are moving further ahead in using allogeneic stem cells as opposed to autologous cells. This has resolved the challenges pertaining to inadequate donors to a large extent, by showing improved variability and differentiation potential. The most commonly used allogeneic stem cells include:

- Adipose-derived stem cells (ADSCs)
- Induced Pluripotent Stem Cells (iPSCs)
- Mesenchymal stem cells (MSCs)

Cynata Therapeutics has been applying its proprietary Cymerus Technology[8] for the development of MSC based therapies. In June 2018, Evotec announced the achievement of the second milestone in the development of iPSC based stem cell therapy for diabetes in collaboration with Sanofi. Together, the companies are at the forefront of their research for the development of beta cell replacement therapy based on beta cells derived from human iPS cells.

Challenge 2: High Cost of Treatment & Outdated Payment Models Create Accessibility Issues

- Potential game-changing strategy – Recalibration of value-based payment models to align with outcome timelines

While the cutting-edge CAR-T cell therapies are transforming the very treatment landscape, skyrocketing prices and non-availability of reimbursement are having large-scale implications for the very adoption of these therapies. Especially for Novartis' Kymriah, which has been developed for a niche population, a price tag of $475,000 is turning out to be a major limiting factor. Globally, there are only 6,000 new cases of ALL, for which it is indicated. Of these, only 10% to 15% of the cases show a relapse, which is ideally the target population for Kymriah. To add to its woes, the cost of therapy is exclusive of hospitalization charges, which

can go up to about $79,000, further imposing cost burdens on the payers. The result, first quarter revenues were four times[9] lower than the anticipated values.

Still, Gilead's Yescarta is priced lower than Kymriah at $373,000, and also targets a larger population of Non-Hodgkins' Lymphoma. As compared to Kymriah, the product has been successful in achieving its revenue targets with Q1 revenues of $40 million and Q2 amounting to $68 million[10]. However, despite being priced lower than Kymriah, the product has been facing reimbursement challenges causing lower-than-estimated product uptake.

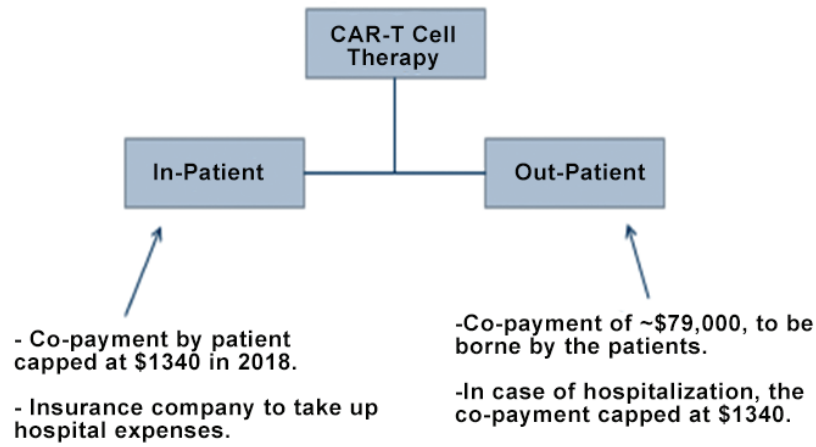
Cell Therapy is a niche market and is in a nascent stage with ongoing R&D activities on a global scale. While the market has been following the traditional one-time payment model, the high cost of these specialized therapies makes it redundant, paving way for more innovative models.

The Centers for Medicare and Medicaid (CMS) is playing a pivotal role in devising a suitable payment solution for patients as well as payers. The agency initially had announced a value-based payment arrangement with Novartis, which relied on assessing the treatment outcome of Kymriah, 1-month post administration. Nonetheless, citing data collection challenges, this arrangement did not fend well and in early 2018, CMS made an exit.

Regardless, this was not a lost opportunity, as CMS along with Gilead came up with an out-patient-based payment model, which essentially is an extension of the value-based model. According to this arrangement, any CAR-T Therapy administered on an out-patient basis will be reimbursed[11] at 6% above the wholesale acquisition cost, as per CMS guidelines. An out-patient arrangement will enable Medicare to reimburse the providers at a net price (post inclusion of discounts and rebates) with an additional 6%. Similarly, for new drugs, such as Kymriah and Yescarta, the agency will pay the manufacturer's wholesale acquisition cost with an additional 6% amount for the first three quarters.

This new arrangement entitles the agency to pay $500,839 and $395,380 for Kymriah and Yescarta treatment, respectively, when administered in an out-patient department (OPD) set-up. Additionally, the agency has clearly set the co-payment for Yescarta specifically at $79,076, while capping[12] the patient costs at an annual in-patient hospital deductible amount of $1,340 in 2018. Experts suggest that this arrangement is the first step toward being paid for the CAR-T Cell therapies, by increasing the uptake across its key markets.

FIGURE 4



In-Patient Versus Out-Patient Payment Arrangements for CAR-T Cell Therapies

Challenge 3: Longer Time to Market

- Potential game-changing strategy – Provision for fast-track approval

The US accounts for almost 40% of the global cell therapy clinical trials. With the growing focus on stem cell and CAR-T cell therapies, the US FDA has been upfront in providing fast-track approval designations to most of the life-saving medicines. In August 2018, the FDA granted fast-track designation to Sellas Life Sciences' cancer vaccine Galinpepimut-S.

As we move toward a better future of curative therapies, several other regional governments are contributing their share by providing conditional approval facilities for these life-saving medicines. Japan's inclusion of the Pharmaceuticals and Medical Devices Act (PMD) and Safety of Regenerative Medicines Act (SRMA)[13] in 2014, is set to transform the Japanese market paradigm by providing conditional approval for Phase III molecules in case of such life saving therapies.

Challenge 4: Challenges in Maintaining Manufacturing Timelines

- Potential game-changing strategy – Manufacturing automation

Despite being the first ever Car-T Cell therapy, Novartis' Kymriah has been facing issues pertaining to commercial production owing to variability issues. Personalized therapies such as these require the stringent following of timelines between blood sample extraction and re-infusion into the patient. To meet these needs, companies need to adopt the following manufacturing automations:

- Single-use/disposable bioreactors to support "small volume, large value manufacturing"
- Implementation of IT-based solutions for real-time monitoring of the manufacturing process
- Investment in green field manufacturing facilities for setting up requirement-specific manufacturing facilities

As the therapeutic landscape evolves and transitions toward personalized and value-based care, regenerative medicine will play an increasingly important role. Moreover, the success of these therapies offers promising opportunities for previously untreated diseases areas. Hence, Regenerative medicine truly holds the potential to be the ultimate medical panacea. ◆

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13. Institutional Framework for Promoting the Future Implementation of Regenerative Medicine - https://www.mhlw.go.jp/english/policy/health-medical/medicalcare/dl/150407-01.pdf

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BIOGRAPHY

Aarti Chitale, a Senior Research Analyst at Frost & Sullivan, has 8 years of experience in market research. Her areas of expertise include regenerative medicine, with a keen focus on tracking market and technology trends in cell therapy. In addition to authoring numerous reports in the area of Regenerative Medicine, she has been tracking game- changing companies in this field by identifying some of the disruptive business models such as risk-sharing models, co-development, and fast-to-market models. She earned her MBA in Marketing and International Business from Balaji University, Pune, and her Bachelor's degree in Biotechnology from Osmania University, Hyderabad.

THERAPEUTIC VACCINES

Exploring the Potential of Combining Cancer Vaccines With Immune Checkpoint Inhibitor Therapy

By: Nina Baluja, MD

INTRODUCTION

Reality has largely failed to meet expectation when it comes to the development of therapeutic cancer vaccines. Despite considerable efforts, the clinical translation of vaccines into efficacious cancer therapies has been challenging for decades. However, advances in our understanding of tumor immunology are rekindling interest in cancer vaccines, particularly in combination with breakthrough immunotherapies, such as immune checkpoint inhibitors.

CANCER VACCINES TODAY

Cancer vaccines can be either prophylactic or therapeutic. Prophylactic vaccines are designed to prevent disease in healthy individuals, and have been used in preventing cancers of viral origin, such as hepatitis B virus (HBV) and human papillomavirus (HPV). In contrast, the development of therapeutic vaccines has been problematic, with many promising Phase 2 studies failing to show survival benefit in Phase 3 trials.

To date, only two therapeutic cancer vaccines have been approved by the FDA: sipuleucel-T and talimogene laherparepvec.

- Sipuleucel-T (marketed as Provenge®) received approval in April 2010 for advanced prostate cancer.[1] In a Phase 3 trial of sipuleucel-T, only one of the 341 patients in the treatment arm exhibited a partial response by standard Response Evaluation Criteria in Solid Tumors (RECIST) criteria. However, the study showed a 4-month improvement in overall survival. The FDA deemed this survival benefit to be significant in a patient population that has few, if any, other effective therapeutic options.[2] Unfortunately, market uptake of this vaccine has been low.

- Talimogene laherparepvec (T-VEC, marketed as Imlygic®), a genetically modified live oncolytic herpes virus therapy, was approved in October 2015 for treatment of melanoma lesions in the skin and lymph nodes.[3] T-VEC is injected directly into the lesions, where it replicates inside cancer cells and causes cell death. T-VEC was evaluated in a multi-center study of 436 patients with unresectable metastatic melanoma. The study showed that participants who received T-VEC experienced a significant (and lasting) decrease in the size of their melanoma lesions, compared to participants who received comparator therapy. However, T-VEC has not been shown to improve overall survival, or to have an effect on melanoma that has metastasized to the brain, bone, liver, lungs, or other internal organs.[4]

Oncolytic virus therapies like T-VEC may be the next breakthrough in cancer treatment following the recent success in immunotherapy using immune checkpoint inhibitors. Oncolytic virus therapy mediates tumor regression through two distinct mechanisms. First, many viruses possess an affinity for cancer cells where they can preferentially replicate and kill established tumor cells. Secondly, the dying tumor cells can serve as a target for tumor-specific immune responses to generate systemic anti-tumor immunity.[5] Other oncolytic viruses that may be nearing approval in North American and Europe include pexastimogene de-

"The renewed interest in cancer vaccines doesn't end with immune checkpoint inhibitors. In fact, investigators are also exploring whether vaccines can potentiate conventional treatment, including surgery, radiation, and chemotherapy. Only time will tell, but there is no doubt that cancer immunotherapy has come of age, and cancer vaccines will likely play role in the future of cancer treatment."

vacirepvec (a vaccinia virus) for hepatocellular carcinoma, GM-CSF-expressing adenovirus CG0070 for bladder cancer, and palavered (a wild-type variant of reovirus) for head and neck cancer.[6]

CHALLENGES OF DEVELOPING THERAPEUTIC CANCER VACCINES

The issues that have hampered the development of therapeutic cancer vaccines are related to both the nature of vaccines and the fundamentals of tumor immunology.

- The vaccine initially induces an immune reaction against the vaccine itself, not the tumor.
- Each tumor has different antigens. As a result, a therapeutic cancer vaccine would need to involve autologous tumor cells.
- Most immune-responsive tumors autovaccinate, but immune regulation prevents an effective response.

Due to these challenges, vaccines are unlikely to have a major anti-tumor effect without control of immune checkpoints.

IMMUNE CHECKPOINT INHIBITORS: A REVOLUTION IN CANCER THERAPY

Immune checkpoints refer to the myriad inhibitory pathways in the immune system that maintain self-tolerance and modulate immune responses. With advances in our understanding of tumor immunology, it is now clear that tumors can co-opt immune checkpoint pathways as a mechanism of immune resistance. This has led to the development of immune checkpoint inhibitors, cancer therapies that prevent cancer cells from turning off T cells, enabling those T cells to infiltrate the tumor and stop it from growing.

The first immune checkpoint inhibitor, ipilimumab, was approved by the FDA in 2011 for the treatment of metastatic and non-resectable melanomas.[7] In 2015, pembrolizumab (marketed as Keytruda®) and nivolumab (marketed as Opdivo®) were the first of the anti-programmed cell death (PD)-1 pathway family of checkpoint inhibitors to gain accelerated FDA approval for the treatment of ipilimumab-refractory melanoma.[8] Since then, both pembrolizumab and nivolumab have also been approved for metastatic non-small-cell lung cancer (NSCLC) indications.[9]

CANCER VACCINES MAY POTENTIATE RESPONSES TO IMMUNE CHECKPOINT INHIBITOR THERAPY

While immune checkpoint inhibitors have revolutionized cancer therapy, they are only effective in 10 to 50 percent of patients with select solid tumors. Many patients with cancer do not respond to immune checkpoint inhibitor therapy, in part due to the lack of tumor-infiltrating effector T cells.[10]

This is where cancer vaccines may play a critical role. Cancer vaccines may help to prime patients for immune checkpoint inhibitor therapy by inducing both effector T cell tumor infiltration and immune checkpoint signals. In turn, immune checkpoint inhibitors may boost the potency of cancer vaccine therapies. Thus, combination therapy with a cancer vaccine and an immune checkpoint inhibitor has the potential to synergistically induce more effective anti-tumor immune responses. This hypothesis has been supported by multiple preclinical studies, and various clinical trials are currently underway.

THE FUTURE OF THERAPEUTIC CANCER VACCINES

The renewed interest in cancer vaccines doesn't end with immune checkpoint inhibitors. In fact, investigators are also exploring whether vaccines can potentiate conventional treatment, including surgery, radiation, and chemotherapy. Only time will tell, but there is no doubt that cancer immunotherapy has come of age, and cancer vaccines will likely play role in the future of cancer treatment. ◆

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BIOGRAPHY

Dr. Nina Baluja is currently Senior Medical Director, Medical Services for Premier Research, where she performs medical and safety monitoring on clinical research projects and provides strategic guidance on protocol development, study design, regulatory filings, and study execution. She has more than 15 years of clinical research, medical marketing, and drug safety experience in the CRO and pharmaceutical fields. Prior to joining Premier Research in 2017, Dr. Baluja was Senior Medical Director at PRA Health Services. Before that, she oversaw global regulatory consulting at PPD and worked extensively in the pharma sector in positions that included Medical Scientific Advisor at Boehringer-Ingelheim, Associate Medical Director at Wyeth Pharmaceuticals, and Trial Delivery Manager at AstraZeneca. Dr. Baluja's areas of specialty include oncology, hemato-oncology, and rare diseases. She has significant clinical development regulatory experience, having prepared and participated in numerous scientific meetings with the FDA, EMA, and Health Canada. She earned her MBBS from Pune University in India and her Master's in Surgical Oncology from Bombay University.

Drug Development
EXECUTIVE

Theresa Bankston, PhD

Director, Technical Services Group

BD Medical – Pharmaceutical Systems

BD

Advancing the world of health

BD Integrated Systems: From Innovation to Integration

The growing complexity and regulatory rigor of combination products has called for increasingly innovative delivery devices. To learn more about the advantages of using an integrated system for these drug-device combination products, *Drug Development & Delivery* recently interviewed Theresa Bankston, PhD, Director of the Technical Services group for BD Medical – Pharmaceutical Systems, who is responsible for providing technical support, solutions and services around delivery systems for injectable drug therapies.

Q: Can you begin by describing what an "integrated system" is, and why it is necessary?

A: The number of biological therapies in development to treat chronic diseases has risen steadily throughout the years. The fact that many of these therapies are designed for home delivery by patients or caregivers via subcutaneous injection, combined with the increasing complexity of longer acting formulations, larger injection volumes, and longer injection durations, has raised the bar for seamless injection delivery technology. Patients today receive these drugs inside prefilled injection devices, known as combination products.

To bring a drug-device combination product to market, pharmaceutical companies must select and assemble multiple components that work together effectively to deliver the drug formulation safely and effectively. These components include a primary container consisting of a syringe barrel, stopper, plunger rod, and backstop; a secondary delivery system, such as an auto-injector or wearable injector; and an add-on needlestick safety guard. These components are available from a variety of suppliers, but pharmaceutical companies who purchase components separately take on additional risks that can be significantly reduced by selecting an integrated system.

"To bring a drug-device combination product to market, pharmaceutical companies must select and assemble multiple components that work together effectively to deliver the drug formulation safely and effectively. These components include a primary container consisting of a syringe barrel, stopper, plunger rod, and backstop; a secondary delivery system, such as an auto-injector or wearable injector; and an add-on needlestick safety guard. These components are available from a variety of suppliers, but pharmaceutical companies who purchase components separately take on additional risks that can be significantly reduced by selecting an integrated system."

Q: What background and specific experience does BD bring to this field?

A: Across BD, we have extensive experience in multiple areas impacting combination products: the drug-container interface, the container-device interface, and the patient-device interface. The latter comes through extensive work developing standards in injection technique across various care settings and preclinical and clinical capabilities in injection science. Specifically, with our long history and expertise in combination products, BD's integrated systems offer a means to incorporate already existing world-class technologies with novel secondary delivery mechanisms to provide a seamless solution.

BD is a leading provider of primary containers globally. We also offer secondary delivery systems, which are designed to integrate with the well-established primary containers already used by most pharmaceutical manufacturers, for a complete combination product solution. This increases convenience, but also enables more flexibility in device selection before manufacturers make downstream decisions about device features and functionality.

BD has developed and currently provides billions of prefillable syringes and components to the pharmaceutical industry every year, meaning that we have the analytical tools and lab test capabilities to optimize the components of combination products to operate cohesively.

Our experience in designing and integrating components into systems, and extensive collaboration with drug developers has led to the development of a range of end-to-end services. These will help pharmaceutical companies in three main ways: first to choose the correct components and system for their application, second, to assess and offer solutions to any potential challenges or sensitivities, and finally to produce the data packages needed to demonstrate the safety and performance of the integrated combination product.

Q: What are the drawbacks and risks of using separate components?

A: Broadly, the risks include the delivery system not functioning as intended, such as primary container breakage, inconsistent system performance, and incompatibility with key container components. These risks may include increases in cost, project management complexity and time, potential delays to launch, and unforeseen problems post-launch. Moreover, such problems may not be revealed until late in development, or possibly after commercialization, when the combination product has already been manufactured in large quantities, and reached patients. The consequences can range from high scrap rates and waste during the filling or assembly process to the loss of costly drugs and therapy delays in the care setting.

Q: And how does BD address these risks?

A: For combination products to perform most effectively, special attention must be paid to component interfaces throughout the product development and delivery process, from the early design phases to manufacturing strategy and execution. At the interface between the drug and primary container, BD leverages its expertise and capabilities in glide force testing to ensure the drug is in the appropriate primary container to meet the manufacturer's needs. Then, between the primary container and the device, BD provides statistical tolerance analysis to specify interface requirements that minimize the risk of system failures. Finally, between the drug and secondary delivery system, BD employs injection time modelling to improve overall device performance.

A well-integrated system anticipates and mitigates performance risks early in development. BD performs system validation and design verification testing on established reference systems, challenging system performance at the limits of process capability. The outputs of this process are provided in summary report documentation.

Q: How does this impact savings for pharmaceutical companies?

A: In terms of time and cost, the most significant savings come from avoiding potentially delayed launch timelines. BD's integrated approach is focused on ensuring that every system component functions cohesively. This approach is intended to develop a seamless delivery system that meets the rigorous regulatory requirements for safety, effectiveness, functionality, and usability.

For example, BD's leading primary container technology designed for biologic drugs, BD Neopak™, ensures a fit with many secondary systems, including BD handheld auto-injectors, wearable injectors, and passive safety devices. This enhanced fit supports greater choice and flexibility for pharmaceutical companies to serve diverse patient groups, therapeutic areas, and markets, minimizing the costs associated with managing multiple component interfaces and suppliers.

Q: What processes are in place to optimize product development?

A: In terms of risk mitigation, because BD produces both primary and secondary systems, we have a unique appreciation of nuances in meeting ISO standards that can help customers. Visibility across secondary system platforms results in product designs that ensure system integration between BD prefillable syringes and secondary systems, both during development and after manufacturing scale-up through commercialization. Internal experts share learnings from implementation across project teams. Moreover, quality commitment is maintained at component and system (including primary container) level, which forces tighter specifications and reduced variability in system performance. This creates a high degree of accountability for BD, as the single party responsible for the performance of the total delivery system.

Finally, BD conducts human factors engineering testing on its most advanced products across a range of representative users to confirm that the integrated devices are safe and user-friendly. While pharmaceutical companies will conduct their own testing with the actual formulation, this early testing increases confidence in usability and reduces the risk of unforeseen issues. Testing for performance feasibility may include in vivo testing, demonstrating that various injection volumes or flow rates are feasible. Combination product support occurs throughout the development process, from matching the right set of components with the formulation in Phases I and II, to validation testing of the system in Phases II and III.

For example, BD integrates its best-in-class BD Hypak™, BD Neopak™, and cannula technologies into our self-injection systems, providing multi-platform flexibility across a range of dose volumes. BD's wearable injector, BD Libertas™, is the leading model of BD systems integration, designed from the bottom up, with an array of proven BD components, including BD Neopak™ technology and cannula.

BD also offers a leading brand of passive needle guards through its BD UltraSafe Passive™ and BD Plus™ Needle Guards. Unlike most add-on safety devices, BD UltraSafe Passive™ and BD Plus™ Passive Needle Guards are designed to work with BD prefillable syringes. Because BD develops both components, we can test compatibility long before a pharmaceutical customer can test the components together with a specific drug.

Q: Can you give specific examples of the most common issues that are solved with integrated systems?

A: First, let's look at cap removal malfunction and wasted drugs. When patients remove the cap from an auto-injector, the rigid needle shield (RNS) may not always be pulled from the needle. The result could be damage to the needle and the drug delivery device, rendering the device unusable. For the pharmaceutical company, this issue may produce complaints, drug wastage, and negative quality perception.

With BD's integrated auto-injectors, the caps are designed to integrate with and remove the RNS so that the needle is not damaged. Knowing that even minor changes, such as tool replacement, can affect RNS dimensions, BD routinely and proactively assesses design and manufacturing updates.

Another issue is that needle extension (depth) is not always well-controlled or understood when the auto-injectors and prefillable syringes are combined. The range of specifications for each component can result in an unexpectedly wide variation when the tolerances are stacked. As a result, unexpected clinical outcomes may occur when bridging from syringe injection to auto-injection, which can lead to pharmaceutical companies needing to repeat clinical studies or perhaps even re-design the auto-injector or prefillable syringe. Either case could result in product launch delays.

And finally, let's look at primary container defects. Like needle extension, component dimensional variability (eg, prefillable syringe variability) is not always well accounted for in the design of the auto-injector assembly. This can lead to higher reject rates and possible primary container breakage.

Q: And in what ways do your key products address these integration issues?

A: I'll focus on just two core products to answer your question: BD Physioject™ and BD Intevia™. Let's start with the BD Physioject™: a disposable auto-injector that fully integrates with the BD Neopak™ 1-mL glass prefillable syringe or the BD Hypak™ for biotech 1-mL glass prefillable syringe. With BD's clear vision on detailed, proprietary prefillable syringe component specifications, critical dimensions that incorporate both BD Physioject™ and prefillable syringes are factored in within the assembly process design.

In an ISO 11608 drop test (1 meter drop) study comparing BD Physioject™ with one of the most commonly marketed disposable auto-injectors, BD Physioject™ outperformed the comparator auto-injector in terms of prefilled syringe breakages and successful complete injections.

Clinical studies conducted by BD show how injections with BD Physioject™ (compared to injection with a syringe alone) provide evidence of more predictable clinical outcomes with BD's integrated system.

And then there's the BD Intevia™: an auto-injector platform technology specifically designed for high-viscosity drug delivery. It supports biotech's evolving needs for high dosages, while offering integration with BD Neopak™ technology and BD Hypak™ for biotech, and providing manufacturers with the flexibility to accommodate formulation changes.

The team went a step further to optimize the system by setting out to eliminate the variability of requiring a skin pinch upon injection, simplifying the process for the patient. BD's ability to tightly control variability of components enables consistent targeting of the subcutaneous space. Preclinical studies have demonstrated that, without the use of a skin pinch, BD can reliably control injection depth, greatly improving the injection experience all round.

Q: How would you summarize BD's solutions in a nutshell?

A: Combined with BD's continuous process and service improvements, BD integrated solutions are designed to mitigate system performance risks, facilitate cost savings, and prevent launch timeline delays to help pharmaceutical companies succeed in bringing their drug-device combination products to market and achieve commercial success. ◆

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GENETIC MODIFICATION THERAPIES

Clinical Applications & Technology Platforms

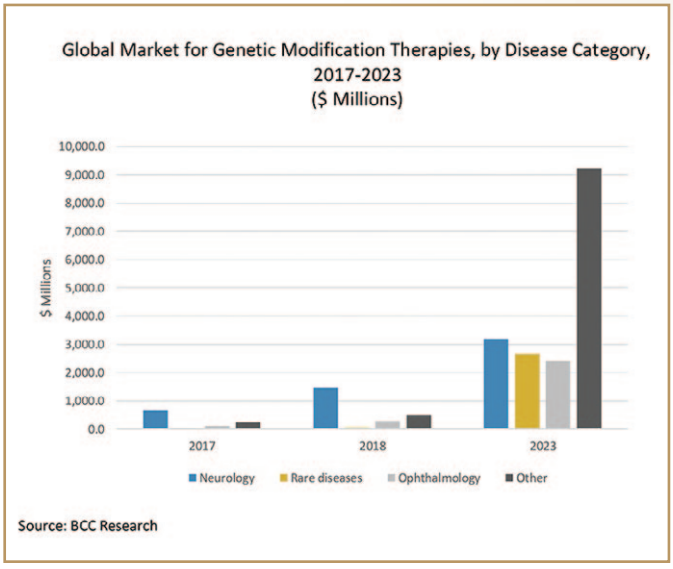
By: Laurie L. Sullivan and John Bergin, MS, MBA

INTRODUCTION

Genetic modification therapies are changing the landscape of medicine. These advanced therapies have the unprecedented ability to offer a one-time cure for severe, debilitating diseases that were previously untreatable. BCC Research found that this industry is segmented by technology platform, delivery method (viral versus nonviral), and clinical application. This specialization enables companies to build significant barriers to entry and competitive advantage.

Strong patent and licensing arrangements also contribute to these competitive positions. Manufacturing to meet the large-scale demands of the industry will play an important role in the future. The interest level in corporate partnerships has been enhanced by recent clinical successes and regulatory approvals for genetic modification therapy candidates. Industry alliances have been centered on several objectives, including access to genetic modification therapy technologies by large pharma/biotech, access to delivery technologies, and entry into new therapeutic markets.

The global market for genetic modification therapies is estimated at $2.3 billion in 2018. It is forecast to expand at an impressive compound annual growth rate of 49.9% to reach $17.4 billion in 2023. Growth in the market for genetic modification therapies is being driven by applications in oncology, neurology, rare diseases, and ophthalmology. In rare diseases, genetic modification therapies create new profit streams. In fields such as oncology, neurology, and ophthalmology, genetic modification therapies have the potential to disrupt current markets.



Key factors for meeting revenue forecasts include continuing demonstration of genetic modification therapy efficacy and safety in clinical settings, migration to earlier-line settings in cancer, and success in efforts to standardize and scale up the manufacture of viral delivery vectors. The following sections examine the main genetic modification therapy platform technologies: gene therapies, genetically modified cell therapies, RNA therapies, and gene editing.

GENE THERAPIES

A rich late-stage pipeline of gene therapies is being developed for a wide range of disease categories. In the next 5 years, gene therapy is poised to exert a significant influence on genetic

modification therapies. Gene therapies seek to permanently replace defective genes in a cell's DNA. This can restore cellular function and has the potential to totally eliminate a disease. Monogenic diseases, for which a specific disease-causing gene can be identified, are well-suited for gene therapies.

Payload and delivery are the main components of a gene therapy. The payload contains the gene sequence that encodes for the production of a protein. Also included in the payload are DNA sequences that regulate transcription of the gene. The delivery component of a gene therapy includes the vector that is needed to deliver the payload into target cells. Gene controls can be used to yield more reproducible results. Promoters play an important role because they control the amount and location of therapeutic gene expression. Other control elements, such as insulators, can help with the stability of therapeutic gene expression; however, they also increase the probability of insertional mutagenesis.

The delivery construct that is chosen can play a vital role in the therapeutic. The two main classes of delivery technologies include viral (eg, adenoviruses, adeno-associated viruses [AAVs], retroviruses, lentiviruses) and nonviral (eg, plasmid DNA, transposons, naked DNA/RNA complexes). The optimum delivery vehicle yields high expression of the payload within the target tissue without inducing an immune response in the host. Considerations for choice of delivery method include the cell and tissue type being targeted, systemic versus local delivery, use of tissue-specific versus constitutively active gene controls, and profile of the payload to be delivered.

To be successful, gene therapy candidates must meet important clinical criteria: 1) the pathogenic mechanism should be clear and addressable, 2) the target organ must be accessible to the gene therapy, and 3) there must be a compelling, unmet medical need. Luxturna, which is the first gene therapy to be approved by the FDA, fully meets these criteria. Luxturna is indicated for biallelic RPE65-mediated inherited retinal disorders. In this indication, mutations in the RPE65 gene is the clear and addressable pathogenic mechanism. The target organ (the eye) is easily accessible to the gene therapy, which uses an AAV2 viral vector to carry the correct version of this gene. Finally, there is a clear and pressing medical need for therapies that can restore functional vision in children and adults who have this disorder.

GENETICALLY MODIFIED CELL THERAPIES

Genetically modified cell therapy incorporates a functional gene into a cell-based therapy. The genetic modification occurs outside the body, and the resulting genetic change to the patient's DNA is permanent. The active payload consists of the gene encoding for production of the therapeutic protein and gene controls that regulate production of the therapeutic gene. The vector, which can be either nonviral or viral, delivers the gene and gene control payload to the cells that are to be genetically modified. The most common cell types include T cells, NK (natural killer) cells, and HSCs (human stem cells). The main types of genetically modified cell therapies include chimeric antigen receptor (CAR) T cell, T-cell receptor (TCR), Listeria-based, tumor-infiltrating lymphocyte (TIL), NK, and HSC.

CAR T-cell therapy involves tumor binding and activation domains; CAR T cells recognize specific tumor antigens and kill tumor cells. TCRs have alfa and beta chains that recognize peptides on the surfaces of tumor cells; the T cells then kill the tumor cells. Listeria-based therapy targets dendritic cells, which present tumor antigens and activate tumor-killing T cells. In TIL therapy, a patient's own TILs are isolated and expanded ex vivo. TILs are then infused back into the patient to attack and kill tumor cells. NK cells can be infused into a patient, where they attach to tumor cells and deposit cell-killing granules in the cytoplasm. HSC therapy entails adding a functional gene to HSCs outside the body and reinfusing them into the patient; the genetically modified HSCs carry the therapeutic gene.

In CAR T-cell therapy, the key therapeutic manipulation made to cells is through a gene product that is delivered by a vector. For CAR T-cell, TCR, TIL, and NK therapies, challenges include toxicities, production, and immunosuppressive tumor microenvironment. CAR T-cell therapy has entered the clinic; BCC Research forecasts that CAR T-cell therapy will achieve significant sales revenue.

RNA THERAPIES

RNA therapeutics alter the expression of a gene. The therapeutic consists of an oligonucleotide and a delivery vector. In some cases, the delivery component is the naked oligonucleotide. The oligonucleotide can be either DNA or RNA, which is complementary to the DNA or RNA sequence of the targeted gene. The delivery vector can be viral, nonviral (eg, antibodies, aptamers, nanoparticles), or naked.

"The global market for genetic modification therapies is estimated at $2.3 billion in 2018. It is forecast to expand at an impressive compound annual growth rate of 49.9% to reach $17.4 billion in 2023. Growth in the market for genetic modification therapies is being driven by applications in oncology, neurology, rare diseases, and ophthalmology."

The main RNA therapy segments include RNA interference (RNAi; stops production of the disease-causing protein), antisense interference (inhibits or enhances translation of mRNA into protein), microRNA modulation (miRNA; also inhibits or enhances translation of mRNA into protein), and messenger RNA (mRNA; produces therapeutic protein).

RNAi is in development for a range of indications, including cancers and infectious diseases. RNAi consists of a double-stranded (ds) DNA oligonucleotide, which is delivered to the patient either systemically or locally to specific tissues or organs. RNAi triggers the RISC (RNA-induced silencing complex) pathway, which results in the cleavage of mRNA corresponding to the therapeutic dsDNA sequence. This shuts down specific proteins that cause a disease or disease symptoms.

Antisense technology uses a single-stranded RNA molecule that is complementary to an mRNA. The antisense molecule binds to the mRNA to either inhibit or enhance translation of the mRNA into a protein. miRNA therapy uses short, single-stranded RNA molecules that can regulate protein production. miRNA modulators can either shut down or enhance production of a particular protein. mRNA therapies use mRNA molecules that can produce functional proteins after being introduced into the patient. mRNA does not enter the nucleus but remains in the cytoplasm; thus there is no risk of insertional mutations. mRNA is not classified as a gene therapy because it does not modify the genetic material of living cells.

GENE EDITING

Gene editing technology is still in its early stages of development, with drug candidates just beginning to enter the clinic. Gene editing therapeutic strategies include gene knockout (stops production of a protein), gene correction (replaces or repairs a dysfunctional protein), and gene insertion (starts production of a new protein). Gene editing relies on the use of engineered nucleases, which are artificial proteins composed of sequence-specific DNA binding domains fused to a nuclease that cleaves DNA nonspecifically. Each gene editing technology is designed to perform three functions: recognize a specific (target) DNA sequence, bind to that target sequence, and cut DNA at a specific site within the target sequence.

Meganucleases are engineered forms of restriction enzymes that have DNA recognition sequences (usually 12-40 nucleotides), together with a nuclease activity domain. The ability to target with meganucleases is limited. In addition, their engineering is challenging because the DNA recognition and nuclease activities are combined into a single domain. Due to these challenges, meganucleases will probably remain restricted to gene editing for small-scale research applications.

Zinc finger nucleases (ZFNs) include a DNA recognition domain (the zinc fingers) linked to a Fok1 nuclease. There are typically three to six separate zinc finger repeats, each one comprising 30 amino acids stabilized by a zinc ion, which bind to a specific DNA triplet. Importantly, the Fok1 cleavage domain needs to form a dimer in order to cut the DNA. This requirement for dimerization provides a distinct advantage for target specificity. Extensive biotechnical engineering is required to achieve this superb target specificity. However, once engineered, ZFN therapy has high clinical utility.

Transcription activator-like effector nucleases (TALENs) use the same DNA cleavage domain as ZFNs (Fok1). However, the recognition domain is completely different. This domain is an engineered version of a conserved repeat domain that comes from naturally occurring TAL effectors encoded by phytopathogenic Xanthomonas bacteria. The DNA binding domain has a highly conserved 33-34 amino acid sequence with differing 12th and 13th amino acids, referred to as repeat variable di-residues (RVDs). Each repeat domain binds to a single nucleotide (versus a triplet in ZFNs),

and the RVD determines specific nucleotide recognition. TALENs are easier to engineer compared with ZFNs because their binding mechanism is relatively simple, with basic variations in the RVD needed for determining the target sequence.

Clustered regularly interspaced short palindromic repeats (CRISPR)–based gene editing consists of a guide RNA (gRNA) for DNA recognition and a nonspecific CRISPR-associated endonuclease (Cas9). A key advantage of CRISPR-Cas9 systems is their ease of engineering; the targeting domain can be completely changed by altering only the gRNA. This is accomplished through molecular cloning versus the need for protein engineering as with other systems (ZFN, meganuclease, and TALEN). A second advantage of CRISPR-Cas9 systems is the ability to multiplex (simultaneously target with a single enzyme and multiple guides). The gRNAs used in CRISPR-Cas9 systems do not bind to target DNA as tightly as other systems, resulting in a tendency to make off-target cuts.

Due to these off-targeting safety concerns, CRISPR-Cas9 systems are moving into the clinic with a strategic approach. The initial clinical focus is on treating severe genetic diseases with significant mortality or morbidity and where the benefit-to-risk ratio is high. A second consideration is the delivery vehicle for CRISPR, which currently permits deliveries to the eye, liver, and some blood cells, making these organs a near-term focus of clinical development.

Optimization to develop next-generation gene editing drugs is ongoing, with the focus on improved tissue targeting and greater specificity to minimize off-target edits, improving persistence/engraftment of cells, and treating polygenic disorders.

STRONG PIPELINE BOLSTERS GROWTH OF GENETIC MODIFICATION THERAPIES

Rapid growth in the genetic modification therapies industry is due to a number of factors. Continuing advances in key technologies are driving growth of the genetic modification therapy market. Enabling technologies foster market growth by improving the clinical efficacy, safety profile, organ-targeting specificity, and durability of a given genetic modification therapy candidate. Enabling technologies include such items as expertise in viral and nonviral delivery modalities, promoter design to drive gene expression, cell culture, oligonucleotide and gene design and optimization, viral manufacturing technology, antigen targeting, and gene editing optimization.

The growing interest on the part of large pharma or biotech companies is driving clinical development of genetic modification therapy candidates. The rich late-stage pipeline for genetic modification therapy candidates is a driving force of growth. The Phase III pipeline includes more than 40 product candidates. This pipeline is evidence of the safety and efficacy of the genetic modification therapeutic approach. Genetic modification therapies address real and pressing clinical needs. Many of the indications do not have any effective treatments, leaving only palliative care options. Genetic modification therapies can provide a complete cure in some cases, demonstrating an unprecedented level of clinical success.

Because of the potentially curative nature of these medicines, there is enormous potential in many applications, ranging from cancer to neurology to rare diseases. Genetic modification therapies represent the next wave of medicines, with enormous potential for treating and curing debilitating and serious diseases. As a result of its wide scope, genetic modification therapies will play an important role in the future global medical economy. ◆

This article is based on a market analysis report published by BCC Research titled "Genetic Modification Therapies Clinical Applications: Gene Therapies, Genetically Modified Cell Therapies, RNA Therapies and Gene Editing" (BIO159A) by John Bergin.

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BIOGRAPHIES

Laurie L. Sullivan, ELS, is a Boston-based writer and editor with 20 years of experience in medical communications. She is certified by the Board of Editors in the Life Sciences. She contributes regularly to the BCC Research content on Life Sciences.

John Bergin is the author of previous BCC Research biotechnology reports and has held business development, sales, and marketing positions with a Fortune 500 advanced materials company, as well as executive management positions with a nanotechnology and separations company. Mr. Bergin earned his BS in Chemistry, his MS in Biotechnology, and a Masters of Business Administration.

THE HUMAN MICROBIOME

Advancing New Frontiers in a Rapidly Emerging Market

By: Flo Orim, MD, PhD

INTRODUCTION

The field of Human Microbiome research and development is apparently one of the most popular hubs of the biotechnology industry. While the Human Microbiome Project, MetaHIT and other huge studies of human microbiota, have garnered a lot of attention over that past few years, the microbiome space has literally exploded in terms of both basic and applied biomedical research.

This report focuses on biomedical aspects of research, development, and commercial endeavors in the human microbiome space. It includes essential background information, evolution of the field, advances in basic research, events in the emerging commercial market, deal activity, interviews with experts, and trends in microbiome research and commerce. Primary sources of information for this report include the scientific literature, discussions with experts, and an online survey of individuals working in this space.

In 2009, a PubMed search on the term human microbiome yielded 579 citations, with a radical increase to 4,490 by 2014. Not only has the field seen massive investments from Venture Capital firms and Angel Investors, showing keen interest, but there has also been a flurry of deals and collaborations with the expected flux and knowledge exchange. Another milestone achieved was the first major microbiome IPO issued.

HISTORY & EVOLUTION

After pioneering several milestones in the field of genomics, Craig Venter led an expedition to collect samples of marine bacteria and sequence them en masse using Sanger shotgun sequencing technology. Venter and his team identified more than 1,800 species, a groundbreaking feat that established metagenomics as a sustainable field for investigation and commercial involvement. The arrival of next-generation sequencing (NGS) technologies with the ensuing emphasis on short hypervariable regions of microbial 16S rRNAs enabled the Human Microbiome Project and other similar efforts to comprehensively characterize the human microbiome to encourage full participation in the field. Initial efforts in microbiome research and development helped to identify several enterotypes (classification of living organisms based on its bacteriological ecosystem in the gut microbiome); a solid foundation for subsequent work in personalized microbial medicine. Evidence shows that individual enterotypes seem to change in response to dietary alterations. Another observation is that a well-balanced microbiome can help to maintain weight, whereas disruption or dysbioses can lead to obesity. Several other correlations have been made between dysbiosis and disease. The current wave of increased commercial activity was born out of several studies showing that patients suffering from recalcitrant Clostridium difficile associated diarrhea could be treated with a fecal transplant from a "healthy" matched donor. Antibiotic treatment temporarily alters the gut microbiome and allows the normally dormant commensal C. difficile to overgrow. This fecal microbiota restoration therapy helps to restore balance with success rates of up to 100%.

Advances in Research on the Human Microbiome Initially NGS sequencing of metagenomes was based on the Roche 454 pyrosequencing platform. 454 Life Sciences will no longer support the platform after 2016. The need for more time-saving and cost-effective alternatives shifted attention to mainly Illumina's faster and

FIGURE 1

Company	Technology/Product	Indication(s)	Status
AdvancingBio	Fecal microbiota transplant services	*C. difficile*-associated diarrhea (CDAD)	FMT services to physicians at reduced cost to patients
AOBiome	Topical applications of patented and stabilized ammonia-oxidizing bacteria (AOB)	- rosacea, acne, eczema - diabetic ulcers - bacterial vaginosis	- Phase 2 trials to early 2016 - Discovery phase - Discovery phase
Assembly Biosciences	Targeted oral delivery of microbiome-based therapies	*C. difficile*-associated diarrhea (CDAD)	Pre-clinical development
C3 Jian	Specifically targeted antimicrobial peptides (STAMP): - Therapeutics: C16G2 C3CD17 MRSA-STAMP - Diagnostic: PCR-based test	Dental caries *C. difficile* SSTIs *S. mutans*	- Phase 2 - Preclinical - Preclinical - Validation
Diversigen (a.k.a. Metanome)	Biobanking, molecular analysis, bioinformatics	- Discovery research - Clinical research - Public Health	Metagenomics service provider
Eligo Bioscience	CRISPR/Cas 9 + engineered phage-capsids-platform-derived eligobiotics (ultraprecise antimicrobials)	- Virulent staph.aAureus - Inflammatory Bowel Diseases - Skin Diseases	Development
Enterome	Therapeutic: - FimH Antagonists EB 8018 - EB 110, EB 120 Diagnostic: Biomarkers - IBD 110 - Screening test AIEC IBD 210	- IBD, non-alcoholic fatty liver Dx - Crohn's Dx - Ulcerative colitis - Crohn's Dx, IBD - Crohn's Dx	- IND - Development - Clinical Trials
Evelo Therapeutics	Oncobiotics	Cancer	Preclinical
Evolve BioSystems	Probiotic-based biotherapeutics targeted for infant microbiome	Infant dysbiosis due to pre-term birth, C-section, infant formula	Clinical trials
ExeGi Pharma	- Live biotherapeutic /probiotics - Visbiome High Potency Probiotic - Visbiome	- Pouchitis, UC, IBS - Liver disease	Launch phase Post-marketing
Human Longevity	Integrating genome, metabolome, and microbiome data to probiotics, diagnostics, and therapeutic	Diseases associated with aging	Several, ongoing
Interface Diagnostics	Smart Capsule™ sampling technology, endoscopy multiomics and bioinformatics, therapeutics, diagnostics	Inflammatory, metabolic, and digestive diseases; and oncology	Targets raised with proof-of-concept pilot study
Intrexon	Actobiotics platform based on engineered L. lactis; oral biotherapeutics to deliver targeted microbiome modulators	Microbiome disorders – colon cancers and inflammation	Undisclosed
MaaT Pharma	Autologous FMT Live, frozen inoculum suspension Stool collection and storage device	Severe antibiotic-induced intestinal dysbiosis	Entering clinical stage by early 2016
MetaboGen	Proprietary metagenomics tool MeduzaGen™ and next-generation probiotics	Dysbiosis, various indications	Undisclosed
MicroBiome Therapeutics	- Microbiome modulators (MM) - NM504 - NM505 - MM + Metformin MT303	- Prediabetes and diabetes - Type 2 diabetes - Obesity and diabetes	- Fast-track patent (06/2015) Phase 3 - Preclinical development
Open Biome	- Nonprofit stool bank - FMT capsule G3 - FMP250 lower-delivery MP FMP30 upper-delivery MP	- Recalcitrant *C. diff* infection - *C. difficile* infection - *C. difficile* infection	Commercial (nonprofit) distribution
Pureflora	Microflora Refinement System – automated FMT preparation	*C. difficile* infection	Undisclosed
Rebiotix	- MRT - RBX2660 - RBX7455 - RBX8225 - RBX6376	- Recurrent *C. diff.* infection - Oral *C. diff.* prevention IBD/Ulcerative Colitis Multi-drug Resistant Organisms	Phase 3 (breakthrough status) feasibility
Ritter Pharmaceuticals	Microbiome modifiers or prebiotics, RP-G28	First FDA-approved drug for lactose intolerance	Preparation for a Phase 2b program
Seres Therapeutics	- Proprietary ecobiotics -SER-109 -SER-262 - SER-287 - SER 155 -Metabolic diseases	- Recurrent CDI - Primary CDI - IBD Abx-resistant bacteria Type 2 DM, metabolic syndrome	FDA breakthrough therapy, Phase 3 Preclinical Phase 1 Preclinical discovery
Symbiotic Health	Microbiome-based oral- encapsulated fecal-derived bacteria	*C. difficile* infection	Pilot trial
Symbiotix Biotherapies	Commensal-derived oral polysaccharide A (PSA)	Inflammatory bowel disease, Multiple sclerosis	Translational studies
Synlogic	Synthetic biotic oral therapies	Inborn errors of metabolism (IEM), urea cycle disorder (UCD), phenylketonuria (PKU)	Preclinical development
Synthetic Biologics	SYN-004 SYN-010	*C. diff* infection, antibiotic-associated diarrhea, IBS + constipation (IBS-C)	Phase 2 development
ViThera Pharmaceuticals	VT301	Inflammatory bowel disease (IBD)	Preclinical
Whole Biome	Complete Biome Test™ microbiome discovery platform	Women's health: Early diagnosis of pre-term labor	Offered to select groups of clinicians, other microbiome companies, research institutes
Xycrobe Therapeutics	Probiotic-like xycrobes – skin biotherapeutics	Topical/transdermal therapy for various conditions	Preclinical

Companies Active in the Microbiome Space

"Our interviews and survey results show that persons working in the microbiome field are highly optimistic about the relevance of their work to the future success of microbiome research and development. The market is growing tremendously, and microbiome market potential is projected to rise from $294 million in 2019, to $658 million by 2023."

cheaper short-fragment sequencing systems. Some researchers favor working with combinations of sequencing platforms depending on the application. Other researchers prefer Pacific Biosciences' platform; the latest release P6-C4 provides impressively long reads averaging 10,000 to 15,000 bases. Data analysis remains a challenge in the microbiome space. Informatics workflows can be either gene-centric, preferred when addressing high complexity applications; or assembly-based, favored for lower diversity applications. Either choice requires further selections downstream from the branch point.

Quite a few substantial advances in data analysis have been made recently yet inconsistency among results of metagenomic analyses from different laboratories and technologies/platforms is a huge challenge. Protocols must be standardized and results made consistent across laboratories and technology platforms. In a collaborative effort, researchers from Human Longevity, Inc. (HLI) and the J. Craig Venter Institute (JCVI) recently published a paper calling for standardization of practices across laboratories. The paper highlighted inconsistencies in microbiome work from different library preparation methods and data analysis.

COMMERCIAL ACTIVITY

This report profiles the activities of 28 microbiome companies, most of which are engaged in developing therapeutics for various diseases. The most frequent target indication is C. difficile gastroenteritis; not surprisingly the gut microbiome is the research focus of the majority of the companies. Other diseases include inflammatory bowel disease, irritable bowel syndrome, acne, and diabetes. Particular programs are directed at larger therapeutic areas, such as neurodevelopmental disorders, autoimmune disease, metabolic disorders, and infectious disease. One company works to develop synthetic oral biotics to address the challenges of inborn errors of metabolism. Several companies are committed to developing more refined alternatives to FMT, including oral preparations and storage devices.

Diagnostics in development range from biomarkers to monitor mucosal healing in IBD, to oral preparations for sampling the gut. The report also describes 15 recent microbiome-related deals, including four research partnerships between small companies and Big Pharma. These include an unidentified global Pharma company and Janssen Research and Development unit. The APC Microbiome Institute University of College Cork, Ireland, is collaborating to support two small companies. The National Institute of Allergy and Infectious Diseases (NIAID) and Swiss Foods Company Nestlé are providing collaborative support to smaller companies.

In an online survey of 119 individuals active in the microbiome space, more than half of respondents work in academia compared to less than half who work in commerce. Nearly one-third are addressed as research/development manager, group leader or supervisor. Almost half stated their work involved analytical methods to detect or describe microbiomes in individuals or populations. About two-thirds work on the gut microbiome and by therapeutic area, another two-thirds focus on inflammation. The majority of respondents work on cancer.

None of the participants expect a change in the research focus of their company, and two-thirds expect an increase in the company's microbiome efforts over the next 2 years. One-third of respondents opined that sufficient microbiome-related information has been obtained to warrant translational efforts, while less than one-third disagreed. Nearly one-third use microarrays to detect dysbiosis, while less than a third use short-read next-generation sequencing. Nearly half of respondents agree

that the next decade will see an avalanche of new personalized biotherapeutics.

TRENDS & CONCLUSIONS

Our interviews and survey results show that persons working in the microbiome field are highly optimistic about the relevance of their work to the future success of microbiome research and development. The market is growing tremendously, and microbiome market potential is projected to rise from $294 million in 2019, to $658 million by 2023. Several research efforts are geared toward establishing cause over correlation regarding dysbiosis-related disorders. Groups and consortia have called for a unified global microbiome effort possibly to promote consistency of results and standardized protocols. This is requisite to maintain the highest standards of quality control for human health.

The term human microbiota refers to the 10 to 100 trillion symbiotic microbial cells harbored by an individual, mainly bacteria in the gut; the human microbiome consists of the genes these cells harbor. An unfavorable change of the gut microbiota composition is called dysbiosis, which leads to an overgrowth of potentially pathogenic bacteria (pathobionts) and a decrease in the number of beneficial bacteria (symbionts). Preceding the current wave of interest and investment in microbiome research and development, early work in the field was hampered by an inability to culture the majority of microbes found in humans. Craig Venter, whose application of shotgun DNA sequencing contributed immensely to the Human Genome Project, also played a key role in triggering the current microbiome gold rush. In 2003, he pioneered the Global Ocean Sample Expedition and led a group that traveled the seas collecting samples of bacteria, later identified by Sanger shotgun sequencing. In 2004, Venter's group published results from a pilot study on samples taken from the Sargasso Sea near Bermuda. They identified about 1,800 species, which included 148 new lineages of microbials. That same year, Jo Handelsman in a seminal paper defined Metagenomics as "the genomic analysis of microorganisms by direct extraction and cloning of DNA from an assemblage of microorganisms," thus, introducing a method of analysis that allowed the application of genomics to uncultured organisms. Metagenomics (also referred to as environmental and community genomics) is another important term to use concerning the microbiome. Simply put, this means that a mixture of DNA from different sources, microbes, in this case, could be cut in pieces, the fragments sequenced, and results deciphered to provide information on the types of organisms contributing to the mix. 454 Life Sciences (a Roche company) brought the first next-generation sequencing technologies to market, with the overall approach being introduced in 2005. A major milestone in the field was the application of 454 Life Sciences' next-generation Pyrosequencing technology to the analysis of bacteria in a deep mine ecosystem by Penn State University scientists. Another major boost to the field was when Illumina and others developed alternative methods and instruments more suitable to gathering large amounts of sequence data at reduced costs in a shorter time frame. From classical Sanger sequencing, the field progressed into determining sequences of entire 16S rRNA genes, which in turn evolved into the current more efficient sequencing of small hypervariable regions of these genes. ◆

This executive summary is based on the following market research report published by Insight Pharma Reports: The Human Microbiome: Advancing New Frontiers in a Rapidly Emerging Market by Flo Orim, MD. For more information, visit www.insightpharmareports.com.

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BIOGRAPHY

Dr. Flo Orim is an experienced physician and cancer researcher who brings a passion for the simple communication of complex science to her work as a medical writer. With an MBBS from University of Jos, Nigeria (1999) followed by years of clinical practice, she made a brief foray into managed care/health insurance and rediscovered her love for communication as a lecturer at the medical school in University of Abuja, Nigeria. She was awarded a Japanese Government scholarship and earned her PhD in Medical Sciences (Radiation Research and Life Sciences) from The Atomic Bomb Disease Institute, Nagasaki University (2013), delving into medical/academic writing during the course of graduate school. She then completed postdoctoral training in Molecular Pathology at Aichi Cancer Center Japan (2016). Dr. Orim has several publications, gaining academic and medical writing experience across the clinical and basic medical sciences as well as the life sciences and biotechnology. Dr Orim currently works as a medical writer and editor in Nagoya, Central Japan.

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Ajinomoto Bio-Pharma Services is a fully integrated contract development and manufacturing organization, with sites in Wetteren and Balen, Belgium and San Diego, California, USA, providing comprehensive process development services, cGMP manufacturing and drug product fill finish services of small molecule and biologic APIs and intermediates. Ajinomoto Bio-Pharma Services offers a broad range of innovative platforms and capabilities to rapidly scale from clinical and pilot programs to commercial quantities, including: Corynex technologies, oglionucleotide synthesis, antibody drug conjugations (ADC), high potency APIs (HPAPI), 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.

Large Molecule Manufacturing: One of the industry's top leaders in microbial biologic manufacturing, using patented technologies and providing impeccable quality.

- cGMP Protein and Plasmid Production
- Microbial Cell Banking & Characterization
- Fermentation & Product Recovery
- Purification & Formulation
- Corynex® Protein Expression System

Highly Potent & ADC Services: Ajinomoto Bio-Pharma Services offers dedicated production and laboratory suites for high containment ADC bioconjugates and highly potent compounds, as well as formulation and fill finish services.

- Conjugation & Purification
- Fill & Finish
- Lyophilization
- Dedicated labs and manufacturing

Oligo & Peptide Synthesis: An industry leader in the synthesis of high quality, scalable, custom oligonucleotides and peptides.

- AjiPhase® Synthesis Technology
- Fast Solid Phase Synthesis

Drug Product Manufacturing: A leader in aseptic filling, offering a wide range of capabilities for vials and syringes.

- Aseptic Formulation
- Aseptic Fill Finish
- Packaging, Serialization & Aggregation Services

Development Services: Our highly knowledgeable Process Development team will establish and characterize a robust manufacturing process to ensure consistent cGMP manufacturing performance.

- Process Development
- Optimization & Scale Up

Product Quality & Analytical Services: Our well-designed product quality and analytical programs work to ensure the success of your small and large molecule products through their life cycle.

- On-Site Laboratories
- Phase Appropriate Analytical Method Development & Lot Release Testing
- ICH – Compliant Stability Programs

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

You have the power to make a difference by delivering therapeutics that improve quality of life and inspire a healthier world. You need a manufacturing partner who has the power to make your every challenge their own and who shares your unwavering tenacity and dedication from clinical studies through commercial success. Together, we have The Power To Make.

CDMO SERVICES:

- Small & Large Molecules
- Process Development
- Oligos & Peptides
- High Potency & ADC Services
- Drug Product Manufacturing

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Alcami is a world-class contract development and manufacturing organization (CDMO) headquartered in North Carolina, with executive offices in Durham and Wilmington. With over 1,000 employees operating at 10 global locations, our combined capabilities include API development and manufacturing, solid state chemistry, formulation development, analytical development and testing services, clinical and commercial finished dosage form manufacturing (oral solid dose and parenteral), packaging, and stability services. Alcami offers an exceptional end-to-end outsourcing opportunity as well as individualized development and manufacturing services that can be integrated for a less fragmented and faster pathway for your products. From early-stage development and scale up to integrated manufacturing and commercial success, our expertise ensures the best possible outcome for your product at every level.

Alcami makes it easy for our partners to bring their products through the clinic to commercialization. We embrace an approach that integrates program, project, and process in a unique and highly effective way and where a product's potential is turned into reality day-after-day. We meet all applicable local, state, and federal regulatory requirements, including current GMPs and country guidelines for the US, Canada, EU, and EU Member State regulatory bodies (eg, EMA, MPA, IMB). We also incorporate international standards as part of the Quality Management System and meet expectations established by the USP, EP, and JP. We comply with all regulations and standards, including those regarding controlled substances (DEA), radioactive materials (NRC), environmental protection (EPA), child-resistant container-closures (CPSC), and employee safety (OSHA).

Alcami offers all phases of pharmaceutical development for small and large molecules through two laboratories located in Durham and Wilmington, NC. These facilities have supported more than 500 Investigational New Drug (IND) filings and over 50 NDAs, ANDAs, and NADAs since 1985. Two cGMP API facilities in Germantown, WI, and Weert, Netherlands, support Alcami's process development/scale up and clinical and commercial supply for customers worldwide. The Germantown facility is Alcami's Center of Excellence for API development and manufacturing site. The Weert facility serves as the company's Center of Excellence for Solid State Chemistry. Regional cGMP analytical laboratories in St. Louis, MO, Wilmington, NC, and Edison, NJ, provide comprehensive analytical testing solutions for Alcami customer's new drug entities and biopharmaceuticals, as well as generic drugs, chemicals, and animal health and medicated consumer health products. Alcami's cGMP drug product manufacturing facilities support preclinical, clinical, and commercial supply. Our Charleston, SC, facility is focused on processing parenteral products while the Wilmington, NC, facility provides solid oral dose manufacture. Both manufacturing sites are fully integrated with Alcami's packaging and distribution center. Alcami has international sales offices in Toyko, Japan, Cambridge, Massachusetts, and San Diego, California. The Japanese branch provides a home base for Alcami's local customers and serves Japanese companies interested in developing and manufacturing products for launch in the US.

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Toll Free: (800) 575-4224
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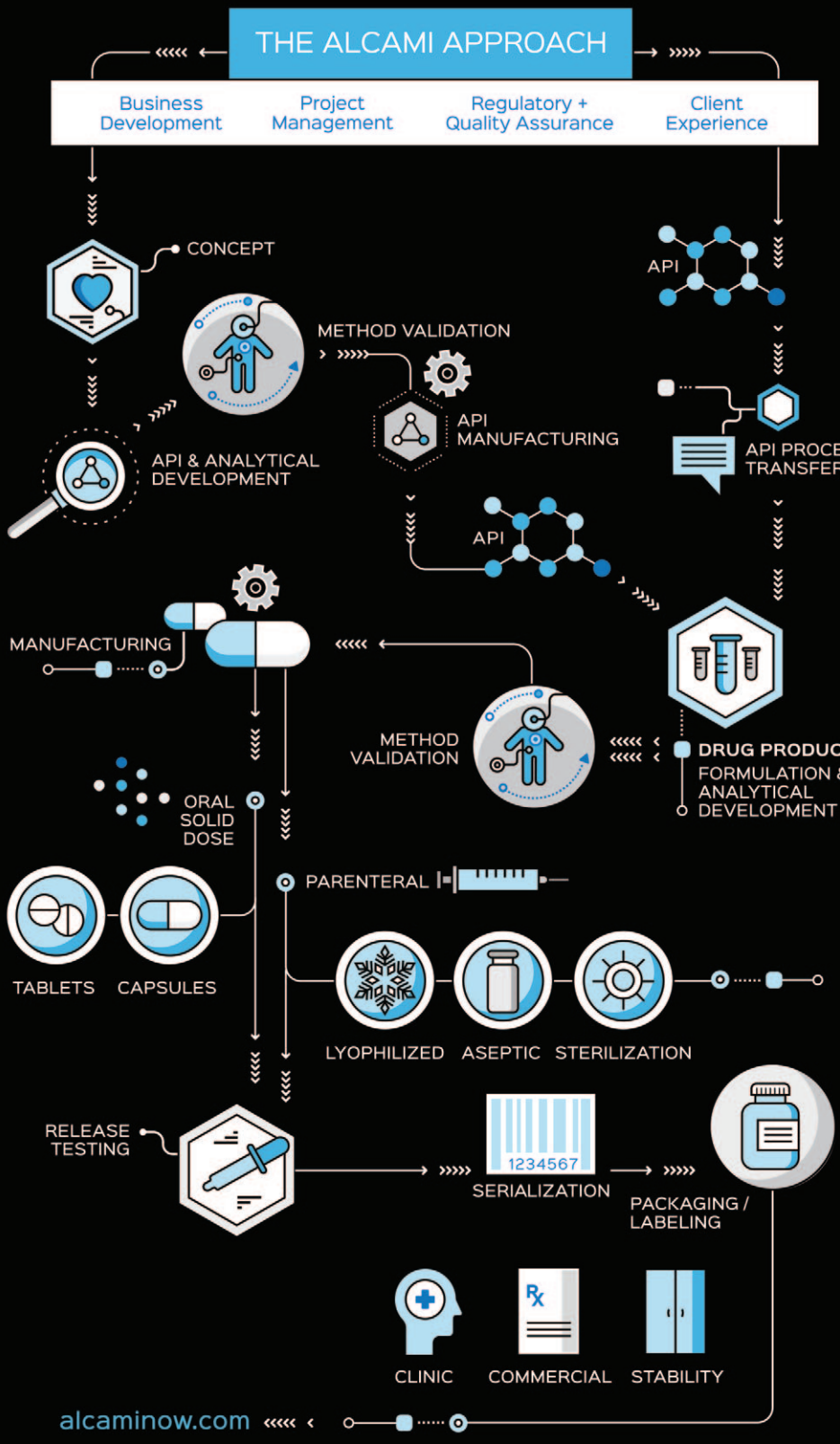

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ASCENDIA PHARMA

Delivering Sophisticated Formulations

Ascendia Pharmaceuticals is a speciality contract development and manufacturing (CDMO) company dedicated to developing enhanced formulations of existing drug products, and enabling formulations for pre-clinical and clinical stage drug candidates. We specialize in creating formulation solutions for poorly-water soluble molecules and other challenging pharmaceutical development projects. Using our suite of formulation capabilities and nano-particle technologies, we can assess the feasibility of a broad array of formulation options in order to improve a drug's bioavailability. Ascendia formulates products for injection (IV, SC, or IM), transdermal, ophthalmic or nasal delivery, and both immediate-release and controlled-release products for oral administration. We execute rapid, comprehensive, and cost-effective programs for our clients.

Ascendia provides complete development services - analytical testing/validation; pre-formulation development and modeling, formulation proof-of-concept, development, and optimization; and cGMP manufacturing/release of clinical trial materials (CTM). Our projects range from discovery-stage molecules, to life-cycle-management projects, to generic product development - always creating formulation solutions with enhanced biopharmaceutical properties suitable for clinical scale-up.

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

We provide contract cGMP manufacturing services for our clients, quickly transitioning projects from formulation optimization to proof-of-concept for a first-in-man study. We conduct turnkey development of control documentation, and product release requirements as necessary to meet our client's specifications. We can manufacture sterile, injectable dosage forms, and work with potent compounds, using our ISO7/8 cleanrooms and aseptic isolator capabilities.

Ascendia also has developed and patented a proprietary pipeline of pharmaceutical product candidates for out-licensing, including ASD-002, a novel, injectable form of the anti-thrombotic drug clopidogrel, and ASD-004, an improved nano-emulsion form of cyclosporin for dry-eye syndrome. Ascendia has a state-of-the-art pharmaceutical research, development, and manufacturing center located in North Brunswick, NJ.

ASCENDIA PHARMACEUTICALS
661 US Highway One
North Brunswick, NJ 08902
T: (732) 640-0058 - (610) 525-0938 W: www.ascendiapharma.com

Avista Pharma Solutions is a contract development, manufacturing, and testing organization, headquartered in Durham, NC. With over 200,000 square feet of laboratory and manufacturing space in the US and UK, Avista Pharma offers a broad suite of scientifically differentiated services ranging from early stage discovery, API and Drug Product development, and cGMP manufacturing to stand-alone analytical microbiology testing support. Our laboratory and manufacturing facilities are located in Durham, NC, Longmont, CO, Agawam, MA, and Edinburgh, UK.

Avista Pharma provides solutions for pharmaceutical companies that need a different kind of partner. Our team of industry veterans brings the experience required to solve our clients' most complex scientific challenges, and our individualized and collaborative approach allows us to be responsive and agile to their needs. We are committed to finding the shortest, most efficient path to success – success that goes beyond science.

To support our clients' needs, we are continuously investing in facility upgrades and expansion. Throughout the past three years, we have expanded our analytical labs in all locations, upgraded and expanded our API manufacturing capacity, expanded our microbiology lab, built a new drug product manufacturing facility, increased our presence in the Boston metro area to support our cleanroom service clients, and acquired an industry-leading provider of solid state chemistry services.

Our full suite of services includes:

- Analytical Development & Testing
- Process Chemistry
- API Manufacturing
- Formulation Development
- Drug Product Manufacturing
- Solid State Science
- Material Characterization
- Discovery, Biology & Parasitology
- Microbiology
- Cleanroom Services

To learn more about our services and find examples of how we have made clients successful, visit www.avistapharma.com.

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SUCCESS

AVISTA PHARMA

BEYOND SCIENCE

Your Premier CMO for Specialized Sterile Injectables

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

FACILITIES

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

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

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

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for Specialized Sterile Injectables

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, versatile solutions–and over 85 years of parenteral experience–to help you achieve your commercialization objectives.

Ultimately, our goal is to make you feel confident and secure in choosing BioPharma Solutions as your CMO–assisting you to avoid the unexpected and guiding you through marketplace complexities to help you achieve the full potential for your molecule.

Learn more about us at
baxterbiopharmasolutions.com

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BD Medical - Pharmaceutical Systems

A Partner of Choice for the Pharmaceutical Industry

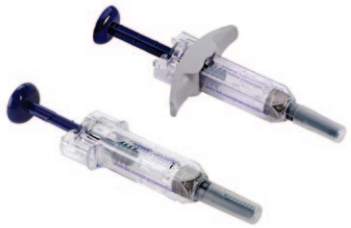
Founded in 1897, BD is one of the largest global medical technology companies in the world and is advancing the world of health by improving medical discovery, diagnostics, and the delivery of care. BD helps customers enhance outcomes, lower costs, increase efficiencies, improve safety, and expand access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

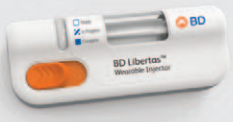
BD Medical - Pharmaceutical Systems at a Glance

- 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

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. **Discover the new BD.**



BD Libertas™ wearable injector

BD Libertas™ wearable injector with Smart option

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BD Libertas™ wearable injector, BD Libertas™ wearable injector with Smart option and BD Intevia™ autoinjector are products in development; some statements made are subject to a variety of risks and uncertainty.

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BIODURO

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BioDuro is a full-service provider for integrated drug discovery and development, including discovery support, API synthesis and optimization, formulation development, and cGMP manufacture of drug products. From drug substance to drug product, discovery to development, small molecule or biologics, BioDuro is your partner for accelerating drug discovery and development and improving efficiency in establishing drug candidate success.

BioDuro Global CMC Solutions

BioDuro provides integrated drug development services from preformulation to clinical trial material (CTM) manufacturing.

Our formulation services cover delivery systems and formulation technologies from simple API-in-capsule to enabled, solubilizing formulations utilizing approaches such as hot-melt extrusion and spray-dried dispersion.

Our analytical expertise drives sound formulation and process development decisions. We provide phase-appropriate method development, validation, in-process, release, and stability testing

BioDuro provides GMP-compliant manufacturing for solids, liquids, and semi-solids, up to Phase III.

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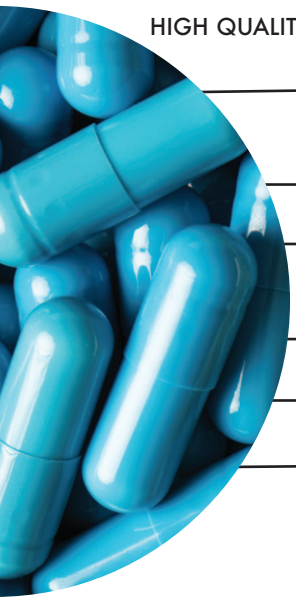
GROUND BREAKING CAPSULE DESIGN:

Our unique combination of science, engineering, formulation and capsule expertise enables us to optimize the bioavailability, targeted delivery and overall performance of our customer's products. We partner with them in over 100 countries to create novel, high-quality and customized solutions that meet their needs and patients' evolving preferences.

Building on our history of innovation in polymer science and capsule engineering, Capsule Delivery Solutions continues to launch ground-breaking capsule designs and equipment technologies that are improving drug development and delivery. Whether you're looking to formulate new products or enhance an existing line, we have the right capsule to help you bring improved products to market faster. With a diverse portfolio including HPMC, Dry Powder Inhalation capsules or specialized clinical capsules, we are a global leader in capsule development and manufacturing, bringing unmatched products and technical support to our worldwide customer base.



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Ligand-owned, Captisol® was invented in 1990 by scientists at the University of Kansas Higuchi Biosciences Center for use in drug development and formulation.

The Captisol® technology is used to address the limitations of currently marketed drugs. Eleven FDA-approved, Captisol-enabled® medications are marketed by: Pfizer, Bristol-Myers Squibb, and Baxter International. Captisol® also has License and Supply Agreements (LSAs) in place with a number of pharmaceutical companies worldwide with Captisol-enabled® product candidates. Routes of administration investigated include parenteral, oral, ophthalmic, nasal, topical, oral, and inhalation.

The regulatory acceptance of Captisol® is supported by extensive safety studies demonstrating its excellent systemic safety profile. In 1999, a Type V Drug Master File (DMF) was filed with the FDA. This regulatory safety data package, which includes greater than 70 volumes, supports the use of Captisol® in parenteral formulations as well as support for other routes of delivery. Multiple FDA divisions and ex-US regulatory agencies have evaluated the data package and permitted the use of Captisol® in clinical trials.

Captisol® is an established enabling technology with substantial characterization, safety documentation and regulatory review. In 1999, a Drug Master File Type V, containing preclinical and clinical safety data for Captisol® was filed with the US Food and Drug Administration. Published in scientific articles and utilized in a number of ongoing clinical trials by leading pharmaceutical and biotech companies, Captisol® is recognized as a valuable and vital delivery technology whose use could mean the success or failure of a development program.

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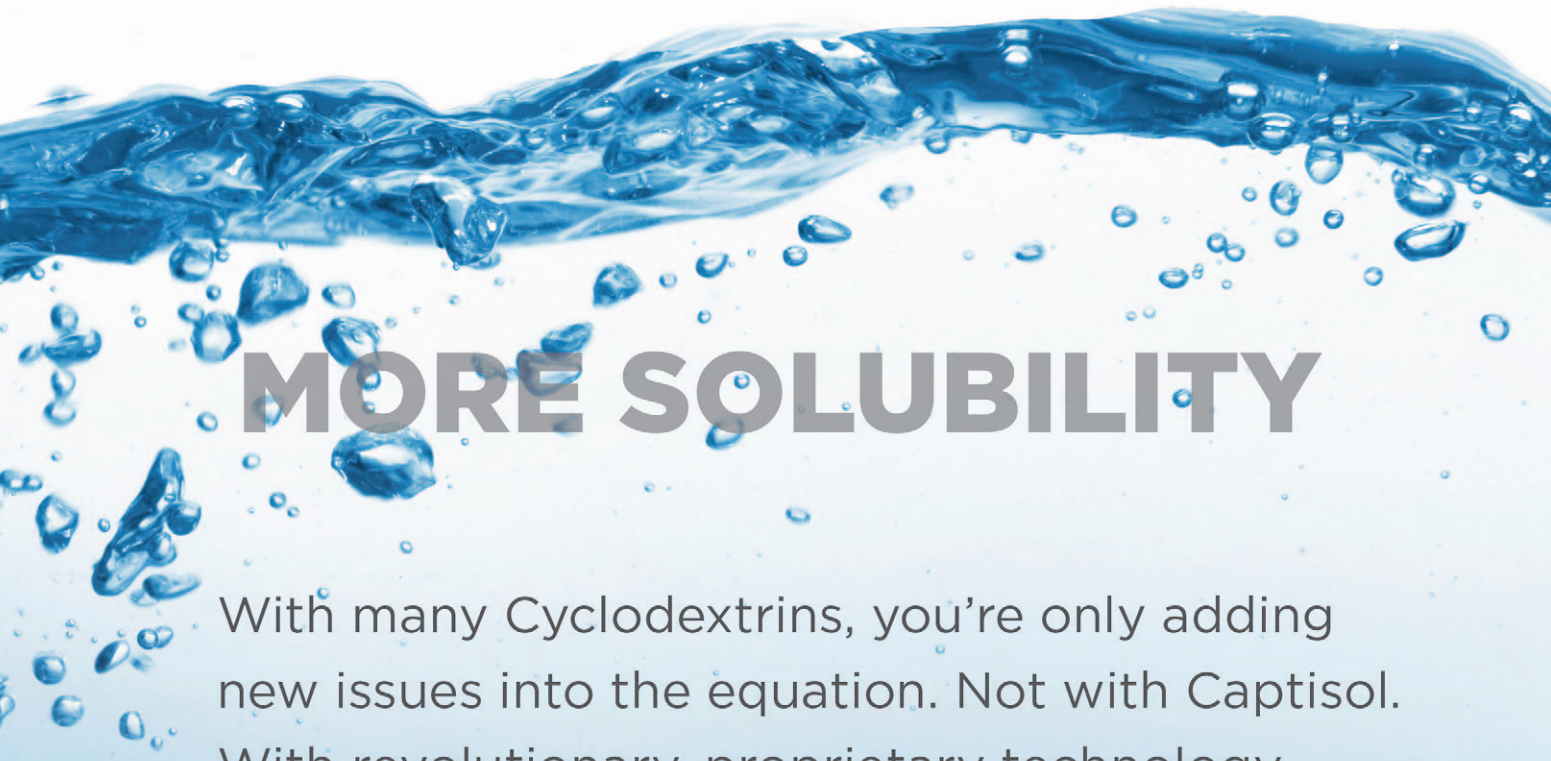

MORE SOLUBILITY

With many Cyclodextrins, you're only adding new issues into the equation. Not with Captisol. With revolutionary, proprietary technology, Captisol is rationally engineered to significantly improve solubility, stability, bioavailability and dosing of active pharmaceutical ingredients.

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Catalent®

Corporate Description

Catalent is the leading global provider of advanced drug delivery technologies and development solutions, providing worldwide clinical and commercial supply capabilities for drugs, biologics, and consumer health products. With over 85 years of experience, Catalent has the proven expertise and flexible solutions at the right scale to bring more customer products to market faster, enhancing product performance, and ensuring reliable supply.

We serve over 1,000 innovator customers - both established and emerging - in over 80 markets, including 90 of the top 100 branded drug marketers, 21 of the top 25 generics marketers, 24 of the top 25 biotech marketers, and 23 of the top 25 consumer health marketers globally. Each year, Catalent manufactures more than 73 billion doses of nearly 7,000 products, which equates to approximately 1 in 20 doses taken each year by patients or consumers.

Our significant intellectual property includes over 1,200 patents and patent applications, and our team of 1,600 talented scientists help introduce more than 150 new products to market every year. Around the world, Catalent is subject to over 50 regulatory audits and more than 400 customer and internal audits a year.

Whether you are looking for a single, tailored solution or multiple answers throughout your product's lifecycle, we can improve the total value of your treatments—from discovery to market and beyond.

Catalent. More products. Better treatments. Reliably supplied.™

Technology Highlights

With our wide range of expert services—including analytical, biologics, pre-formulation, and formulation—we drive faster, more efficient development timelines and produce better products. These include:

- GPEx® technology for advanced cell expression, and advanced biopharmaceutical development, analytical and manufacturing.
- SMARTag® technology for antibody-drug conjugation, affording precision design of next-generation biologic therapies.
- OptiForm® Solution Suite to assist in rapid, optimized dose form development.
- Bioavailability enhancement including lipid-based systems, Pharmatek SD™ spray dry technology, particle-size engineering, and OptiMelt® hot melt extrusion.
- Unique delivery technologies: including OptiShell® gelatin-free capsule technology, the Zydis® orally disintegrating tablet platform, and controlled release dose design, as well as inhaled and injectable dose forms.
- Catalent RP Scherer Softgel is a global leader in innovative oral and topical softgel technologies, and nearly 90% of NCEs approved by the FDA over the last 25 years have been developed by us.

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EARLY PHASE DOSE DESIGN OPTIMIZATION | OVERCOMING COMPLIANCE CHALLENGES IN PATIENTS | IMPROVED PATIENT ACCEPTANCE & ADHERENCE | BETTER OUTCOMES FOR PATIENTS & INNOVATORS

To be successful, new treatments require superior real world outcomes. Through our proprietary Better Treatments by Design™ process, Catalent works with you to determine and address innovator, prescriber, and patient needs at the right point in the development process. With our experience developing thousands of molecules and commercializing hundreds of products, combined with access to the broadest suite of delivery technologies, we can develop the right dose form for your treatment. Contact us today and give your candidate its best chance of success from clinical development to commercial supply.

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CordenPharma is your full-service partner in the Contract Development & Manufacturing (CDMO) of **APIs, Drug Products**, and associated **Packaging Services**. Through a network of fully inspected cGMP facilities across Europe and the US organized under five technology platforms - **Peptides, Lipids & Carbohydrates - Injectables - Highly Potent & Oncology - Small Molecules - Antibiotics** - CordenPharma experts translate complex ideas at any stage of development into high-value products.

Peptides, Lipids & Carbohydrates

- Synthetic Peptide API Production
  -Solid / Liquid-phase, Hybrid Synthesis
  -cGMP & non-cGMP
- Synthetic Lipids & Carbohydrates

Sterile Injectables

- New Development & Commercial Suites for Aseptic Filling with >60.000 units per day
  (Pre-filled Syringes, Liquid or Lyophilized Vials)
- Packaging, Labeling & Logistics
- Sterile Emulsion Technology
- Large Pre-Filled Syringes
- Clinical Trial Services

Highly Potent & Oncology

- API Development & Commercial Manufacturing
  (SafeBridge Category 4, OEL ≤50 ng/m^3)
  -High Containment for Cytotoxic & Cytostatic APIs
  -Low Volume (Clinical Batches > Commercial Manufacturing)
  -Highly Potent Small Molecules & Peptides
  (Solid & Solution-Phase)
  -Highly Potent Purification by Chromatography
- Drug Product Development & Manufacturing
- Oral Solid Dose
  -Full Development Capabilities (from 100g to commercial-scale)
  -Coated & Uncoated Tablets
  -Serialization & 2D Data Matrix Coding

Small Molecules

- Development & Commercial Manufacturing
  -Intermediates
  -APIs & Excipients
  -Clinical Supply from Phase I – III
- Proprietary & Generic Advanced Intermediates & APIs

Antibiotics

- Non-segregated
  -Oral APIs
  -Oral & Sterile Drug Products
  -Primary & Secondary Packaging
- Segregated

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FULL-SERVICE CDMO >>
FOR A GLOBAL MARKET

CordenPharma is your full-service CDMO for a global market. Through our network of technology platforms and cGMP facilities for the manufacture of APIs, Drug Products and pharmaceutical Packing, CordenPharma experts translate your complex processes, ideas and projects at any stage of development into high-value products.

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TECHNOLOGY PLATFORMS

- PEPTIDES, LIPIDS & CARBOHYDRATES
- HIGHLY POTENT & ONCOLOGY
- INJECTABLES
- SMALL MOLECULES
- ANTIBIOTICS

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CPhI North America's Mission

To facilitate the growth and evolution of North American pharma by providing a forum for innovation, learning, sourcing, and networking.

About CPhI North America

CPhI organizes the most important and widespread series of global pharmaceutical events. Our gatherings are both renowned and revered — but it didn't start in North America. With massive events throughout Asia, South America, Europe, and beyond…more than 500,000 powerful and respected pharma players from every aspect of the supply chain understand that CPhI is where they connect to learn, grow, and conduct business. With a 30-year tradition and an infrastructure fine-tuned to unite buyers, sellers, and industry trailblazers, we expanded this iconic worldwide events portfolio into the most progressive mega market on earth. Enter CPhI North America.

It's true, the US alone accounts for 40% of the world's pharmaceutical sales and is home to 6 of the top 11 companies. But much more than that, this is a place of community-building connections. A forum for thought leadership. The hub of innovation. And it all comes to life at CPhI North America.

Headed to Chicago

Home to several of big pharma's powerhouses and the largest medical device cluster in the country, the Midwest's life sciences sector is growing at more than twice the rate of the overall US economy — with capital investments up 53% over the past 10 years. If that's not enough, the region's bioscience industry employs more than 300,000 professionals, topping both California and the East Coast.

Chicago strategically comprises a pharma market unlike any other, and our 2019 event will put attendees right in the middle of the action!

Award Winning Tradeshow

CPhI North America was honored by Tradeshow News Network, taking home the fastest growing award in the attendance category.

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CPhI north america

April 30–May 2, 2019

Lakeside Center at McCormick Place
Chicago, IL, USA
cphinorthamerica.com

For nearly 30 years, CPhI has organized the world's most influential pharmaceutical events. Several annual gatherings comprise our iconic worldwide portfolio, but it's CPhI North America that has become the critical link in a global chain connecting motivated buyers with industry-leading suppliers. We represent the most lucrative pharma market on earth. It's here you will drive your career and your business forward. You simply can't afford to be left behind.

With over 6,500 attendees and 670+ exhibitors together for three days, this is your chance to network with top industry players, learn about the latest trends and regulations, and effectively do business.

Use Promo Code DRUGDEV when you register to claim your FREE Expo Only pass or get an additional $50 off your Conference or VIP Pass.
Go to cphinorthamerica.com/register today!

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UBM

1224_CPhI19

CRODA

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

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

Croda has been actively investing in GMP API technologies and R&D to ensure the continual delivery of exceptional ingredients. We consider future health and wellness needs when creating new specialty products. Croda has developed a proprietary process called Super Refining™ to help create products of superior quality and purity. The process helps to physically remove impurities from pharmaceutical excipients and nutritional oils without altering their fundamental structure.

HIGH-PERFORMANCE PRODUCTS

Croda offers a complete range of excipients for topical dosage forms as well as high-purity solvents, vehicles, and surfactants suitable for parenteral, oral, suppository, and ophthalmic formulations. The company's products include:

- Super Refined™ Range of Excipients
  - Oils: including sesame, soybean, peanut, corn, olive, and cottonseed
  - Oleic acid: high-purity multi-compendial excipient
  - PEGs: high-purity, multi-compendial polyethylene glycols
  - Dimethyl isosorbide: high purity solvent for hydrophilic and lipophilic APIs, enhancing skin penetration
  - Polysorbates
  - Castor oil
  - Propylene glycol
  - Etocas™ 35: high-purity polyoxyl 35 castor oil
- Crodamol™ Range: a range of ester solvents and vehicles
- Polawax™: a complete compendial and self-emulsifying wax
- Synperonic™ Range: a range of monograph compliant poloxamers
- Crodacol™ Range: fatty alcohols
- Crodesta™ Range: sucrose esters for mild emulsification and sustainable release in tablet applications
- Medilan™: medicalgrade lanolin designed to surpass USP requirements for lanolin, modified

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Drug Delivery Experts (DDE Labs) is a contract R&D drug delivery laboratory located in San Diego that specializes in drug product development. We have the expertise to integrate drug delivery formulations with the appropriate device to maximize commercial potential.

DDE Labs was created in 2014 to address the gap of good outsourcing partners in the formulation and drug delivery technology landscape. We specialize in drug-device combination product development and integration of formulation and delivery system approaches with commercial strategy and life-cycle plans. We work in the injectable products space as well as alternate delivery systems.

OUR TEAM

- Specialists in combination drug product development
- Extensive industry experience in biologics drug development
- Highly-qualified Ph.D. scientists from pharma backgrounds
- State-of-the-art R&D lab, including process suite for clean fill
- Pharmaceutical development scientists from various disciplines

Each of our experts has more than twenty years of experience in pharmaceutical research, development, and commercialization. Our experts can customize a drug delivery solution that best meets your product's need.

OUR WORK PRODUCT

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

NEW! Proprietary Technologies

BIOLOGICS & BIOPOLYMER SALTS

DDE Labs' proprietary technology involves new salt forms of active pharmaceutical ingredients, including peptides, proteins, antibodies, oligonucleotides, and polysaccharides.

- Applications in extended-release injection, stabilization, and co-formulation
- High encapsulation efficiency and high drug load for biologics
- Simple and mild aqueous manufacturing process

CAPSULE DEVICE FOR ORAL DELIVERY OF BIOLOGICS

DDE Labs has also developed a novel device technology designed for oral delivery of active agents to the GI tract.

- Oral delivery technology for enhancing bioavailability of biologics
- Device is based on simple parts and principles in pharmaceutical injection systems
- Simple to manufacture, low cost, with bio-compatible materials commonly used in devices

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Twitter: twitter.com/drugdeliveryexp

Partnering With Biopharma to Share Success of Biologic Drugs

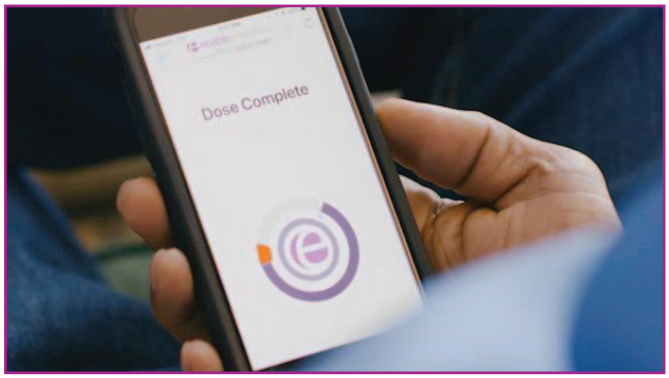
Enable Injections is a combination product company whose enFuse™ drug delivery platform is synonymous with large-volume wearable infusion technology. When biopharma companies want to make their therapeutics more convenient for patients, they partner with Enable Injections to combine their products with the most size efficient body-worn self-administration devices available. These symbiotic alliances support product differentiation that allows Enable Injections, which specializes in subcutaneous delivery of 5-50 ml doses, to share in the commercial success of biologic therapies. The combination of the enFuse technology - which can be used in early stage clinical evaluations - with new therapeutics is expected to increase adherence and positively impact outcomes across a broad range of diseases.

Enable Injections: the Leader in a Fast-Growing Sector

The drugs and devices comprising these combination products will reach the market simultaneously. Enable's technology delivers a subcutaneous flow of the drug and offers a less costly, more convenient alternative to IV administration of viscous, large-volume drugs. It allows patients to easily and comfortably administer the biologic at home or work while continuing their daily routines without the need to sit for hours to receive treatment. In a sector expected to grow at a CAGR of 23% until 2024, Enable Injections' technology is attracting multiple biopharma partners, suggesting it will be a key driver of this growth.

Drugs & Delivery are an Inseparable Combination

By overcoming the barriers to high-volume subcutaneous delivery, and with innovations such as its Smart EnFuse Bluetooth connectivity for HIPAA-compliant data capture to help patients adhere to regimens, Enable Injections has placed itself in a strong position in the sector. Continuous patient-centered innovations ensure that Enable Injections remains the partner of choice for companies that want to differentiate biologics or prolong lifecycles of existing large-volume drugs.



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EVONIK
POWER TO CREATE

Corporate Description

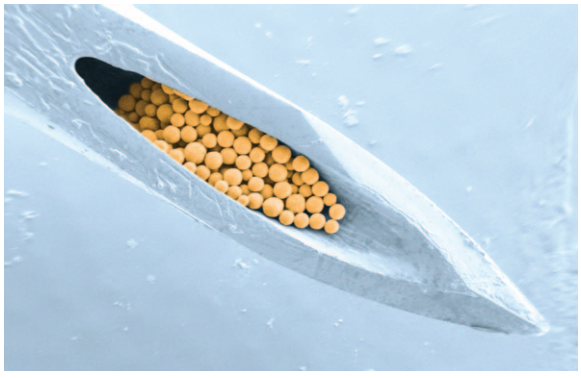
Evonik is one of the world leaders in specialty chemicals, with more than 36,000 employees across more than 100 countries and €14.4 billion in annual sales in 2017. The Business Line Health Care is a strategic partner to the world's pharmaceutical companies, helping customers transform their APIs into high-performance medicines for more than 60 years. For oral and parenteral drug delivery, Evonik combines market-leading portfolios of functional excipients with best-in-class formulation development and manufacturing services. We are also one of the world's largest and most specialized CMOs for API, HPAPI and intermediates. Our global strength, expertise, and flexibility can help reduce project risk, accelerate the path to market, improve drug safety and efficacy, strengthen supply security, differentiate product brands, and improve patient compliance.

Oral Solid Dosage Forms

- With our EUDRAGIT® portfolio of functional polymers, Evonik provides pharmaceutical companies with unrivalled versatility to match any release profile for oral solid dosage forms. Being easy to handle, consistently manufactured to a high-quality standard, and compatible with all relevant process technologies, EUDRAGIT® polymers have a history of excellence for safety and performance that spans more than 60 years.
- Best-in-class formulation services and drug delivery technologies can be leveraged to protect the drug, improve targeting, and boost performance.
- With a global network of formulation and application experts, Evonik can reduce complexity from initial concept to final dosage form.
- Additional services include the clinical production and scale-up of oral solid dosage forms, and local regulatory support.

Specialized Parenterals

- Evonik is a global CDMO partner for specialized parenterals with strong backward integration in the design and production of excipients.
- RESOMER® is a broad portfolio of standard and custom bioresorbable polymers for parenteral controlled release with a proven track record for safety and supply security that spans more than three decades.
- As a global formulation and process development leader for polymeric microparticles, lipid nanoparticles, and implants, we provide advanced formulation solutions for systemic and local delivery across drug areas including siRNA, mRNA, oligonucleotides, peptides, and HPAPIs.
- In addition to project services from feasibility review through to clinical and commercial cGMP manufacturing, Evonik also provides aseptic filling services for powders, liquids, and suspensions.



EVONIK INDUSTRIES AG
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Exelead

Complex Drug Product Formulations

Exelead is a CDMO dedicated to the development and commercialization of therapeutics to treat life-threatening diseases for small populations. The company specializes in liposomal and PEGylated formulations for sterile drug products, offering rare dedication to the customer who needs a partner.

Exelead's development capabilities can be utilized to improve drug delivery and drug product characterization. At their Indianapolis, Indiana manufacturing facility, the Exelead team produces proprietary parenteral pharmaceuticals for oncology and enzyme replacement treatment, as well as for the treatment of numerous infectious diseases.

Exelead staff is a balance of chemists, chemical engineers, microbiologists and pharmaceutical manufacturing experts. Senior Exelead management is comprised of seasoned executives from the pharmaceutical and biotechnology industries. The company is a wholly owned subsidiary of Essetifin S.p.A. (Rome, Italy) and is led by John Rigg, CEO.

SERVICES OFFERED

End-to-End Solution

- Method Development & Transfer
- Process Development and Optimization
- Technical Transfer
- Clinical Manufacturing
- Process Scale Up
- Commercial Manufacturing
- Project Management and CMC Support

Flexible Production

- Liposomal Formulation
- PEGylation
- Aseptic Fill
- Automated Inspection
- Packaging
- Quality Control
- Sterility Assurance
- Quality Assurance
- Supply Chain

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CREDENCE MEDSYSTEMS

INNOVATION WITHOUT CHANGE

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.

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.

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Note: This product has not been evaluated by FDA.

Scienced-Based CDMO

Hovione offers customized services and innovative solutions from drug substance to drug product with high standards of quality and technical expertise. We provide reliable supply with flexible manufacturing to bring medicines to market faster. Utilizing innovative technologies and methodologies, and with a global footprint, Hovione is an integrated supplier to the pharmaceutical industry having the privilege of serving patients.

From Drug Substance to Drug Product

Hovione's expertise and methodologies that were used to develop complex API synthesis and world-leading spray-drying approaches are applied to inhalation and oral drug product with the new Drug Product Center. The facility is prepared to handle high potency compounds and operate within tight environmental control.

Hovione can manufacture drug substance all the way to commercial supplies and perform formulation development and production of early clinical supplies, as well as clinical supplies manufacturing for drug products. With blending, granulation, dry granulation, milling, tableting, film coating, and encapsulation equipment, we can supply few grams batches, for formulation evaluation, to Proof-of-Concept (POC) clinical batches.

The Leader in Commercial Spray Drying

Combining the largest capacity, the best scale-up science, and the most experienced team, we can handle projects from development to market. Our particle engineering technologies can address oral bioavailability, lung delivery, modified release, and taste masking. In each technology, we can support you from proof-of-concept to commercial manufacturing.

Our Particle Engineering manufacturing assets are spread over three sites (Cork, Loures, New Jersey) and range from pilot to very large-scale equipment. We can also handle highly potent compounds at our Loures and New Jersey sites in response to meet our customer's needs. Our Development-by-Design methodology allows our customers to save costly API, to shorten development timelines and get guaranteed results.

Everything for Inhalation

Inspired by innovation, Hovione's world-leading expertise in particle engineering, customized high-performance APIs, and formulation development are the ingredients for a partnership starting from clinical programs and into commercial supply.

The Company

Hovione has over 55 year of experience as a CDMO and is currently a fully integrated supplier offering from drug substance to drug product intermediate to drug product. With four FDA-inspected sites in the US, Ireland, Portugal, and China and development laboratories in Portugal and the US, Hovione provides branded pharmaceutical customers services for the development and compliant manufacture of innovative drugs, including highly potent compounds. Hovione employs 1,900 people worldwide and has more than 1300m3 of flexible production capacity.

We do well what is difficult, to give our customers what they cannot find elsewhere. Please visit www.hovione.com.

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Frontage Laboratories, Inc. Your Drug Development Partner

Frontage is a CRO providing integrated, scientifically driven research, analytical, and development services throughout the drug discovery and development process to enable biopharmaceutical companies to achieve their drug development goals.

We offer our clients comprehensive services in analytical testing and formulation development, drug metabolism, and pharmacokinetics (DMPK), bioanalysis, preclinical safety and toxicology, and early phase clinical studies. We have enabled many innovator, generic and consumer health companies of all sizes to file IND, NDA, ANDA, BLA and 505(b)(2) submissions in global markets allowing for successful development of important therapies and products for patients.

We successfully assist clients to advance hundreds of molecules through development to commercial launch in global markets. We are committed to providing rigorous scientific expertise to ensure the highest quality and compliance.

Integrated:
Capability and Expertise to Solve Complex Problems

Expertise:
Deep Pool of Talented & Highly-Qualified Scientists

Quality:
Strong Track Record of Regulatory Inspections

Chemistry, Manufacturing, and Control (CMC) Services

With an outstanding compliance history, the CMC team at Frontage operates under strict adherence to ICH and US FDA GMP guidelines.

Our broad portfolio of services spans drug product development, analysis, and clinical trial materials' delivery and supply, from preclinical stages through Phase II clinical trials. We support a range of delivery systems including oral solids, topical, and sterile.

We have extensive experiences in formulation development, analytical method development and validation, technical transfer, and clinical trial materials (CTM) manufacturing, as well as commercial product release and stability testing for US, EU, and Asian markets.

- Analytical Services for Small Molecule and Biologics
- Product Stability Storage and Testing
- Pre-Formulation and Formulation Development
- GLP Batch Production and Testing for Preclinical Study
- GMP Batch Production and Testing for Clinical Study
- Strong Quality & Compliance Track Record

Website: www.Frontagelab.com
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Quality > It's how you get from formulation to the pharmacy.

With an outstanding compliance history, the CMC team at Frontage operates under strict adherence to ICH and US FDA GMP guidelines. Our broad portfolio of CMC services spans drug product development, analysis, and clinical trial materials' delivery and supply, from preclinical stages through Phase II clinical trials.

To learn more, visit our website at **frontagelab.com/service/cmc/**

FRONTAGE
YOUR DRUG DEVELOPMENT PARTNER

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OR VISIT US AT: *frontagelab.com*

Gattefossé

We provide specialty excipients and drug delivery solutions to the health industries worldwide. With a service and distribution network that spans more than 60 countries, we ensure responsiveness to the pharmaceutical industry's needs from both regional and global perspectives.

Gattefossé Corporation serves customers in the USA, Canada, and Mexico.

Products

Each excipient is designed to meet a unique set of formulation and functionality objectives while conforming to the highest safety, quality, and regulatory standards. Our product offer includes solubilizers, emulsifiers, bioavailability enhancers, sustained release matrix formers, and skin penetration enhancers for all routes of administration. Additionally, we develop and share formulation technologies that are designed to transform lipid excipients into viable drug delivery systems.

Formulation Development Support

The new **Gattefossé Technical Center** in the USA works closely with drug developers in the region, providing hands-on assistance to advance drug pipelines, to speed up drug delivery projects, and essentially shorten the development path. Free of charge services include excipient screening, formulation characterization and ultimately development of prototype formulations for oral, topical, transdermal, and other routes of administration.

Investing in the USA

With a significant surge in hiring and personnel additions to our technical teams, our group continues investments in the region - including new facilities, new equipment and most importantly human capital and talent.

Core Values

The conviction that achieving an innovative edge benefits all concerned is rooted in the 135-year history of the Gattefossé enterprise. This vision is supported by our direct involvement in R&D and learning initiatives that foster knowledge sharing. Sponsoring St-Remy conferences for 50 years and AAPS scientific awards since the 1990's are examples of such initiatives.

Safety, Regulatory & Quality Support

Gattefossé characterizes each excipient's physico-chemical properties and safety profiles and ensures each product has global regulatory acceptance. Every product is supported with full dossiers including safety data, regulatory standing, and updated Drug Master Files with the FDA.

Our Goal

We aim to simplify formulation decisions that minimize attrition rates and shorten the drug development path. For existing drugs that could benefit from improved dosing, better patient compliance, or extension of product life cycle, we emphasize innovative formulation technologies. For new drug entities that suffer from solubility and bioavailability issues, we focus on guidance for pre-formulation decisions that may be combined with innovative drug delivery approaches.

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We Offer

- Innovative excipients
- Expertise in LBDDS
- Simplified decisions
- Shorter development time

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GATTEFOSSÉ

People make our name

GatewayAnalytical
A ChemImage Company

INDUSTRY LEADING TURNAROUND TIME | MULTI-DISCIPLINED ANALYTICAL EXPERTS | FULLY CERTIFIED & ACCREDITED LAB | PERSONALIZED CUSTOMER SERVICE

Gateway Analytical is an innovative analytical laboratory that specializes in providing expert testing services to the pharmaceutical, medical device, and materials science industries. Built with quality as our cornerstone and timeliness, and customer service as our core values, we are able to offer project turnaround in as fast as 24 hours in a GMP-compliant environment. Our new, fully equipped 8,000-sq-ft laboratory space features HEPA-filtered controlled environments, ISO 9001 and ISO 17025 accreditations, specialized sample preparation capabilities, and a dedicated space for handling cytotoxic drug materials. Gateway is able to provide industry leading materials analysis services tailored to support a variety of unique drug development projects.

Identify Foreign Particulate

We identify and source foreign particulate using:

- Microscopy (optical, polarized light, fluorescence)
- FTIR spectroscopy
- Raman spectroscopy
- SEM-EDS

Count, Size & Identify Particle Populations

We count, size, and characterize your wanted (API, excipients, etc.) and unwanted (foreign particulates) particles using:

- Light obscuration (HIAC)
- SPE (automated Raman/LIBS)
- Automated SEM-EDS
- Raman Chemical Imaging

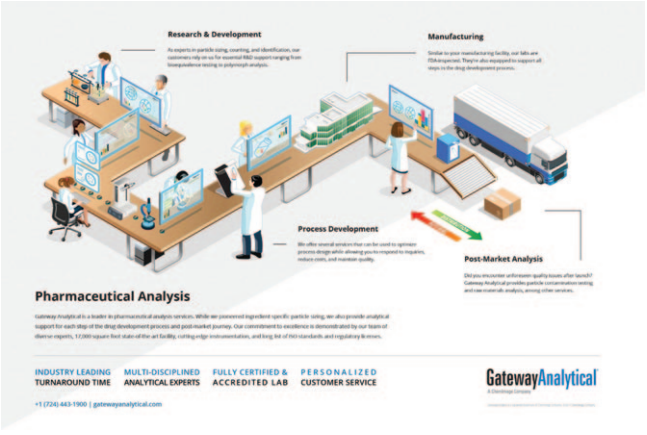
Specialized Testing Services

We provide specialized testing services, such as:

- Chemically specific counting, sizing, and identification of API, excipient, and foreign particles
- API distribution using automated SEM-EDS
- Glass delamination
- Cytotoxic materials handling
- Cleanroom garment shedability testing

Provide Support for R&D, Specialized Projects & Method Transfer

Drug development is more than just clinical trials. Our pharmaceutical analysis services provide support for your company at all stages of development, from preclinical decisions to post-market regulatory inquiries. Pharmaceutical products are evaluated on two critical metrics: efficacy and safety. While these two measuring sticks guide your clinical trials and determine primary and secondary endpoints, you know there are many more metrics that contribute to successful drug development. The quality of raw materials, the particle size distribution of drug ingredients and even the composition of a storage container can affect process outcomes. These data points may not make headlines, but they can make or break an application for marketing approval. To learn more about Gateway Analytical and how we are helping to make the world healthier and safer, visit our website at www.gatewayanalytical.com.



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Founded in 1977, JRF Global is one of the oldest (40+ years) and most respected non-clinical Contract Research Organization in Asia. JRF's capabilities spanning from Discovery to Development phase provides integrated services to both innovator and generic pharma companies.

Salient Features

- GLP & AAALAC accredited
- 300+ employees, 700+ clients across 60+ countries
- Spread across 6 locations worldwide (USA, Canada, Spain, UK, India & Japan)
- 29000+ GLP studies across all industries and have been well received by US FDA, EMA, MHRA, and other regulatory agencies
- State-of-the-art animal house facility among the best in Asia
- Experienced in handling small molecules, biologics/biosimilars, vaccines & herbal products
- JRF's fully integrated chemistry and toxicology services offer an attractive value proposition in terms of efficiency, deliverables & cost.

Unique Solutions for our Sponsors

- **A Research Foundation:** No bureaucracy quick decision-making
- **Re-invest Top $ Back to the Organization:** New services & people
- **Integrated Services Under One Roof:** Custom Synthesis/Medicinal Chemistry, P-C Chemistry, Analytical/Bioanalytical Chemistry, ADME/PK, Exploratory & GLP Toxicology, Safety Pharmacology & IND-Enabling Studies
- **Extensive Experience in Regulatory Submissions Globally**
- **Client Dedicated Project Management**

Services at a Glance

- P-C Chemistry, Analytical/Bioanalytical Chemistry
- Med-Chem & Custom Synthesis
- *In vitro* DMPK
- *In vivo* Pharmacokinetics
- Efficacy Models
- Safety Pharmacology
- Genotoxicity
- DART - Segment I, II, III
- Carcinogenicity
- IND-Enabling Studies
- Dermal Absorption Studies (in vitro & in vivo)
- Impurity Profiling
- Zebra Fish Discovery Assays
- Environmental Risk Assessment (Tier I & II)
- Expertise in Niche Areas (eg, Ophthalmology, Inhalation & Dermal Studies)

Quality & Project Management Support

- JRF Global's top management is committed and actively involved in the establishment, management and monitoring of quality systems. This is achieved by documenting quality policies and objectives and ensuring that both are understood and implemented by all scientists' at all the levels.
- Ensuring that appropriate GLP focused processes are implemented to fully satisfy the GLP needs, thereby ensuring satisfaction of the customers' expectations and company objectives.
- Project Management team at JRF Global ensures various non-scientific elements of the collaboration are appropriately coordinated and bridged for a smooth operational flow resulting in agreed turnaround times.
- Manages information flow to all stakeholders in a timely manner.
- Periodical updates about the progress of the project.

Lonza Pharma & Biotech

As one of the world's most renowned companies for contract development and manufacturing, Lonza Pharma & Biotech is recognized for our reliable, high-quality services, our global capacity, our innovative technology platforms, and our extensive experience. From 2013 to 2016, our contributions supported 36% of launches with small-molecule breakthrough designation. In 2016 alone, we provided manufacturing services for more than 50 commercial molecules and conducted more than 250 development programs. We have helped launch pioneering autologous cell therapies.

Success for us is when you, as our partner, are fully satisfied. We continuously improve and innovate to meet your expectations and improve your chances of business success. Our broad capabilities span across biologics, small molecules, bioconjugates, and cell and gene therapies. We manage projects from pre-clinical stage through to commercialization, and our expertise covers both drug substance and drug product.

We believe that the best outcome – for you and for your patients – can only come as a result of a successful collaboration. Together, we can solve the next challenge and bring your next medicine to life.

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metrics contract services

Company Overview

Metrics Contract Services is a full service pharmaceutical development and manufacturing organization serving clients worldwide. We deliver proven scientific and operational excellence for oral dosage forms. Today, as a subsidiary of Mayne Pharma Group, we offer clients more resources and capabilities than ever before.

Pharmaceutical Development and Clinical Trial Materials Manufacturing

We offer comprehensive formulation development services 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 more than 100 chemists on staff, Metrics analyzes 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 total engineered containment through customized, hardwall isolation technologies. Containment is achieved at 30 nanograms per cubic meter of room air; 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-Man (FTIM) Studies

Metrics Contract Services has successfully delivered materials for over 150 FTIM 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

The parent company of Metrics Contract Services, Mayne Pharma, recently invested $80 million to significantly expand facilities and equipment at its site in Greenville, NC. The new 126,000 sq ft, oral dose commercial manufacturing facility quadruples the company's US manufacturing capacity, and the repurposing of existing space creates 10+ new analytical laboratories and formulation development suites.

Metrics Contract Services can now offer a complete "concept to commercialization" solution in one contiguous location for clients, providing larger scale and increased capabilities for seamless scale-up, eliminating the need for site transfers.

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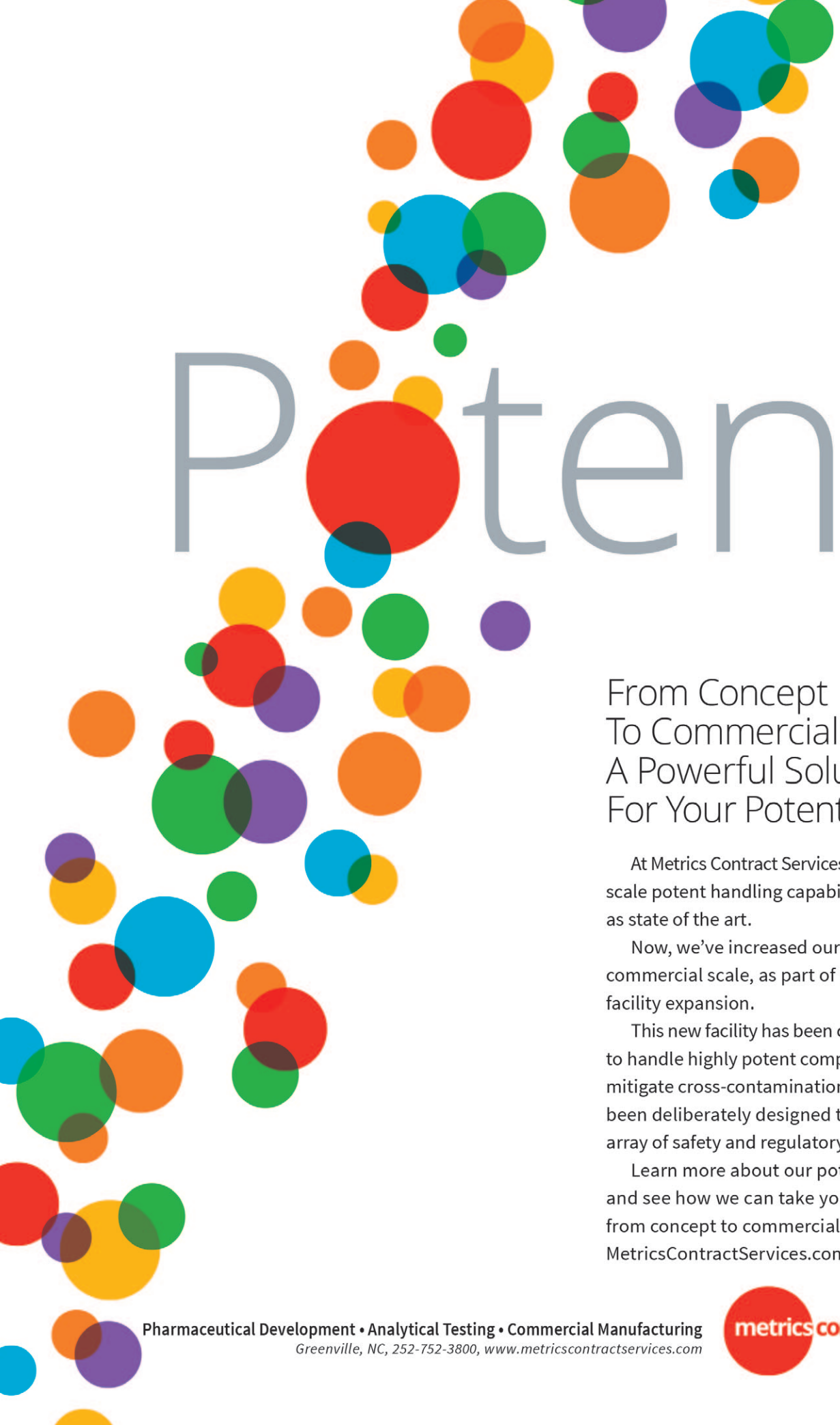


From Concept To Commercialization. A Powerful Solution For Your Potent Projects.

At Metrics Contract Services, our development scale potent handling capabilities are regarded as state of the art.

Now, we've increased our capacities to commercial scale, as part of our $80-million facility expansion.

This new facility has been custom engineered to handle highly potent compounds and mitigate cross-contamination risks. Plus, it's been deliberately designed to meet a diverse array of safety and regulatory requirements.

Learn more about our potent services and see how we can take your potent product from concept to commercialization. MetricsContractServices.com/potent.

Pharmaceutical Development • Analytical Testing • Commercial Manufacturing

Greenville, NC, 252-752-3800, www.metricscontractservices.com

metrics contract services

Customized, Activated/ Functionalized Polyethylene Glycols (PEGs)

We are your trusted global partner for the development and supply of commercial quantities of functionalized PEGs (polyethylene glycols). Those in turn, are essential for your PEGylated therapeutic proteins for drug delivery. Our offerings include high-purity materials for use in investigational products in every phase of clinical development and in commercialized products. We understand that you care about rapid and cost-effective time to market. Therefore, setting the right quality attributes for the functionalized PEG is crucial for the manufacturing and stability of your PEGylated product — we can help you get it right. And during the marketing phase, expertise in life-cycle management and regulatory affairs can help you safeguard your compliance.

Our portfolio of ready-to-use functionalized PEGs

- Linear MPEGs (up to 40kDa)
- Branched PEGs
- Linear bifunctional PEGs (linkers)
- Multi-arm PEGs
- Monodisperse PEGS - Backbone chemistry and activation

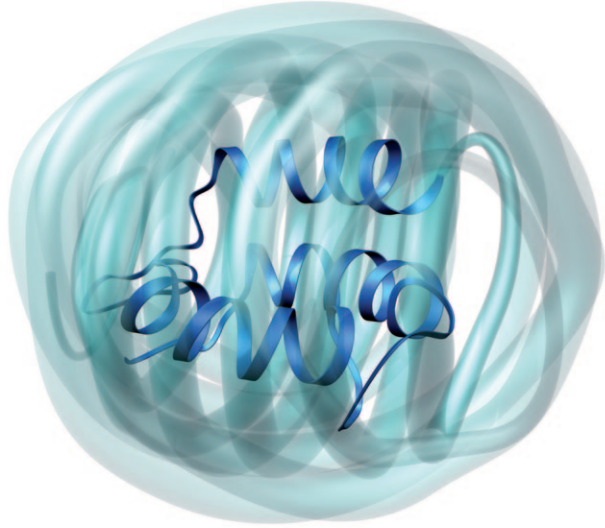
Applications

- For the PEGylation of therapeutic proteins at every phase of clinical development and commercialization
- Linker substances for Antibody Drug Conjugates (ADC)
- As part of medical devices (e.g. biodegradable hydrogels)

Custom development expertise for functionalized PEGs

Our experience in the development and scale-up of functionalized PEGs — ranging from pre-clinical evaluations to large-scale commercial quantities — has a long tradition. Our development projects can be highly customized to your individual needs supported by our dedicated experts and worldwide presence. We can assist you in exploration of synthetic pathways (feasibility), process development, manufacturing under GMP, as well as analytical test methods and validation.

All backed by the required QA and QC and an excellent audit record. At the respective development stage, quality and supply agreements will support your supply security on a commercial scale. With MilliporeSigma, you have a partner you can count on to help you get your product to market more quickly.



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MilliporeSigma
Polyethylene Glycol Technical Expertise
EXPLORE PURITY
Optimize your pegylation process with our high-purity, polyethylene glycols (PEGs). Backed by our expert support from feasibility to scale-up, our broad product line and customized, functionalized PEGs will help you achieve higher yields at every scale of production.
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The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.
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 Advanced Business Development Division in 2015 for tackling a variety of today's problems, and the division created OXYCAPT™ Multilayer Plastic Vial & Syringe to solve some issues of existing primary packaging for injectable drugs.

Products

OXYCAPT™ Vial & Syringe consists of three layers. The inner and outer layers are made of cyclo-olefin polymer (COP), the most reliable polymer in the pharmaceutical industry. The middle layer is made of state-of-the-art polyester developed by MGC.

The oxygen-barrier property is almost equivalent to glass and much better than COP. 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 & syringe. All of the containers are 100% inspected by the machinery.

There are 2-mL, 6-mL, and 10-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 & tub formats. As customizability is one of the features for plastic, MGC is able to consider developing customized OXYCAPT™ containers if requested.

Biologics is a target application for OXYCAPT™ because it is 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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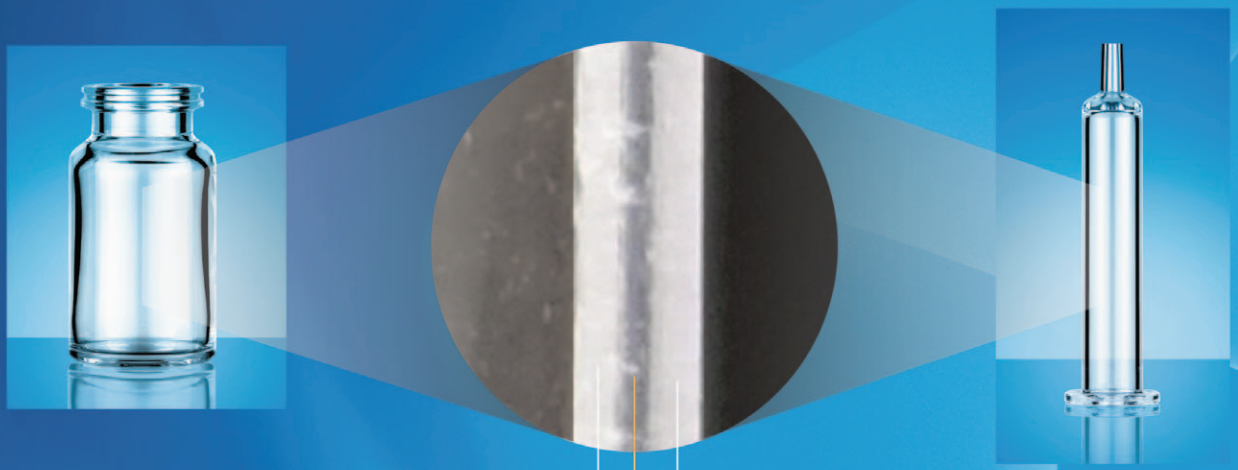
OXYCAPT™ Plastic Vial & Syringe

Multilayer Configuration



Water Vapor Barrier Layer (COP)
Oxygen Barrier Layer
(Oxygen Absorbing Polymer)
Drug Contact & Water Vapor Barrier Layer
(COP)

- ✓ Excellent Oxygen Barrier
- ✓ Excellent Water Vapor Barrier
- ✓ Very Low Extractables
- ✓ Excellent pH Stability
- ✓ Low Protein Adsorption
- ✓ Excellent UV Barrier
- ✓ High Transparency
- ✓ High Break Resistance
- ✓ Easier Disposal than Glass
- ✓ Much Lighter than Glass
- ✓ Customizable
- ✓ Suitable for Biologics

MITSUBISHI GAS CHEMICAL

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https://www.mgc.co.jp/eng/products/abd/oxycapt.html

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NEMERA is a **world leader in the design, development, and manufacturing of drug delivery devices** for the pharmaceutical, biotechnology & generics companies. **Nemera always puts patients first**, providing the most comprehensive range of devices in the industry. Nemera's services and products cover several key delivery routes:

OPHTHALMIC

0% PRESERVATIVES IN THE DRUG, 100% EYE PROTECTION

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

NASAL, BUCCAL, AURICULAR

EASY USE, EASY BREATHE

The number of drugs delivered through the nasal, buccal and auricular route is expanding. **Patients need high-performance and reliable spray systems.** Nemera offers **various technologies** with a full range of metered pumps and valves platforms, for Prescription and OTC applications: **Advancia®, SP270+ and SP370+, SP27, and SP37.***

DERMAL & TRANSDERMAL

CONVENIENT DEVICES FOR DERMAL DELIVERY

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

PARENTERAL

COMPLEX DEVICES, SIMPLE PATIENT CARE

Parenteral drug administration exposes patients and healthcare professionals to many hazards. **Patients need safe, reliable, and easy-to-use devices.**

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

INHALATION

NEMERA, A PARTNER OF CHOICE

The pulmonary route is widely used for drugs treating lung diseases but it can also be the pathway for systemic treatments. **Over 10 million patients use devices manufactured by Nemera every day. From concept generation to large scale manufacturing,** Nemera is the key partner for your inhalation device.

ELECTRONIC

KNOW-HOW & CAPABILITIES TO ANSWER PATIENTS' NEEDS

Nemera also developed electronic know-how and capabilities to answer patients'needs. Nemera's innovation department leverages multi-skilled teams to develop tailored electronic solutions across multiple device platforms.

we put patients first

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-grades of multi-compendial Mannitol and Sodium Succinate NF (Anhydrous & Hexahydrate) have been launched 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 was launched in 2014 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 will soon celebrate 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

PFANSTIEHL, INC.
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Founded in 1994, Noble® is the global leader in medical device training solutions, patient onboarding strategies, and multisensory product development for the world's top pharmaceutical brands and biotechnology companies. Focused on driving innovation, Noble works closely with brand, device, and commercialization teams to develop turnkey solutions that improve onboarding and adherence, bringing value to clients and patients alike.

We have the expertise to make a difference for patients and brands

As a fully integrated product development company, Noble's in-house design, development, and manufacturing expertise enables the seamless transition of concepts from design/engineering to manufacturing. Noble's experience and platforms in these disciplines are supported by an award-winning cross-functional team of industrial, mechanical, material, manufacturing, and quality engineers who consistently develop novel solutions related to mechanical demonstration device requirements. Such solutions result in unparalleled demonstration devices that accurately mimic the behavior of key device features, all while having the ability to be reset and function reliably over the lifetime of the product.

Our exclusive industry-leading collaborations uniquely position us to serve our clients and deliver unrivaled value and quality. Through cooperative agreements with prominent device manufacturers, Noble is provided key product specification information and insights, thereby ensuring that all training and demonstration devices not only simulate commercial drug delivery device functionality, but also provide patients a hyper-realistic simulation experience.

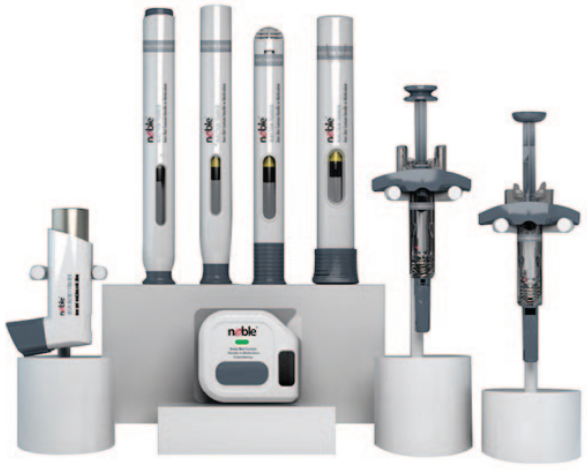
Beyond Noble's device manufacturer partnerships, our device agnostic technologies allow us the versatility to accommodate a wide variety of autoinjector, prefilled syringe, on-body, and respiratory device form factors – all while being a low-cost reusable solution to safely and effectively onboard users.

We're more than a product development company – we're your go-to resource

In addition to developing innovative training platforms and holistic-based solutions, Noble also offers a variety of services designed to provide clients with comprehensive support through pre-and post-launch. We provide clients with in-depth market research, ranging from device usability and preferences, competitive analysis to training and onboarding benchmarking. We also prepare you to get the most out your launch with customized utilization and commercialization strategies, including forecasting, best practices for training devices and patient support, lifecycle management, a revolutionary Train the Trainer program, and more. Plus, Noble's reach spans the globe – with major facilities located in Orlando, FL, and Ningbo, China – so when you're ready to ship, we are well equipped to handle your global logistics management and help you navigate the nuances of shipping your patient training resources worldwide.

Experience the Noble difference

Noble is changing the future of adherence and onboarding through research-driven insights, innovative technologies and patient-focused solutions. Our products drive innovation to make a true impact, and our advanced strategies – from development to commercialization to utilization – are purpose-built to help transform your bottom line. Find out how Noble can make a world of difference for your patients and your brand



Help patients get past the *sticking point* of injections

Prefilled Syringe Demonstrators

Designed to Match BD UltraSafe™ 1mL & 2.25mL Product Line

Device Replication
Resettable Safety Mechanisms+
Locking Needle Guard
Optional Custom Flange

Locking Needle Guard
Designed to simulate safety and shielding systems while also allowing users to reset for multiple practice sessions

Simulation Tip Options

ENCASED

AGITATOR

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Find out how Noble's prefilled syringe demonstrator platforms can increase user confidence and help patients get past the point of needle anxiety.

Contact us today **888.933.5646** or **GoNoble.com/PFSPlatforms**

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.

FACILITIES

State-of-the-art cGMP facilities in North America, Europe and Australia support products destined to over 100 countries; site segregation for Sch II-V Controlled Substances, Animal Health, Hormonal Products, Penicillin Products, Cytotoxins, SafeBridge™ Band 1-4 Potent Compounds; Cold Chain packaging and distribution at 2-8°C, -20°C, -40°C, -80°C, and -196°C for Advanced Therapeutic Medicinal Products (ATMPs); low humidity packaging; and modified environments for oxygen and light sensitive products.

DRUG DEVELOPMENT:

Full service Formulation Development including Analytical Development/Characterization. We are able to offer formulation development services for a variety of dosage forms including: tablets, capsules, powders, gels, creams, liquids, solutions, suspensions, emulsions, suppositories, pessaries, granules for reconstitution, and drug in capsule/vial.

CLINICAL TRIAL SERVICES:

Tablet, Capsule, Powder and Liquids Manufacturing, Analytical Development, Stability Testing, Clinical Packaging & Labeling including product Blinding & Randomization, Global Storage & Distribution, sterile & non-sterile drug manufacture for early stage studies, as well as Returns Management & Destruction.

COMMERCIAL SERVICES:

Commercial drug manufacturing including Commercial scale-up. Packaging Services for Oral Solids, Powders, Liquids, Creams, and Gels, as well as Injectable & Parenteral Delivery forms including Device Assembly. Analytical & Stability Services in support of commercial supply.

POTENT COMPOUNDS:

Contained manufacturing and packaging services for clinical and commercial medicines. PCI's state-of-the-art, purpose-built, contained manufacturing site handles potent compounds with OEL's down to 0.01µg/m3, and was recognized by ISPE as a Facility of the Year in 2013. Contained potent compound manufacturing is further supported by segregated, purpose-built packaging facilities in both Europe and North America.

SERIALIZATION

Leveraging over 7 years of commercial Serialization services to domestic and emerging markets, PCI offers clients both integrated and stand-alone Serialization solutions.

RECENT DEVELOPMENTS

In the last year, PCI acquired Millmount Healthcare, located in Dublin Ireland in the European Union, Pharmaceutical Packaging Professionals located in Melbourne, Australia, and Sherpa Packaging Professionals located in San Diego, CA.

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Our Pledge,
The Industry Leading Experience

PCI Pharma Services – a market leader for integrated drug development and commercialization

The foundation of a successful partnership is trust. At PCI, we pledge our unwavering commitment to provide the industry leading customer experience. This focus enables us to be a trusted partner to 19 of the top 20 pharmaceutical companies in the world. We earn trust by providing our clients flexibility and responsiveness, outstanding operational performance, and the support of uncompromising quality and regulatory standards. By this commitment we deliver our clients an end-to-end development and commercialization solution including drug development and scalable drug manufacturing, integrated clinical trial services, and commercial packaging services. We are trusted to support lifesaving medicines destined to over 100 countries around the world.

We invite you to learn more about what the PCI pledge can do for the success of your business.

pci MANUFACTURING SERVICES

pci CLINICAL SERVICES

pci COMMERCIAL PACKAGING

Industry Leading Serialization Expertise and Technology with More Than 7 Years Supplying Domestic and Emerging Markets

- 80+ serialization installations across global network
- DSCSA & FMD ready
- Primary, secondary, and tertiary packaging
- In-line product aggregation offering
- Secure data exchange

pci PHARMA SERVICES

pciservices.com

Portal Instruments, a clinical-stage medical device company is developing a next- generation needle-free drug injection platform to transform the drug delivery experience for patients suffering from chronic diseases, such as ulcerative colitis, multiple sclerosis, rheumatoid arthritis, and psoriasis.

Today, patients suffering from many chronic conditions have access to biologic drugs that can greatly improve their well-being. Unfortunately, those drugs must often be self-injected via a needle and syringe, which can lead to patient anxiety and uncertainty. In some cases, patients may refuse treatment or skip injections and then might not be able to reach the outcomes that they wish.

Founded 4 years ago, Portal is looking to transform the experience for patients who are on these life-changing therapies. Originally developed in Ian Hunter's lab at MIT, the Portal's digital jet-injector is the only computer controlled needle-free drug delivery device technology available for clinical evaluation.

Previous jet-injectors used a mechanical means (eg, a high-powered spring, compressed air or gas cartridges like CO2 or Nitrogen) to generate, essentially, an "explosion" to inject the shot. These devices were loud, limited in delivery volume and often painful.

The Portal system, in contrast, uses a computer-controlled linear actuator that pressurizes the medication and injects it in a very fine jet. It can administer up to 1 mL of medication, is relatively quiet, fast, and automatically adapts to both viscosity and temperature of the medication. Studies have shown that patients perceive less pain and prefer the Portal Needle-free injector versus needle and syringe injections.[1]

A key part of the needle-free injection platform and patient experience are the companion digital tools to track injection timing and remind patients when it's time for injection. The platform also has the potential to aggregate anonymized patient data on adherence, which can offer useful insights into treatments across a population set.

Portal Instruments is a Series B-funded medical device company and its Quality Management System is ISO 13485 certified.

Portal is looking to develop strong partnerships with all major biologics players seeking to gain an edge by offering their therapeutics fully integrated with an optimum delivery system.

1. Kojic, N., et al. (2017). An Innovative Needle-free Injection System: Comparison to 1 ml Standard Subcutaneous Injection. AAPS PharmSciTech. doi: 10.1208/s12249-017-0779-0.

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E: partnering@portalinstruments.com W: www.portalinstruments.com

Needle Free Injections

Portal Instruments

PATIENT PREFERRED*

<1 SECOND DELIVERY TIME

ADAPTIVE TO DRUG VISCOSITY

1 ML DELIVERY VOLUME

Portal Instruments *connected needle free injector.*
Innovative technology for your innovative science.

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DRUG DELIVERY PARTNERSHIP | **JAN 28-30** | WEST PALM BEACH, FL
PHARMAPACK EUROPE | **FEB 6-7** | PARIS, FRANCE

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*Kojic, N., Goyal, P., Lou, C.H. et al. *AAPS PharmSciTech* (2017) 18: 2965. https://doi.org/10.1208/s12249-017-0779-0

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.

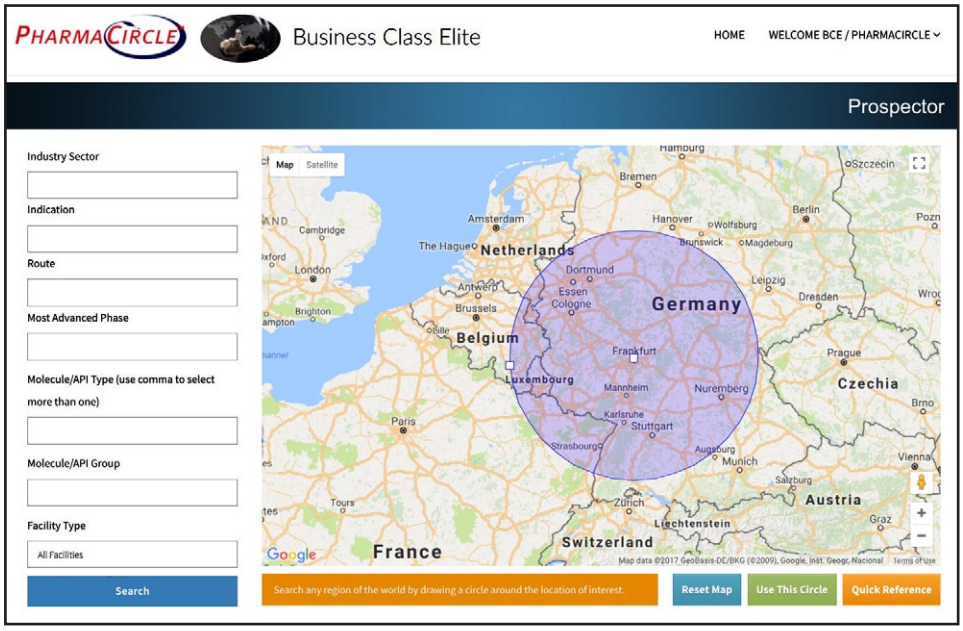
PharmaCircle's premier database tracks drugs, biologics and combination products in all stages of development, connecting pipeline and product information with formulation and component details. The database delivers seamless integration of scientific, clinical, safety, regulatory, manufacturing and commercial information, and detailed analyses on over 6,000 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
- Veterinary Market Data

To learn more about how PharmaCircle can help your company, please see our ad on pages 16 & 17 and 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

ProMed
Molding for Life

For over 20 years, ProMed Molded Products has specialized in the molding of small, intricately designed silicone components and sub-assemblies. In 2006, ProMed Pharma leveraged this expertise to begin production of polymer-based drug-releasing implants and combination device components. Working with both established and early stage medical device and pharmaceutical companies, ProMed develops robust manufacturing processes and platforms for controlled release of drugs from a variety of materials.

Key markets for our services include cardiovascular, neurology, and ophthalmology. Representative drug-device applications include steroid-eluting pacing leads, drug-eluting stents and balloons, and antimicrobial catheters. ProMed also supports pharmaceutical companies developing extended release formulations utilizing subcutaneous implants, intrauterine devices, intravaginal rings, and ophthalmic implants.

Specific capabilities include:

- Silicone molding - transfer, liquid injection, insert and compression molding
- Plastic injection molding and extrusion - biomaterial options such as ethylene vinyl acetate (EVA), polyurethanes, and poly (lactide co-glycolide) (PLGA)
- Experience with steroids, hormones, antibiotics, and microbicides
- Micro molding of parts as small as 0.1 mg
- Design assistance, rapid prototype tooling, molding, and assembly
- Dedicated processing and mixing equipment for APIs
- Class 10,000 clean rooms, Class 5 isolators
- More than 10,000 square feet of available manufacturing space for new manufacturing operations

ProMed utilizes both in-house anlaytical testing and partnerships with state-of-the-art facilities to ensure that drug content, drug elution, purity, mechanical strength, and dimensional specifications are consistently met. ProMed Pharma's Quality Assurance is dedicated to delivering drug-eluting components of the highest quality that can be used in implantable pharmaceutical products and life- sustaining medical devices. Our Quality System was designed using the 21 CFR 820 Quality System Model and supplemented with applicable sections of the Pharma cGMPs. ProMed Pharma is ISO13485 certified and FDA registered and inspected.

ProMed Pharma, LLC
15600 Medina Road
Minneapolis, MN 55447
T: (763) 331-3800 F: (763) 331-3888
E: info@ promedpharmallc.com W: www.promedpharmallc.com

Year Founded: 1878
Number of Employees: 1,900 in Life Sciences worldwide; 95,000 in the SGS Group

WHO WE ARE

SGS Life Sciences is a leading contract service organization providing analytical development, biologics characterization, utilities qualification, biosafety and quality control testing for over 40 years. SGS operates a global, wholly-owned network of 18 Life Science laboratories with facilities in the US, UK, Canada, Belgium, France, Germany, Italy, Switzerland, China, and India. Our customers include large multinational companies as well as midsize or small local enterprises. The Top 20 pharmaceutical companies trust SGS as a partner for their quality control testing.

We serve a variety of Life Science companies including pharmaceutical, biopharmaceutical, biotechnology, and medical device manufacturers. SGS offers laboratory services that include analytical chemistry, microbiology, stability studies, method development, and protein analysis. SGS is the world's leading inspection, verification, testing and certification company.

SERVICES OFFERED

cGMP Analytical Testing & Development

- Quality control testing of raw materials, APIs, and finished products
- Monograph testing (USP, EP, BP, and JP)
- Analytical method development and validation
- Container testing (extractables and leachables)
- Stability testing according to ICH guidelines or customer specifications
- Microbiological testing
- Utilities qualification (air, gas, water and surface)
- Medical device testing

Biopharmaceutical/Bioanalytical/Biosafety

- Protein/peptide analysis and quantification
- Glycosylation analysis
- Biologics safety testing (endotoxin, virus and mycoplasma)
- Cell-line characterization
- Host-cell impurity testing (residual DNA)
- Virus testing (cell bank and virus seeds characterization)
- Antibody product analysis
- Bioanalysis (mass spectrometry, immuno- and cell-based assays)

SGS Life Sciences
E: lss.info@sgs.com
W: http://www.sgs.com/en/life-sciences

LIFE SCIENCES

LABORATORY SERVICES

LIFE INSPIRED, QUALITY DRIVEN

GET TO MARKET QUICKLY, SAFELY & EFFICIENTLY

SGS Life Sciences enables the medical and health innovators of the world to deliver life-changing solutions in the quickest, safest and most efficient way, helping improve the lives of many.

SERVICES INCLUDE:

- Biologics Characterization
- Extractables & Leachables
- Stability
- Biosafety
- Microbiology
- Analytical Chemistry

CONTACT

Lss.info@sgs.com

www.sgs.com/lifescience

WHEN YOU NEED TO BE SURE

SGS

SGW Pharma Marketing is dedicated to connecting drug development companies with audiences that matter most: development partners, technology and service seekers, and investors. With 27 years of consumer and B2B pharma experience, you can count on us to deliver innovative solutions that make a difference.

Public Relations/Media Relations

Working as your sole strategic partner or as an extension of your communications staff, our dedicated team has the direct industry experience and knowledge necessary to develop your unique message and target only the most appropriate B2B vehicles that will result in the most valuable editorial coverage.

Social Media Development/Management

Promote your business through the major social media channels via all leading social media platforms, blogs/RSS, viral content, online communities, news aggregators, and social influencers the smart way! We can help effectively engage with your online audience, both present and potential, by developing and executing a comprehensive Social Media Plan based on your specific requirements.

Multimedia/Interactive/Web Design

Building web applications that help your business run and grow takes a set of unique skills and talent. We can be your architect, project manager, analyst, designer, developer, internet marketing specialist, social media strategist, quality assurance tester, and hosting support staff.

SEO/SEM

Today, more marketers are realizing SEM and SEO are not separate disciplines. Instead, they are complementary programs that can benefit each other to increase conversion rates and share of voice. SEM and SEO teams should work together to improve results on their respective programs, increase return on search marketing investment, and drive a lasting lift in conversion across the board. Let us show you how.

Advertising Design

We employ unique, big picture solutions that get to the heart of the real advertising issues, challenges, and opportunities facing the ever-evolving B2B life science industry. Our specialized active and passive campaigns (online or print) and collateral design/corporate ID positioning, including logo development and branding, accommodate any size budget and are geared directly toward complementing and supporting your life science business development initiatives.

Full-Service Video Production

Through the years, we've created the commercials, videos, social media content, multi-media presentations and animation used in all of SGW Integrated Marketing Communications / LifeScience PR integrated strategies and distribution touch points. In 2016 we reorganized the division, made significant investments in equipment, our facilities and people. Our working philosophy is simply to operate smarter, faster and more efficiently for our clients. And while we're very proud of the hundreds of creative awards we've won over the years, we're much prouder for the successful results we deliver for our clients.

Traditional/Online Media Planning & Placement

Analyzing, planning, and buying media is a time-intensive, multi-pronged approach that requires dialogue with the client, defining the target audiences, focused research, a media strategy that maximizes efficiency of the available budget, and strategic placement capabilities.

Tradeshow/Event Planning

Access to potential clients is at an all-time high, so let us help you ensure your competitive advantage through our tradeshow & event logistics management, booth design capabilities, high-tech lead generation, and promotional materials.

SGW Pharma Marketing
219 Changebridge Road
Montville, NJ 07045
T: (973) 585-1264
W: www.sgwpharma.com Contact: Amy Bunn (abunn@sgw.com)

Reaching your audience is important. **Engaging** them is paramount.

SGW Pharma Marketing is dedicated to connecting drug development companies with the audiences that matter most: development partners, technology and service seekers, and investors.

We never lose sight that branding a technology or service is more engaging when you make a real connection with people. Our formula blends the "human factor" into each of our brand-building strategies.

Whether you're talking to R&D scientists, business development professionals, or C-level executives, we focus on creating tailored messaging to each group and delivering it via a wide range of services.

For more information, contact Amy A. Bunn
O 973.585.1264 C 919.412.2470 E abunn@sgw.com
or visit us online at sgwpharma.com

SGW | Pharma MARKETING

Your brand's formula for success.

STRATEGIC PLANNING • CREATIVE • VIDEO/AUDIO • MEDIA PLANNING
DIGITAL • MOBILE • SOCIAL MEDIA • PUBLIC RELATIONS

SHL is a world-leading solution provider in design, development, and manufacturing of advanced drug delivery systems. We work with leading biotechnology and pharmaceutical companies to develop drug delivery devices, including compact disposable auto injectors, reusable pen injectors, and complex inhaler systems. These devices use standard pre-filled syringes and cartridges, as well as novel primary containers.

SHL has always invested significantly in research and development. The investment has especially intensified over the past 10 years, allowing us to upgrade our broad pipeline of next-generation drug delivery devices. These innovative devices include advanced reusable and disposable injectors that can be enhanced through digital implementations and can accommodate high volume and high viscosities. Our investments have strengthened our support in the advancement of drug development and digital healthcare.

With locations in Taiwan, Sweden, Switzerland, China and the US, our experienced engineers and designers develop product enhancements and breakthrough drug delivery solutions for clients globally.

As SHL is determined to provide the most comprehensive range of solutions and services, we maintain all key capabilities and processes in-house to ensure the best quality and time-to-market. SHL offers:

- Innovative device design based on customer/patient needs
- An advanced in-house tooling center for drug delivery devices
- An extensive range of molding solutions
- Customized assembly and testing equipment
- Semi-automatic and fully automatic assembly solutions
- Analytical sciences responsible for full test method development, validation, and transfer
- Final assembly, labeling, and packaging services for drug delivery devices

- ISO13485- and FDA 21 CFR 820-compliant systems
- 510K clearance and compliance to medical device cGMPs
- A wide range of own patented solutions, significant licensing opportunities, and strong commitment to protecting customers' IP
- Proven track record of successful devices on the market
- Dedicated experienced professionals to ensure the success of your project
- Forward-looking initiatives exploring new technologies and future developments, including comprehensive connectivity offers

With over 4,000 staff worldwide, our organization consists of several distinct group companies:

SHL Medical
Designs, develops and manufactures advanced drug delivery devices, as well as provides final assembly, labeling and packaging services for leading pharmaceutical and biotech companies across the globe.

SHL Healthcare
Develops and manufactures equipment solutions for home, hospital and long term care use.

SHL Technologies
Provides contract manufacturing and engineering services for the production of complex medtech and industrial products.

SHL Group
Gubelstrasse 22, 6300 Zug, Switzerland
T:+41 41 368 00 00

Email: info@shl-group.com
URL: www.shl.group

SHL GROUP

We Bring Innovation to Life

Supporting high volume drug delivery

Bring your innovation to life with Molly® 2.25, a high-volume variation of SHL's classic Molly®, designed with improved anti-rolling features for enhanced safety.

www.shl.group

UPM Pharmaceuticals®
Formulating Your Future™

UPM Pharmaceuticals® is a Bristol Tennessee based contract development and manufacturing organization (CDMO) serving the pharmaceutical and biotechnology industries. UPM provides high-quality pharmaceutical drug development services that include formulation development, cGMP manufacturing and packaging, analytical method development, and testing from concept through commercialization.

UPM is your partner with a strict sense of quality, timeliness, sound scientific fundamentals, and affordability with which we complete all our projects. We focus on drug development and manufacturing for solid oral dosage forms, such as capsules and tablets, and semi-solid creams and ointments.

Scientific Expertise — UPM's scientific team includes some of the industry's best analytical chemists, formulators, and manufacturing specialists. Our experienced scientists provide innovative ideas and guidance to address our clients' unique product development challenges, such as low dose content uniformity, high dose compressibility, controlled drug release rates, and experimental designs for limited API availability.

Rapid and Responsive Turnaround — Our scientists and managers utilize daily planning meetings and a master scheduling process to ensure that every project will be completed on time, every time.

Quality Assurance Documentation — Our highly experienced quality assurance personnel manage complete cGMP quality systems that support formulation development, clinical and commercial manufacturing, and analytical testing.

TABLETS
- Capacity for 3.5 B units per year
- Single and bi-layered
- Mini-tablets and orally disintegrating
- Controlled humidity suite
- DEA controlled substances (CII-CV)
- Clinical and commercial scale

CAPSULES
- Capacity for 680 M units per year
- State-of-the-art encapsulation technology
- Range of 150-100,000 capsules per hour

CREAMS & OINTMENTS
- Capacity for 138,000 kg units per year
- Automated packaging lines for tubes and jars

DEA Licensed / FDA Inspected

UPM Pharmaceuticals, Inc.
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UPM Pharmaceuticals®
Formulating Your Future™

FROM CONCEPT TO COMMERCIAL FOR **SOLID DOSE & SEMI-SOLIDS**

UPM Pharmaceuticals is an independent, award-winning CDMO. We offer development and manufacturing of tablets, capsules and semi-solid dosage forms – including DEA controlled substances (CII–CV) and a controlled humidity suite. At our 476,000 sq ft facility in Bristol, Tennessee, our experienced personnel can advance your project from lab scale to commercialization in a single location. UPM has successfully implemented its serialization program.

Visit us at the following show

AAPS PharmSci 360
November 4-7, 2018, Booth# 2014
Walter E. Washington Convention Center
Washington, DC

To learn more, visit **www.upm-inc.com**
or call **+1 423 989 8000**

Processing Capabilities

- Dry blending
- Wet & dry granulation
- Fluid bed processing/drying
- Controlled substances (CII-CV)
- Clinical & commercial packaging
- Full analytical support

Tablets & Capsules

- Capacity for 3.5 billion tablets and 680 million capsules per year
- Sophisticated tableting and encapsulation technology
- Multi-layer tableting

Creams & Ointments

- Capacity for 138,000 kg units per year
- Automated packaging lines for tubes and jars

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E: infoUS@vetter-pharma.com





YOUR PARTNER IN ASEPTIC FILLING

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, and Vetter currently manufactures 5 of the world's top 10.

Collaborating with the top 20 (bio-)pharmaceutical companies worldwide, Vetter supports products from preclinical development through global market supply. Through its US and European facilities, Vetter Development Service provides state-of-the-art support for early stage products, with seamless transfer at Phase III to Vetter Commercial Manufacturing for large-scale production. We offer state-of-the-art technology and innovative processes to promote product quality and maximize API yield.

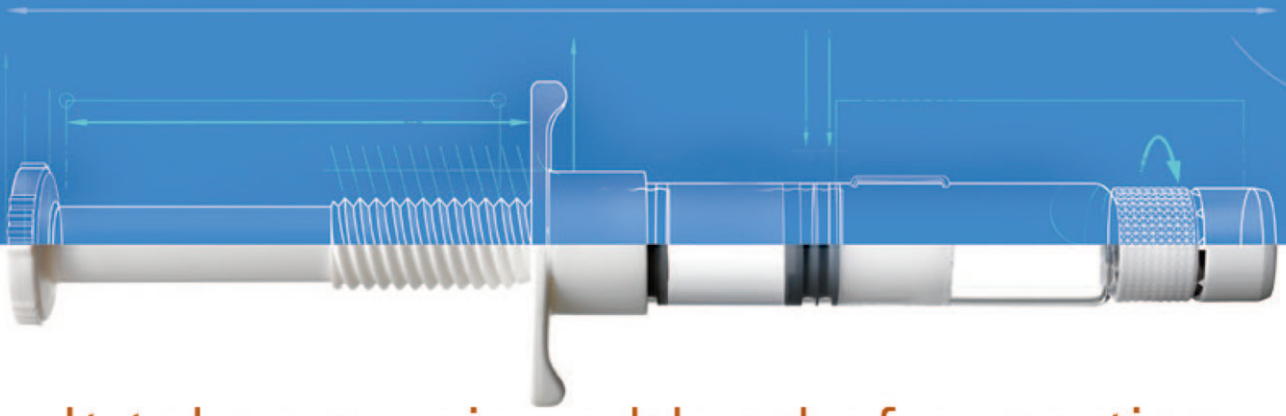
VETTER AT A GLANCE

- Headquarters in Ravensburg, Germany
- Additional clinical development facility in Chicago, US
- A Representative offi ce for Asia Pacific in Singapore and a subsidiary in Japan and South Korea
- Approximately 4,400 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 for more information.

From clinical development to commercial production



It takes a unique blend of expertise to deliver the right results

At Vetter, we look at your product from every angle. And help you find answers that make a difference in efficiency, productivity, safety, quality, and growth. From initial process design through high-speed fill and finish, learn how a partnership with Vetter will keep your product moving smoothly towards success.

- More than 35 years of experience in aseptic filling
- Expertise with many compound classes, including biologics
- Highly trained experts in key technical areas
- Integrated life cycle management
- Innovative drug delivery options
- State-of-the-art cGMP manufacturing
- Excellent global regulatory support

Vetter Development Service | **Vetter Commercial Manufacturing** | **Vetter Packaging Solutions**

CMO LEADERSHIP AWARDS 2018

FOYA 2018 Facility of the Year Awards
CATEGORY WINNER
Facility of the Future

Awarded state-of-the-art technologies and innovative processes

VETTER
Answers that work
www.vetter-pharma.com

US inquiries: infoUS@vetter-pharma.com • Asia Pacific inquiries: infoAsiaPacific@vetter-pharma.com •
Japan inquiries: infoJapan@vetter-pharma.com • EU and other international inquiries: info@vetter-pharma.com

West Pharmaceutical Services, Inc.

Committed to quality, collaboration, service and innovation

West is a leading global manufacturer in the design and production of technologically advanced, high quality, integrated containment and delivery systems for injectable medicines. We are a trusted partner to the world's top pharmaceutical and biotechnology companies—working by their side to improve patient health.

West Offers Proprietary Packaging, Containment and Drug Delivery Products

- **Stoppers and seals for injectable packaging systems:** to help ensure drug compatibility and stability, while also supporting operational efficiency
- **Syringe and cartridge components:** including custom solutions for the specific needs of injectable drug applications
- **Self-injection systems:** innovative, patient-centric technologies that are easy to use and can be combined with connected health technologies that have the potential to increase adherence
- **Containment and delivery systems:** including Daikyo Crystal Zenith®—a high performance polymer alternative to glass that can meet the challenges of sensitive biologics

Contract Manufacturing – Pharmaceutical, Biotech and Diagnostic

West contract manufacturing harnesses a powerful combination of innovation, technology, infrastructure and expertise to serve the pharmaceutical, medical and consumer industries. Along with more than 50 years of experience, we bring customers quality, safety and reliability in injection molding, contract assembly and finished packaging from our eight locations throughout North America and Europe.

- **NYSE: WST**
- **7,500 global employees**
- **Founded in 1923**
- **2017 sales: $1.6 billion**
- **West products used on a daily basis: approximately 112 million units***

*Based on 2017 annual sales.

Headquartered in Exton, Pennsylvania, USA, West has more than 50 locations, including 28 manufacturing facilities around the world:

- Australia
- Brazil
- China
- Denmark
- England
- France
- Germany
- India
- Ireland
- Israel
- Japan
- Mexico
- Serbia
- Singapore

A Commitment To Quality

An integral part of the healthcare industry, West's top priority is delivering quality products that meet the exact product specifications and quality standards customers require and expect. This focus on quality includes excellence in manufacturing, scientific and technical expertise and management. At the manufacturing level, this means producing clean, sterile, high-quality components to minimize disruptions to the supply chain and bringing safe, effective drug products to market—and to the patient—quickly and efficiently.

A Caring Corporate Citizen

West has a long and distinguished history of giving back to our communities, and a commitment to philanthropy is embedded in all that we do. The Company contributes to a wide range of organizations working to improve our world. The Herman O. West Foundation, an independently managed 501 (c) (3) entity sponsored by West, is committed to giving to children with special needs in the areas and communities where West employees live and work. Additionally, the West without Borders employee-led fundraising campaign encourages active participation at every local West site.

West Pharmaceutical Services, Inc. I 530 Herman O. West Drive, Exton, PA 19341

For complete contact information please visit www.westpharma.com.

#9724 1018

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.**

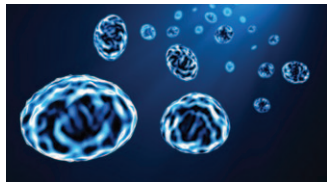
CDMO Services

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.**

Oral Solid Dosage Forms

Specialized to manufacture oral solid dosage (OSD) forms, Alcami's Wilmington, NC, site supports preclinical production through commercial launch and supply. Our cGMP manufacturing technologies are arranged in flexible suites designed for novel, advanced, and complex projects. Embedded within the manufacturing facility, our formulation development experts assist in product development and lifecycle management, including formulation changes and qualification of additional indication with expert small volume product support with small lot sizes made as needed. Development and manufacturing of OSD products are carefully tailored for orphan drug and niche dosage forms where micro batches and flexibility in processing equipment is critical to preserving API. Alcami gives you the capability to formulate a safe, stable medicine and develop a robust manufacturing process that is scalable for your commercial supply with OSD formulations and manufacturing teams being housed in the same state-of-the-art building. For more information, visit Alcami at **www.alcaminow.com.**

Nanoparticle Formulations



Ascendia Pharmaceuticals is a contract development and manufacturing (CDMO) company offering services for formulation development of poorly soluble drugs and other challenging development programs. Our formulation options include nanoemulsions, amorphous solid dispersions, nanoparticles, liposomes, and oral controlled release. These technologies are suitable for oral, topical, or injectable dosage forms. NanoSol is our technology for production of nanoparticle formulations. Ascendia has the capability to make nanoparticles from native drug crystals using ball milling, or lipid-based nanoparticle composites for lipophilic drugs. When the nanoparticle is delivered to the body there is greater surface area for dissolution, and by using enhancers in the formulation higher bioavailability can be more readily achieved. Ascendia can optimize nanoparticle formulations and produce clinical trial materials for first-in- man studies. For more information, contact Ascendia at (732) 640-0058 or visit **www.ascendiapharma.com.**

Development, Manufacturing & Testing

Avista Pharma Solutions is a contract development, manufacturing and testing organization, headquartered in Durham, North Carolina. With over 200,000 square feet of laboratory and manufacturing space in the US and UK, Avista Pharma offers a broad suite of scientifically differentiated services ranging from early stage discovery, API and Drug Product development, and cGMP manufacturing to stand-alone analytical microbiology testing support. Led by our broad experience and collaborative approach, we are committed to finding the shortest, most efficient path to success for our clients – success that goes beyond science. For more information, visit Avista Pharma Solutions at **www.avistapharma.com.**

Specialized Sterile Injectables

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

Parenteral Delivery Devices

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

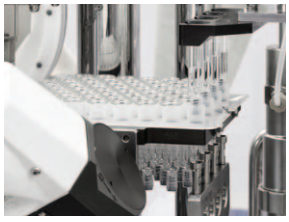
Platform Technology

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 12 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.**

Intelligent Dose Design

Leveraging its global early phase development centers of excellence in the UK and US, and its network of manufacturing sites around the world, Catalent offers its partners end-to-end solutions, encompassing early drug-product development, formulation, and delivery technologies, through to manufacturing and clinical supply services. By adapting for each molecule's unique characteristics and challenges, Catalent uses its formulation and development experience, and a wide range of tools and technologies to create dose forms that benefit patients. Catalent's multi-award-winning OptiForm® Solution Suite platform can assist in the development of innovative dose forms that can improve a drug's clinical efficacy and commercial success. OptiForm Solution Suite is fast, flexible, and fact-based, combining the broadest selection of enabling technologies to ensure the right decisions are made at each stage of development. For more information, contact Catalent Pharma Solutions at (888) SOLUTION or visit **www.catalent.com.**

Full-Service CDMO



CordenPharma is your full-service CDMO partner in the Contract Development & Manufacturing of APIs, Drug Products, and associated Packaging Services organized under 5 technology platforms - Peptides, Lipids & Carbohydrates – Injectables - Highly Potent & Oncology - Small Molecules - Antibiotics. With multiple cGMP manufacturing facilities across Europe and the US, CordenPharma experts translate your complex projects into high-value products at any stage of development. CordenPharma provides proprietary peptide, lipid, and carbohydrate technologies for cGMP-compliant products and services. We additionally specialize in Clinical (Phase I-III) and commercial supply of small molecules, unique expertise in both SPPS & LPPS technology for efficient peptide manufacturing, aseptic & terminal sterilization fill & finish, highly potent APIs (with exposure limits as low as 1 ng/m^3) and formulations (solid forms), segregated antibiotics, oncology drug products, and labeling/packaging. For more information, visit CordenPharma at **www.cordenpharma.com.**

Super Refined™ Excipients

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.**

On Body Delivery System

Enable Injections' on body delivery system (OBDS) delivers high-volume, often viscous drugs subcutaneously for patients to conveniently and discreetly inject at home, work, or on the move. The design is based upon over 12 years of research in minimizing injection pain with a strong emphasis on the end-user and Human Factors. The platform consists of a single injector up to 5-ml, 10-ml, 20-ml, 30-ml, 40-ml, 50-ml capacity - and associated transfer system. One of the three transfer systems (Syringe, Vial, or Fully Automated Reconstitution) is combined with each injector to provide the user with a simple disposable package. This package transfers the drug from the original container closure to the injector in a few intuitive steps. For more information, visit Enable Injections at **www.enableinjections.com.**

Enteric Coatings

New platinum standard for enteric coatings: Evonik has created an advanced combination polymer solution for enteric coatings to reduce processing complexity, lower preparation times and save costs. EUDRAGIT® FL 30 D-55 combines the respective benefits of two existing polymers with well-accepted monographs including EUDRAGIT® L 30 D-55: the gold standard for enteric coatings since 1955. Being highly flexible, plasticizer-free and able to be sprayed with a smooth, fast and no-stick process, it is ideal for microparticulates and other dosage forms that require excellent adhesion. As a single product, preparation times can be reduced by up to 70%. With only a thin film able to provide reliable enteric protection, it creates options for higher drug loadings. Formore information, contact Evonik at AAPS (booth 2127) or email **healthcare@evonik.com**

Liposomal & PEGylated Formulations

Exelead
Complex Drug Product Formulations

Exelead is a CDMO dedicated to the development and commercialization of therapeutics to treat life-threatening diseases. Exelead's core technologies focus on the manufacture of sterile drug products specializing in liposomal and PEGylation formulation technologies. Exelead has development capabilities that can be utilized to improve drug delivery and drug product characterization. The Indianapolis, Indiana manufacturing facility produces proprietary parenteral pharmaceuticals for oncology and enzyme replacement treatment, as well as for the treatment of numerous infectious diseases. Exelead manufactures drug products that are distributed globally and offers solutions at every phase of the drug development process (Pre-Clinical, Phase I/II/III, and Commercial). For more information, visit Exelead at **www.ExeleadBioPharma.com.**

CMC Services

FRONTAGE
YOUR DRUG DEVELOPMENT PARTNER

Ensure comprehensive product analysis with Frontage's team of experienced analytical scientists. We specialize in analytical method development, validation and transfer for product development and clinical trial materials (CTM) manufacturing support, as well as commercial product release and stability testing. Our services are designed to help sponsors throughout the drug development process in their effort to fully characterize drug substances, developmental formulations and commercial drug products. Our facilities house a wide range of the latest analytical instrumentation for a comprehensive array of methods. And, we continually keep pace with technology to ensure compliance with evolving regulatory and market requirements. Our development team can solve your analytical challenges efficiently. For more information, contact Frontage at (610) 232-0100 or visit **www.frontagelab.com.**

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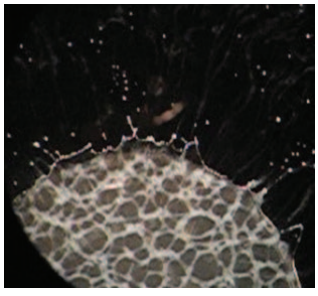
Gateway Analytical is an innovative analytical laboratory that specializes in providing expert testing services to the pharmaceutical, medical device, and materials science industries. Built with quality as our cornerstone and timeliness and customer service as our core values, we are able to offer project turnaround in as fast as 24 hours in a GMP-compliant environment. Our new, fully equipped 8,000-sq-ft laboratory space features HEPA-filtered controlled environments, ISO 9001 and ISO 17025 accreditations, specialized sample preparation capabilities, and a dedicated space for handling cytotoxic drug materials. Gateway is able to provide industry leading materials analysis services tailored to support a variety of unique drug development projects. For more information, visit Gateway Analytical at **www.gatewayanalytical.com.**

Self-Emulsifying Delivery



Gattefossé self-emulsifying drug delivery systems (SEDDS) are a simple and efficient solution for the delivery of poorly soluble compounds, and as of late for oral peptide delivery. Scientists have successfully developed SEDDS for delivery of Leuprorelin, Desmopressin, and Insulin, which has a MW of 5.8 KDa. This is made possible by hydrophobic ion-pairing of the peptide molecules and subsequently cloaking them with SEDDS formulations using Gattefossé excipients. SEDDS solubilize the peptides in the digestive tract while protecting them from enzyme degradation and glutathione reduction. Suitable excipients for effective peptide delivery include Labrasol® ALF, Gelucire® 44/14, Labrafil® M 2125 CS, and Peceol™. Solid SEDDS are also possible using processes such as granulation and hot melt extrusion. For more information, visit Gattefossé at **https://bit.ly/2xaa5BU.**

Pharmaceutical-Grade Oils

Gattefossé offers USP/NF-grade high-purity vegetable oils by ADM-SIO in the USA and Canada. Suitable for oral, topical, and other routes of administration, SIO's pharmaceutical-grade Soybean Oil IV, Olive Oil IV, and Sesame Oil IV-1 are highly refined by a process that removes impurities and yet preserves the natural antioxidants of the raw material. This ensures clarity, reduced pigmentation (lighter color), and most importantly, a higher stability throughout the product's shelf-life guaranteed 3 years after date of manufacture. SIO high-purity oils are ideal for solubilization of poorly soluble and/or sensitive API in capsule, soft gel, and injectable dosage forms. For more information, contact Deandra Wolfe of Gattefossé at **dwolfe@gattefossecorp.com.**

Contract Development & Manufacturing

Hovione is an international company with over 58 years of experience as a Contract Development and Manufacturing Organization (CDMO) and is currently a fully integrated supplier offering services for drug substance, drug product intermediate, and drug product. With four FDA-inspected sites in the US, China, Ireland, and Portugal, and development laboratories in Portugal and the US, the company provides branded pharmaceutical customers services for the development and compliant manufacture of innovative drugs, including highly potent compounds. For generic pharmaceutical customers, the company offers niche API products. Hovione also provides proprietary product development and licensing opportunities for drug products. In the inhalation area, Hovione is the only independent company offering a complete range of services. For more information, visit Hovione at **www.hovione.com.**

Non-Clinical CRO

Founded in 1977, **JRF Global** is one of the oldest (40+ years) and most respected non-clinical Contract Research Organization in Asia. JRF's capabilities spanning from Discovery to Development phase provides integrated services to both innovator and generic pharma companies. We offer fast, transparent, cost effective, and hassle-free services in Toxicology, Eco-toxicology, Chemistry, Environmental Fate and Metabolism, and other regulatory testing requirements. Our experienced and knowledgeable scientists have worked with pharmaceutical and biopharmaceutical, agrochemical, specialty chemical, industrial biotech, biocidal, cosmetic, and veterinary products. With locations in India, USA, UK, and Japan, we are the obvious partner-of-choice of over 600 companies for non-clinical safety data generation. For more information, visit **www.jrfglobal.com.**

Lonza Pharma & Biotech

At **Lonza Pharma & Biotech** we provide contract development and manufacturing services that enable pharma and biotech companies to bring medicines to patients in need. From the building blocks of life to the final drug product, our solutions are created to simplify your outsourcing experience and provide a reliable outcome, at the time when you expect it. Our extensive track record includes commercialization of pioneering therapies and manufacturing of a wide variety of biological and chemical drugs. We continuously invest to solve not just the current, but also the future challenges. Together, we can bring your next medicine to life. For more information, visit Lonza Pharma & Biotech at h**ttp://pharma.lonza.com.**

Capsugel® Colorista™

Capsule Delivery Solutions, part of Lonza Pharma & Biotech, launches the new Capsugel® Colorista™, a high-quality capsule based on an all-colorants™ formulation. This new capsule contains a broad selection of colorants suitable for use in major markets, allowing pharmaceutical customers to have access to a wide array of colors, and is available in both Vcaps® Plus (HPMC) and Coni-Snap® gelatin. Colorista™ capsules meet the demand of pharmaceutical developers who look for solutions that cut down on development time, while giving them flexibility to progress with technical development before the final commercial color decision is taken. To learn more on Colorista™, visit **https://www.capsugel.com/biopharmaceutical-products/colorista-capsules.**

Fast Track to Clinical Trials

With more than 140 successful FTIM fast track to clinical trial studies and materials completed, **Metrics Contract Services** understands what it takes to deliver this challenging and critical service. We offer a commitment to a 16- to 24-week timeline from receipt of a well-characterized NCE to shipment of clinical materials, plus specialized equipment, like our Xcelodose 600 micro dosing system, and a standardized internal process to ensure both speed and accuracy. For more information on our Fast Track to Clinical Trials services, visit **www.MetricsContractServices.com.**

Polyethylene Glycols (PEGs)

MilliporeSigma is your trusted global partner for the development and supply of commercial quantities of functionalized PEGs (polyethylene glycols). Those in turn, are essential for your PEGylated therapeutic proteins for drug delivery. Our offerings include high-purity materials for use in investigational products in every phase of clinical development and in commercialized products. We understand that you care about rapid and cost-effective time to market. Therefore, setting the right quality attributes for the functionalized PEG is crucial for the manufacturing and stability of your PEGylated product — we can help you get it right. And during the marketing phase, expertise in life-cycle management and regulatory affairs can help you safeguard your compliance. For more information, visit MilliporeSigma at

Functional Chemicals

MITSUBISHI GAS CHEMICAL

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

Nemera

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

Device Training Platforms

noble®

Noble works with drug delivery device manufacturers and biopharmaceutical companies to develop self-injection training devices, including autoinjectors, prefilled standard and safety syringes, wearables, and respiratory platforms to provide biopharmaceutical companies improvements in launch strategies and patient adherence. Noble's training and onboarding platforms are built true to form and function to device specifications and are available as off-the-shelf and customized solutions, with the optional inclusion of proprietary technologies for products ranging from mechanical training devices to smart error-correcting training platforms. These devices are designed to emulate a device's form factor and functionality, including tactile feedback, operational forces, and administration steps to provide patients with accurate simulation of actual delivery devices while being a low-cost reusable solution to safely and effectively onboard users. Companies providing reusable, device-comparable training products will be well positioned for competitive differentiation through improved patient satisfaction, adherence, and outcomes. For more information, contact Noble at (888) 933-5646 or visit **www.gonoble.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

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.**

Needle-Free Injection

Portal Instruments

Portal Instruments, a clinical-stage medical device company is developing a next- generation needle-free drug injection platform to transform the drug delivery experience for patients suffering from chronic diseases, such as ulcerative colitis, multiple sclerosis, rheumatoid arthritis, and psoriasis. Today, patients suffering from many chronic conditions have access to biologic drugs that can greatly improve their well-being. Unfortunately, those drugs must often be self-injected via a needle and syringe, which can lead to patient anxiety and uncertainty. In some cases, patients may refuse treatment or skip injections and then might not be able to reach the outcomes that they wish. For more information, visit Portal Instruments at **www.portalinstruments.com.**

Silicone Components

For over 20 years, **ProMed Molded Products** has specialized in the molding of small, intricately designed silicone components and sub-assemblies. In 2006, ProMed Pharma leveraged this expertise to begin production of polymer-based drug-releasing implants and combination device components. Working with both established and early stage medical device and pharmaceutical companies, ProMed develops robust manufacturing processes and platforms for controlled release of drugs from a variety of materials. Key markets for our services include cardiovascular, neurology, and ophthalmology. Representative drug-device applications include steroid-eluting pacing leads, drug-eluting stents and balloons, and antimicrobial catheters. For more information, visit ProMed at **www.promedpharmallc.com.**

Contract Service Organization

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

Advanced Delivery Devices

SHL Group (Scandinavian Health Ltd) is a world-leading solution provider in design, development, and manufacturing of advanced drug delivery systems. We work with leading biotechnology and pharmaceutical companies to develop drug delivery devices, including compact disposable auto injectors, reusable pen injectors and complex inhaler systems. Significant investment in R&D has allowed us to enhance our broad pipeline of "next-generation" drug delivery systems. These include a range of disposable and reusable injectors with fixed or variable dosing, high dose accuracy, and the ability to accommodate high volumes and high viscosities. With locations in Taiwan, Sweden, China, and the US, our experienced engineers and designers develop product enhancements and breakthrough drug delivery solutions for pharma and biotech clients globally. For more information, visit SHL Group at **www.shl.group.**

Development Services

UPM Pharmaceuticals is an independent, award-winning contract development and manufacturing organization (CDMO). The Bristol, TN-based CDMO serves the pharmaceutical and biotechnology industries with its offering in tablet, capsules, and semi-solid dosage form manufacturing – including DEA controlled substances (CII-CV) and a controlled humidity suite. Experienced personnel at UPM can provide high-quality pharmaceutical drug development services that include formulation development, cGMP manufacturing and packaging, analytical method development and testing from concept through commercialization all in one 476,000-sq-ft facility. UPM is characterized by its strict sense of quality, timeliness, sound scientific fundamentals, and affordability with which they complete all projects to ensure success to clinic/market. For more information, contact UPM Pharmaceuticals at (423) 989-8000 or visit **www.upm-inc.com.**

Full-Service CDMO

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

Integrated Delivery Systems

West is a leader in developing and manufacturing pharmaceutical delivery systems. The company has unique technologies in self-injection systems, including the SmartDose® drug delivery platform and the award-winning SelfDose® patient-controlled injector, that enable patients to self-administer injectable medicines at home. West is also collaborating with HealthPrize Technologies on a connected health offering that is designed to improve and reward medication adherence with unique technologies. The offering integrates HealthPrize's Software-as-a-Service medication adherence and patient engagement platform into injectable drug delivery systems, providing biopharmaceutical companies and their patients with an end-to-end connected health solution. For more information, contact West at (800) 345-9800 or visit **www.westpharma.com.**

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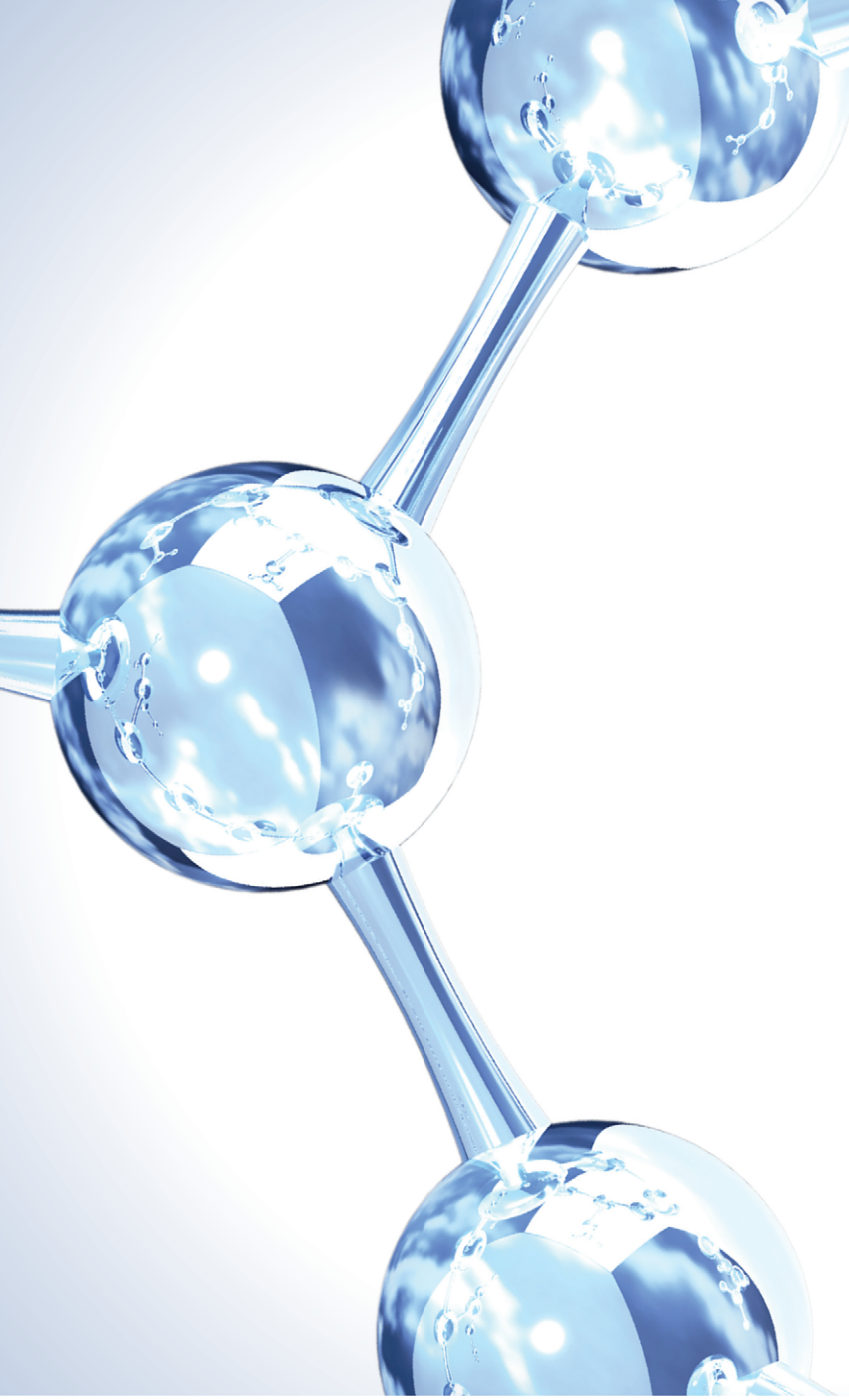

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EARLY DEVELOPMENT

your molecule has potential. our passion is to help you start smart and move faster.

As the #1 global leader in drug development, we have the passion to help you start smart and get to clinic faster. Selecting the right molecule, understanding its challenges, and applying the right formulation technology early, are the keys to success. Give your molecule its best chance! Catalent can design a customized accelerated program based on deep experience across hundreds of development programs, broadest technology portfolio, strong analytics and integrated manufacturing.

BROAD EARLY DEVELOPMENT OFFERINGS:

SOLUBILITY SCREENING FOR CANDIDATE SELECTION
DMPK MODELING
API OPTIMIZATION
SOLID STATE SERVICES
PREFORMULATION TESTING
BIOAVAILABILITY ENHANCEMENT
GLP FORMULATIONS

OPTIFORM® SOLUTION SUITE

One accelerated, flexible, and data-driven solution combines all analytics, services and materials your molecule needs from candidate selection into Phase 1.

CANDIDATE SELECTION → PRE-CLINICAL → BIOAVAILABILITY SOLUTIONS → PHASE 1 MATERIAL

DEVELOPMENT DELIVERY SUPPLY

Catalent. More products. Better treatments. Reliably supplied.™

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