Drug Development & Delivery

November/December 2017 Vol 17 No 8 www.drug-dev.com

Market Forecasts & Corporate Capabilities

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

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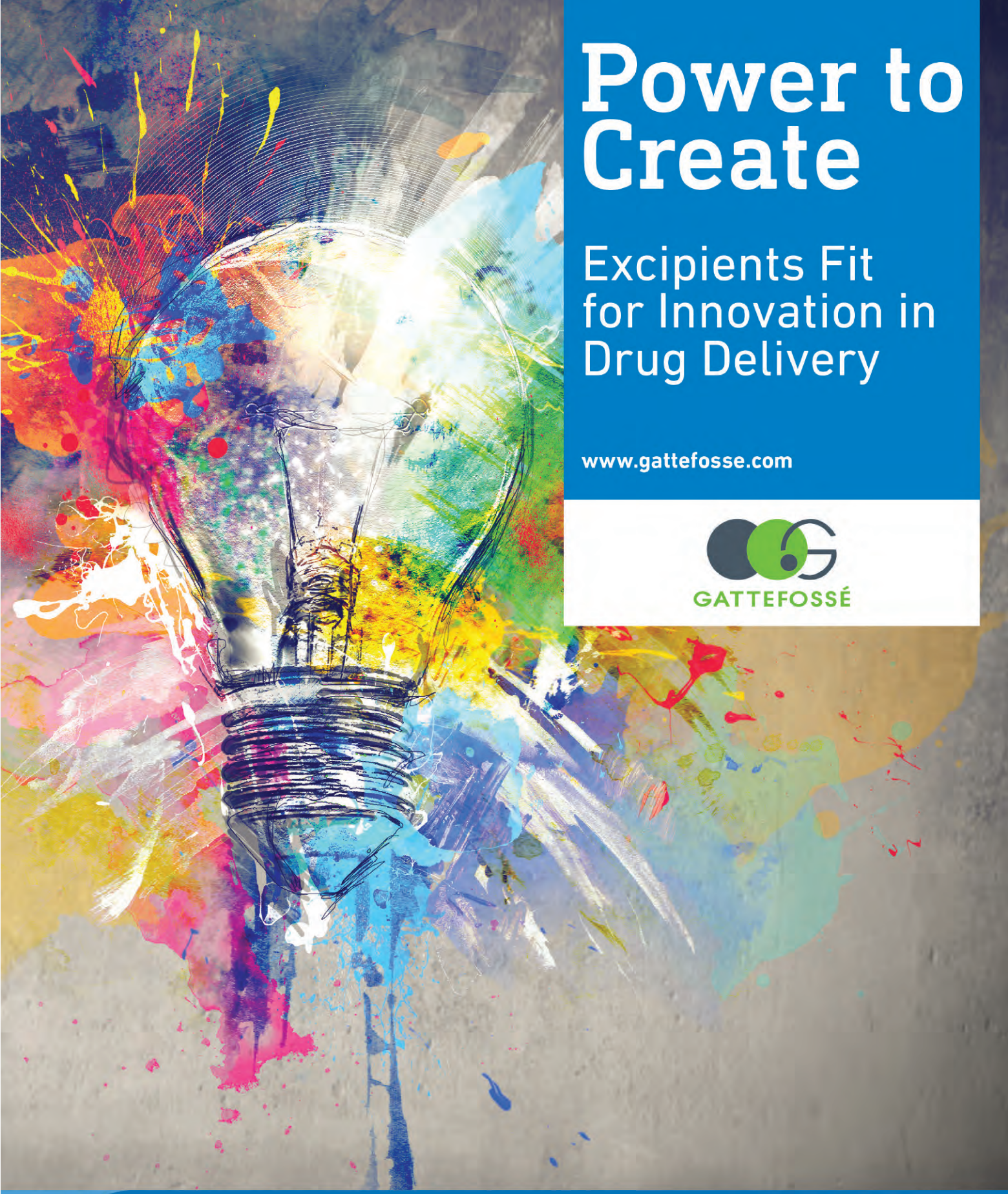

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November/December 2017 Vol 17 No 8

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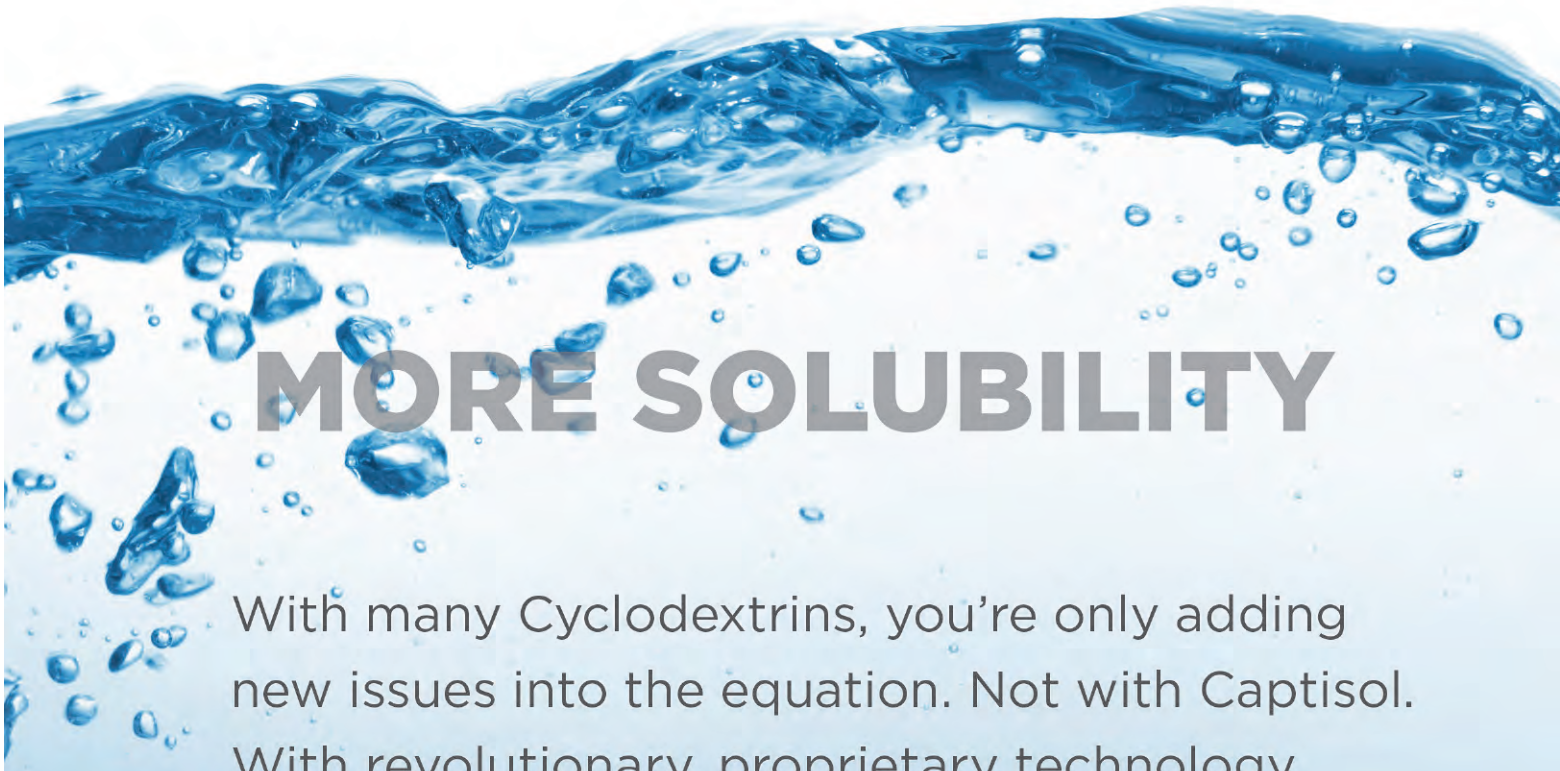

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Integrated Solutions for Cold Chain Pharmaceuticals

Helping to Make Cold Storage Less Complicated

Patient safety is of utmost concern in the pharmaceutical industry, with the FDA requiring drug manufacturers and their manufacturing partners to have strong quality management systems.

Temperature-sensitive drugs require storage solutions that not only meet the needs of the drug product, but also ensure compliance with regulatory guidelines in a properly monitored and sustained environment. Any deviation from the ideal environment can affect patient safety and jeopardize the drug's quality, resulting in loss of potency, efficacy or even the need to discard the product entirely.

Drug products such as biologics, vaccines, and products whose chemical and physio-chemical stability depends on temperature put an added emphasis on pharmaceutical manufacturers to ensure proper handling, storage, transportation and dispensing.

The West Contract Manufacturing team can support integrated device assembly solutions that meet regulatory and U.S. Food and Drug Administration guidance for temperature sensitive drug handling. This can help simplify the supply chain and reduce overall risk by improving production efficiencies.

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- Aggregation
- MES infrastructure
- Work cell history and analytics

As one of the largest custom manufacturers of reusable pens and auto injectors, the West Contract Manufacturing team can provide proper cold chain solutions – helping to ensure that temperature sensitive drugs are delivered to the patients who need them without compromising the integrity, efficacy, safety or security of the drug.

For more information visit **www.westpharma.com**

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Aytu BioScience Receives Market Approval for the MiOXSYS System for Male Infertility

Aytu BioScience, Inc. recently announced that the Australian Government Department of Health and Therapeutic Goods Administration (TGA) has approved the MiOXSYS System for inclusion on the Australian Register of Therapeutic Goods. MiOXSYS has been approved by the TGA as an aid in the diagnostic assessment of semen quality for patients undergoing male infertility evaluation.

Josh Disbrow, Chief Executive Officer of Aytu BioScience, commented "MiOXSYS continues to gain traction with its international commercial expansion as regulatory bodies, like Australia's TGA, approve the product for clinical use in the assessment of male infertility. In Australia, approximately one in six couples suffer from infertility, and almost half of these cases can be attributed to male factor infertility. Therefore, male infertility assessment remains a significant area of clinical need. We are pleased to now be able to offer MiOXSYS to clinicians and laboratories throughout Australia who seek to better identify and treat men with suspected infertility and for which oxidative stress may be implicated."

With Australian TGA approval, the Company has engaged in Australian market development activities and is in early discussions with distribution partners. The Company expects to announce a distribution partner and launch MiOXSYS for clinical use in the coming quarters.

Aytu BioScience is a commercial-stage specialty life sciences company focused on global commercialization of novel products in the field of urology, with a focus on products addressing vitality, sexual wellness, and reproductive health. The Company currently markets two prescription products in the U.S.: Natesto, the first and only FDA-approved nasal formulation of testosterone for men with hypogonadism (low testosterone, or "Low T") and ProstaScint (capromab pendetide), the only FDA-approved imaging agent specific to prostate specific membrane antigen (PSMA) for prostate cancer detection and staging. Additionally, Aytu is developing MiOXSYS, a novel, rapid semen analysis system with the potential to become a standard of care for the diagnosis and management of male infertility caused by oxidative stress. MiOXSYS is commercialized outside the US, where it is a CE Marked, Health Canada cleared product, and Aytu is planning US-based clinical trials in pursuit of 510k medical device clearance by the FDA. Aytu's strategy is to continue building its portfolio of revenue-generating products, leveraging its focused commercial team and expertise to build leading brands within growing markets. For more information, visit aytubio.com.

Aytu also now owns wholly owned subsidiary Aytu Women's Health (formerly Nuelle, Inc.), a personal health and wellness company focused on women's sexual wellbeing and intimacy. Aytu Women's Health markets Fiera, a personal care device for women that is scientifically proven to enhance physical arousal and sexual desire. Fiera is a consumer device and is not intended to treat, mitigate, or cure any disease or medical condition.

SOTIO Completes Enrollment of Phase III VIABLE Study

SOTIO, a biotechnology company owned by the PPF Group, recently announced the enrolment of the last patient into the VIABLE study, a global Phase III clinical trial evaluating DCVAC/PCa in combination with docetaxel in patients with metastatic castration resistant prostate cancer (mCRPC).

The VIABLE study (Eudra CT: 2012-002814-38: IND: 015255) is a randomized, double blind, multicenter, parallel-group Phase III study to evaluate the efficacy and safety of DCVAC/PCa as an add-on therapy to first-line standard of care chemotherapy in men with metastatic castration resistant prostate cancer (mCRPC). The study is being conducted in around 200 clinical sites in 21 European countries and the US. Since its launch in 2014, 1182 patients were randomized in the VIABLE study. Data on the overall survival of patients in this study are expected in 2020.

Ladislav Bartonicek, CEO of SOTIO, said "The completion of the patient enrolment to the VIABLE study is an important milestone. It is a major step toward registration of our active cellular immunotherapy and making it available for routine clinical use. We are grateful to all our medical partners, the patients and their families for their ongoing support of this study. After finalization of treatment and follow-up period we expect to finalize the primary analysis of the data in 2020."

"This pivotal clinical trial is building on many years of scientific research at Charles University and University Hospital in Motol in Prague and intensive development efforts of SOTIO," said Radek Spisek, Chief Scientific Officer of SOTIO. "Completing the enrollment underlines the significant progress SOTIO has made in the assessment of the innovative, dendritic cell-based active cellular immunotherapy for late-stage prostate cancer and other cancer indications. We believe that adding DCVAC/PCa to standard chemotherapy can prolong patients' lives and slow down disease progression."

DCVAC is an active cellular immunotherapy treatment that is produced individually for each patient using the patient's own dendritic cells (that are part of the immune system), to induce an immune reaction against tumor antigens. SOTIO is developing three product candidates using the DCVAC platform to affect multiple different cancers in various stages of disease - DCVAC/PCa for patients with prostate cancer, DCVAC/OvCa for patients with ovarian cancer and DCVAC/LuCa for patients with lung cancer. DCVAC/PCa was the first SOTIO investigational medicinal product to enter clinical research. The company is currently evaluating the safety and efficacy of DCVAC in multiple Phase I to Phase III clinical trials.

SOTIO is an international biotechnology company leading the efforts of PPF Group to build a diverse biotechnology portfolio through its own research & development, collaborations, in-licensing, investments, mergers and acquisitions. The company is developing new medical therapies, focusing on the treatment of cancer and autoimmune diseases. SOTIO's most advanced project is its proprietary platform of active cellular immunotherapy (ACI) based on dendritic cells. SOTIO is conducting multiple Phase I to Phase III clinical trials verifying the safety and efficacy of its DCVAC products.

G1 Therapeutics Announces Publication in Cancer Discovery

G1 Therapeutics, Inc. recently announced the publication CDK4/6 Inhibition Augments Anti-Tumor Immunity by Enhancing T Cell Activation, is available online in the journal Cancer Discovery.

The research, conducted in collaboration with leading academic cancer centers, demonstrates that transient inhibition of cyclin-dependent kinases 4 and 6 (CDK4/6) with trilaciclib (and other selective CDK4/6 inhibitors) activates effector T cells and enhances anti-tumor immunity in preclinical models. While chronic exposure to CDK4/6 inhibitors can block T cell proliferation, in vivo studies showed that short-term exposure to CDK4/6 inhibitors results in increased T cell recruitment and enhanced effector cell function in tumors, which significantly augments anti-tumor efficacy of checkpoint inhibitors.

"This research reinforces our hypothesis that transient inhibition of CDK4/6 is critical for enhancing anti-tumor immunity," said Mark Velleca, MD, PhD, Chief Executive Officer of G1. "We're excited about the findings, which further support our rationale for combining trilaciclib with chemotherapy, as well as checkpoint inhibitors."

"We believe that the addition of trilaciclib to chemotherapy/checkpoint combinations will not only preserve immune system function, but will also directly enhance effector T cell activity," added Raj Malik, MD, Chief Medical Officer of G1. "Trilaciclib, the only short-acting, intravenous CDK4/6 inhibitor in development, is currently being tested in four Phase 2 trials, including a study in small-cell lung cancer patients receiving chemotherapy and Tecentriq, with or without trilaciclib (ClinicalTrials.gov Identifier: NCT03041311)."

G1 Therapeutics is a clinical-stage biopharmaceutical company focused on the discovery and development of novel therapeutics for the treatment of cancer. G1's two clinical assets, trilaciclib and G1T38, are CDK4/6 inhibitors, a validated and promising class of targets for anti-cancer therapeutics. Trilaciclib and G1T38 have broad therapeutic potential in many forms of cancer and may serve as the backbone of multiple combination regimens. In addition, G1 is advancing G1T48, a potential first/best-in-class oral selective estrogen receptor degrader, or SERD, which is targeted for the treatment of ER+ breast cancer. G1 is based in Research Triangle Park, N.C. For additional information about G1, please visit www.g1therapeutics.com.

Organovo & Viscient Biosciences Collaborate to Develop Custom Research Platform

Organovo Holdings, Inc. and Viscient Biosciences recently announced a collaboration to develop a custom research platform for studying liver disease. The partnership is expected to expand upon Organovo's current service portfolio for compound screening in disease models, which aids the drug discovery work of the Company's customers. Viscient is targeting early discovery work for non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH).

"We continue to have excellent traction with a wide range of biopharmaceutical companies in evaluating our tissue systems to facilitate the discovery and development of novel drug candidates to treat liver disease," said Taylor J. Crouch, CEO, Organovo. "Our 3D disease models have the unique capability to demonstrate drug mechanisms of action and efficacy in a setting that closely mimics human livers. We're proud to collaborate with Viscient's talented team as they have a strong understanding of our expertise. Our aim is to establish a custom platform that will support high-value drug profiling, and ultimately move our collaboration into a steady-state relationship."

"Viscient is a strong believer in unlocking the power of 3D bioprinting to bring cures and treatments to patients with few options today," said Keith Murphy, CEO, Viscient Biosciences. "In our pursuit of breakthrough therapies in important areas of medicine, we're eager to tap into novel, complex and more accurate disease models. Organovo's technology provides the potential for valuable and unprecedented insights as we target new drugs in areas of unmet medical need and strong commercial potential."

Deteriorating liver function is a growing and serious public health concern, with an estimated 100 million adults in the US afflicted with NAFLD, while up to 20 million more Americans are projected to have NASH. Left unchecked, these diseases can progress to cirrhosis and cancer, with NASH being the second leading cause of liver transplants in the US. Despite decades of intense research worldwide, the understanding of NAFLD progression and the development of novel therapeutic approaches have been limited by the lack of advanced systems that mimic human liver biology over an extended period of time.

Organovo designs and creates functional, three-dimensional human tissues for use in drug discovery, clinical development, and therapeutic applications. The Company develops 3D human tissue systems through internal research programs and in collaboration with pharmaceutical, academic, and other partners. Organovo's 3D human tissues have the potential to transform the drug discovery process, enabling treatments to be developed more effectively and with greater relevance to performance in human trials and commercialization. The Company's ExVive Human Liver and Kidney Tissues are used in high-value drug profiling, including compound screening in disease models, toxicology, target and marker discovery/validation, and other drug testing.

Catalent Collaborates With Grid Therapeutics to Develop Novel Targeted Immuno-Oncology Therapy

Catalent Pharma Solutions recently announced it has signed a multi-year agreement with Grid Therapeutics, LLC, for the development and manufacture of Grid's lead therapeutic candidate for the treatment of solid tumors. Grid is an oncology-focused biotech company building on the innovative science first developed by Edward F. Patz, Jr. MD, and his team of scientists at Duke University Medical Center.

Under the agreement, Catalent Biologics will employ its proprietary GPEx cell line technology to develop cell lines and manufacture antibodies with a view to optimizing the process for cGMP bulk drug production. The project will be undertaken at Catalent's state-of-the-art Madison, WI, biomanufacturing facility.

Grid's research is based upon a novel approach to identify specific tumor immunoglobulin G (IgG) antibodies from patients with early stage cancer. Grid used a unique strategy to obtain the sequence of its lead IgG3 antibody directly from B cells in cancer patients.

"Grid Therapeutics is excited to partner with Catalent to develop this novel, human-derived antibody for the treatment of cancer. We feel Catalent Biologics is well positioned to bring this novel antibody to the clinic," commented Edward F. Patz, Jr. MD, CEO of Grid Therapeutics.

"Catalent regularly and successfully partners with innovator companies looking to bring new, important therapies to market faster, and a patient derived IgG3 monoclonal antibody would be a significant advancement in optimized treatments," commented Mike Riley, Vice President & General Manager of Catalent Biologics.

Catalent's proprietary GPEx technology creates stable, high-yielding mammalian cell lines with high speed and efficiency. The advantages of applying GPEx technology span from early feasibility studies, to clinical manufacturing, through to commercial-scale production. To date, seven GPEx-based antibody and protein products are approved and marketed, and 34 therapeutic candidates are currently in the clinic across the world.

Catalent performs GPEx programs at its state-of-the-art commercial biomanufacturing facility in Madison, WI, which was completed in June 2013. Designed for flexible cGMP production from 10 liters up to 1,000 liters, and non-GMP production up to 250 liters, the site features extensive single-use technologies and unidirectional flow to maximize efficiency and safety. In 2016, Catalent announced the commencement of work to extend its Madison facility and add 22,000 square feet of space accommodating two x 2,000-liter bioreactors that will allow the company to support late-phase clinical and commercial production of up to 4,000-liter batches. This extension is due to be commissioned in the last quarter of 2017.

Grid Therapeutics is a biotech company based on the innovative science first developed by Edward F. Patz, Jr., MD, and his team of scientists at Duke University Medical Center. Located in Durham, NC, Grid is developing the first human-derived targeted immunotherapy for cancer.

Arcturus Therapeutics & Synthetic Genomics Announce Strategic Alliance

Arcturus Therapeutics, Inc. and Synthetic Genomics, Inc. recently announced they have entered into a research collaboration and worldwide license agreement to develop self-amplifying RNA-based vaccines and therapeutics in both human and animal health. The collaboration will bring together Arcturus's LUNAR lipid-mediated delivery platform with Synthetic Genomics' RNA replicon platform to potentially enable more efficacious and lower cost vaccines and therapeutics.

Under the collaboration, Synthetic Genomics will have exclusive access to LUNAR technology for vaccines and therapeutics, using self-amplifying RNA. Arcturus will receive an upfront cash payment, R&D support, and preclinical, development, and sales milestone payments, as well as royalty payments on any future sublicensed products.

"This agreement with Synthetic Genomics is in line with our corporate strategy to form strategic collaborations that leverage our proprietary technologies," said Joseph Payne, President and Chief Executive Officer of Arcturus. "This collaboration gives us the opportunity to apply our LUNAR technology to address unmet needs in both vaccines and therapeutics."

Synthetic Genomics' RNA replicons provide the genetic instructions to the body's own cells to produce ample amounts of protein and unleash a powerful immune response. These replicons carry the RNA code for a self-replication engine as well as multiple antigens that signal for immune response. The self-amplifying RNA-based therapeutic triggers rapid and immediate antigen expression within host cells, stronger T-cell response (including when the host is already infected), and lower dose requirements compared to traditional RNA-based vaccine and therapeutic approaches.

Combining Synthetic Genomics' replicons with Arcturus' LUNAR technology may enable the replicon RNA to avoid degradation and target the tissues and cell types needed to promote a protective immune response or drive expression of therapeutic proteins. In this way, the combination of both platforms may yield preventative and therapeutic treatments for a variety of diseases.

"We have made tremendous progress in programming our replicon RNA system to develop next-generation vaccines and therapeutics," said Oliver Fetzer, PhD, Chief Executive Officer of Synthetic Genomics. "We are excited to collaborate with Arcturus to explore how their delivery technology can contribute to the shared goal of developing innovative RNA-based medicines."

Synthetic Genomics is programming the operating system of life to create sustainable solutions for humankind's most pressing issues, from the wellbeing of our population to the health of our planet. With an unmatched understanding of how DNA drives the function of cells — the basic biological units of all living organisms — Synthetic Genomics modifies and writes genomes to enable transformative products in the areas of vaccines, medicines, nutrition, and biotechnology research. In addition to designing novel organisms that overcome fundamental hurdles of scientific research and medicine, Synthetic Genomics pursues partnerships with organizations seeking to dramatically improve upon existing products in health care, energy and other sectors.

Novoteris Investigator Receives Health Canada Clearance to Start Phase 2a Clinical Trial

Novoteris, LLC recently announced that the Therapeutic Products Directorate of Health Canada has cleared an investigator sponsored, pilot clinical trial application exploring the treatment of Non-Tuberculous Mycobacteria (NTM) with Novoteris' Thiolanox inhaled nitric oxide gas, using its unique computerized trace-gas delivery system.

This single center open label trial will recruit 10 subjects to the Vancouver clinical site. This trial will enable the testing of nitric oxide in patients who have this debilitating disease and who are excluded from the Novoteris Phase 2 placebo controlled trial recruiting patients with Cystic Fibrosis (CF) in North America. Novoteris has demonstrated the broad-spectrum anti-microbial property of nitric oxide effectiveness against mycobacterium both with in-vitro studies and a 4.5 log decrease in sputum bacteria levels in two human subjects with Mycobacterium abscessus that were treated in its pilot clinical trial of patients with Cystic Fibrosis in Europe.

Gaseous nitric oxide's potent antimicrobial properties, lack of bacterial resistance, and small molecule penetration capabilities could provide a promising alternative, non-antibiotic approach to treating infections in people living with this disease.

"The clearances by Health Canada will enable us to expand our work with this novel therapy to a wider range of people with an exceptional need for more effective antimicrobials and represents another important opportunity for Novoteris," stated Alex Stenzler, President of Novoteris.

Non-Tuberculous Mycobacteria (NTM) lung infections are caused by inhalation of these insidious opportunistic organisms in the air. In susceptible people, particularly those with Cystic Fibrosis, bronchiectasis or other chronic lung diseases, it can become a slow and progressively destructive lung disease. In many people, the prolonged use of antibiotics for more than a year may result in multi-drug resistant strains of NTM and with few antimicrobial options, can be lethal. NTM is a significant emerging threat affecting morbidity and mortality in CF patients with an estimated post millennium prevalence median of 13%.

Nitric oxide is a molecule naturally produced by the body and plays an important role in every organ system, including the innate defense system against microorganisms. Externally delivered nitric oxide has been demonstrated to be an effective antimicrobial agent against a broad spectrum of microbes, including drug-resistant strains. A lower concentration of nitric oxide is already an approved drug on the market from other manufacturers for the treatment of pulmonary hypertension in newborns.

"We anticipate that this study of nitric oxide will provide an opportunity to test this novel therapy in this patient population who have been waiting for an effective treatment," added Dr. Miller, Chief Technology Advisor.

Novoteris, LLC is a privately held limited liability company managed by a group of international industry veterans and clinicians involved in developing and producing innovative, cutting-edge medical products.

Rhythm Announces Preliminary Data from Phase 2 Study of Setmelanotide for Treatment of Bardet-Biedl Syndrome

Rhythm Pharmaceuticals, Inc. recently announced the presentation of preliminary data from an ongoing Phase 2 proof-of-concept study evaluating the safety and efficacy of setmelanotide, the company's novel melanocortin-4 receptor (MC4R) agonist, for the treatment of Bardet-Biedl syndrome (BBS). Results are being presented at the ObesityWeek 2017 meeting held October 29 – November 2, 2017, at the Gaylord National Resort & Convention Center in Washington, DC.

Rhythm is advancing clinical research programs evaluating setmelanotide as a first-in-class treatment for a number of rare genetic forms of obesity caused by deficiencies in the MC4 pathway, a key biological pathway in humans that regulates weight by increasing energy expenditure and reducing appetite. Mutations affecting the MC4 pathway are a potential cause of early onset obesity and hyperphagia often associated with BBS, a rare genetic disorder that is also characterized by vision loss, polydactyly, kidney abnormalities, and other symptoms. BBS is estimated to have a prevalence of approximately one in 100,000 in North America.

"There are currently no approved treatment options to manage obesity in people living with BBS," said Keith Gottesdiener, CEO of Rhythm. "We are committed to addressing the unmet needs in the BBS community as well as other patient populations impacted by rare genetic forms of obesity that result from deficiencies along the MC4 pathway and are not treatable with lifestyle modifications or currently available treatment options."

The Phase 2 study includes five BBS patients who presented with morbid obesity and hyperphagia at initiation. Setmelanotide is being administered daily by subcutaneous injection for 52 weeks. Within 6-19 weeks of initiation, four patients experienced cumulative weight loss of 12.1% (17.8 kg), 7.9% (7.9 kg), 9.7% (11.8 kg), and 9.7% (9.5 kg) respectively. One patient showed no weight loss; however, achieved apparent weight stabilization. Hunger scores improved in all patients. Treatment has been well tolerated with adverse effects including mild injection site reactions and increased skin pigmentation.

The preliminary data provide support for continued evaluation of setmelanotide in BBS patients. Rhythm has also demonstrated proof-of-concept in Phase 2 clinical trials that evaluated setmelanotide for the treatment of two additional MC4 pathway deficiencies: pro-opiomelanocortin (POMC) deficiency obesity and leptin receptor (LepR) deficiency obesity. The US FDA granted setmelanotide Breakthrough Therapy Designation for the treatment of POMC deficiency obesity and LepR deficiency obesity, and setmelanotide is currently in Phase 3 development for both conditions.

Rhythm is a biopharmaceutical company focused on the development and commercialization of peptide therapeutics for the treatment of rare genetic deficiencies that result in life-threatening metabolic disorders. Rhythm's lead peptide product candidate is setmelanotide, a first-in-class melanocortin-4 receptor (MC4R) agonist for the treatment of rare genetic disorders of obesity.

Citoxlab Acquires American CRO Xenometrics

Citoxlab Group recently announced the acquisition of Xenometrics, an American CRO specialized in the non-clinical assessment of new drug candidates. This acquisition is the third one made by Citoxlab in North America further to the acquisition of the LAB Research Group (2011) and Accellab (2016). The financial terms of the agreement were not disclosed.

Xenometrics is a non-clinical CRO offering comprehensive services in the fields of safety, pharmacology and pharmacokinetics to customers from the pharmaceutical, biotechnology and chemical industries.

Through this acquisition, Citoxlab Group reinforces its position in the non-clinical CRO arena, with consolidated revenues of $148 million (⇔128M) and a staff of 1,200, spread over seven sites in France (Evreux and Saint-Nazaire), Canada (Laval and Boisbriand), Hungary (Veszprem), Denmark (Copenhagen), and now in the USA (Kansas City).

Dr. Jean-Francois Le Bigot, Chairman and CEO of Citoxlab Group said: "We were actively looking for an investment opportunity in the US as part of our growth strategy. This is important to better serve our US clients and I am very happy that we have identified the right opportunity with Xenometrics and successfully closed this acquisition. This CRO, created as a spin-off from a large pharma company, has tremendous non-clinical expertise and a strong reputation as a flexible organization capable of meeting the customers' needs in project management during early development. This is really key, in particular for biotech companies that fight against time in order to reach milestones in their time-sensitive development plans. Two other criteria were also critical in our decision: - the staff is exceptionally stable, which results in experienced people who not only know their job, but also the specific requests or habits of their clients, - the location in Kansas City which is easy to reach for most American customers. For all these reasons, I am very confident and very excited that this acquisition will allow us to provide more services and additional capacity to our client portfolio with an increase in study slots."

Dr. Alfred Botchway, PhD, DSP, one of the founders and the CEO of Xenometrics, said "We are very proud that a leader like Citoxlab decided to invest in our company. We have been well aware of their excellent reputation as a science-driven CRO. In addition to this, I also realized that they have an impressive long-term development strategy, which is rare nowadays. We are very confident that joining the Citoxlab Group is a true opportunity for the future development of Xenometrics and its staff. We have already defined together several very concrete short and long term investments goals to improve and broaden our capabilities and services in Kansas City."

Cognition Therapeutics Announces Issuance of Patent for a First-in-Class Alzheimer's Disease Clinical Candidate

Cognition Therapeutics, Inc. recently announced the USPTO has issued a composition of matter patent for a family of novel compounds including CT1812, Cognition's first-in-class, orally available Alzheimer's disease drug candidate.

US Patent No. 9,796,672, "Isoindoline compositions and methods for treating neurodegenerative disease," arises from the inventive work of Cognition's scientific team led by Cognition co-founders Susan Catalano, PhD, and Gilbert Rishton, PhD, as well as colleague Gary Look, PhD. The small molecules covered by this patent were designed to inhibit the binding of beta amyloid oligomers to neuronal receptors and facilitate clearance of beta amyloid oligomers into the cerebrospinal fluid, with the goal of mitigating the toxic effects of beta amyloid oligomers that lead to the synapse loss characteristic of Alzheimer's disease and other neurodegenerative conditions. The newly issued patent provides Cognition with protection for CT1812 in the US through 2034. Additional time may be secured through patent term extension based upon regulatory review. Cognition also has filed corresponding patent applications to seek similar patent protection in key markets throughout the world.

"This patent is the result of the focused efforts of researchers dedicated to developing novel medicines against Alzheimer's disease," commented Cognition President & CEO Kenneth I. Moch. "CT1812 has a unique mechanism of action that blocks the binding of beta amyloid oligomers to the synapses on neurons, a process that has been directly implicated in the cognitive decline associated with Alzheimer's disease. Looking to 2018, we will be building on the results of our recently completed CT1812 Phase 1b/2a study by undertaking additional mechanism of action clinical studies and a larger Phase 2 study of CT1812 in patients with Alzheimer's disease."

Cognition's lead product candidate, CT1812, has completed a Phase 1b/2a clinical study (COG0102) in patients with mild-to-moderate Alzheimer's disease and has been granted Fast Track designation by the US FDA. This highly brain penetrant compound targets the sigma-2 receptor complex on neuronal synapses, displacing toxic beta amyloid oligomers from their binding sites on brain cells and clearing them into the cerebrospinal fluid. CT1812 has been shown in multiple Alzheimer's disease models to stop memory loss. Results from Study COG0102 will be announced in a late-breaker oral presentation at the CTAD (Clinical Trials on Alzheimer's Disease) meeting in Boston taking place November 2-4, 2017.

Cognition Therapeutics is a privately held biopharmaceutical company developing a pipeline of disease modifying small molecule drug candidates to treat neurocognitive disorders. Cognition's lead candidate, CT1812, is a proprietary first-in-class, orally available small molecule in development for the treatment of mild-to-moderate Alzheimer's disease. CT1812 and Cognition's other pipeline candidates were identified using the company's disease-relevant screening and novel chemistry platforms.

R&D PARTNERSHIPS

Partnering for Progress: How Collaborations Are Fueling Biomedical Advances

By: Neil Lesser and Matt Hefner

INTRODUCTION

In today's era of rapid scientific progress, public- and private-sector researchers are seeking to leverage their strengths in collaborative ways to accelerate innovation in patient treatment and care. Biopharmaceutical companies increasingly are partnering with a diverse set of healthcare stakeholders to address scientific and technological challenges, create greater efficiencies in research and development (R&D), and accelerate the discovery, production, and delivery of critical new treatments for patients in need. Forward thinking biopharmaceutical companies serve not just as partners, but often also act as integrators in this ecosystem, bringing together diverse players and providing scientific, regulatory, and delivery system insights; operational capabilities; and financial resources.

Deloitte was contracted by the Pharmaceutical Research and Manufacturers of America (PhRMA) to analyze the various types and number of biopharmaceutical partnerships created throughout the past several decades. Based upon a comprehensive database of partnerships formed between 1980 and 2014, we found that R&D-focused partnerships — most notably, non-asset-based, pre-competitive models (those whose primary objectives do not necessarily center on a specific drug candidate) have grown substantially throughout the past decade and highlight the growing role and importance of more open, collaborative approaches to R&D innovation.

NAVIGATING THE BIOPHARMACEUTICAL INNOVATION PROCESS: OPPORTUNITIES & CHALLENGES

R&D activity is increasing to address unmet patient needs. The last decade has seen a steady rise in Food and Drug Administration (FDA) drug approval rates, demonstrating progress in addressing patient unmet needs despite growing R&D and regulatory challenges. Between 2011 and 2016, 204 new molecular entities (NMEs) were approved by the FDA through the Center for Drug Evaluation and Research (CDER), compared to just 131 NMEs approved between 2005 and 2010.[1] Further, the FDA's CBER (Center for Biologics Evaluation and Research) approved 11 new medicines in 2015 in addition to several biological and blood products not formally classified as drugs. There is also significant current R&D activity, with more than 7,000 new medicines in development across the globe.[2]

Throughout the past 10 years, biopharmaceutical companies have increasingly sought to address previously unmet medical needs by building on scientific advances in genomic and molecular medicine. For example, the era of personalized medicine is rapidly changing the way diseases are identified, patients are diagnosed, and treatment decisions are made. Collaboration across the biopharmaceutical R&D ecosystem has been essential in driving important scientific breakthroughs in novel diagnostics technology and in identifying molecular targets for the development of personalized medicines. These advances are reshaping drug development. Biopharmaceutical companies are committed to advancing targeted therapies and medicines to treat serious conditions and unmet medical needs.

AN INCREASINGLY CHALLENGING BIOPHARMACEUTICAL R&D ENVIRONMENT

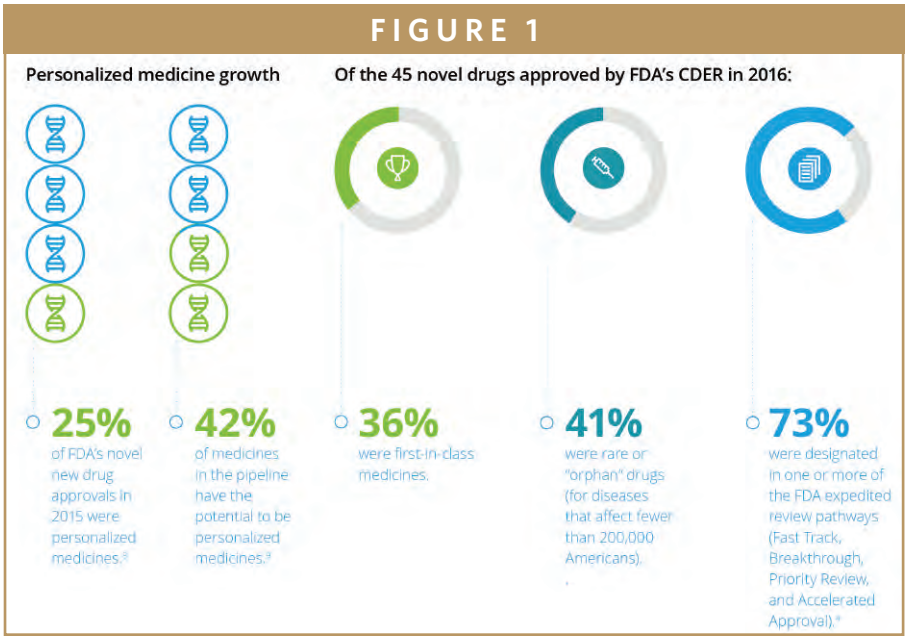
As researchers learn more about the molecular underpinnings of complex diseases, traditional methods for assessing the clinical safety and efficacy of a medicine in development create myriad innovation challenges. Some of the scientific, regulatory, payment, operational, and financial hurdles that complicate the biopharmaceutical R&D process and can increase the cost, time, and risk of drug development include:

- **Scientific Complexity:** Drug developers are pursuing more complex disease areas (eg, rare cancers, neurological conditions, etc) and are using new approaches to fight these diseases, often at the molecular and genetic levels.

- **Regulatory Requirements:** Regulatory requirements have continued to proliferate. The rapid increase in new sources of evidence, including patient-reported outcomes, patient-generated data, and real-world evidence (RWE) present new challenges related to data collection, analysis, storage, and confidentiality. Further, there remains uncertainty around regulatory acceptance of some of the more novel clinical trial designs and endpoints that companies are currently pursuing.

- **"Burden of Proof" for Coverage & Payment:** Health plans, healthcare providers, and patients often have differing views of the value of new medicines. Restrictions on biopharmaceutical companies' ability to proactively engage with health plans to discuss types of evidence prior to product approval may make it more difficult to determine what data would be most useful for coverage and payment decisions.

FIGURE 1



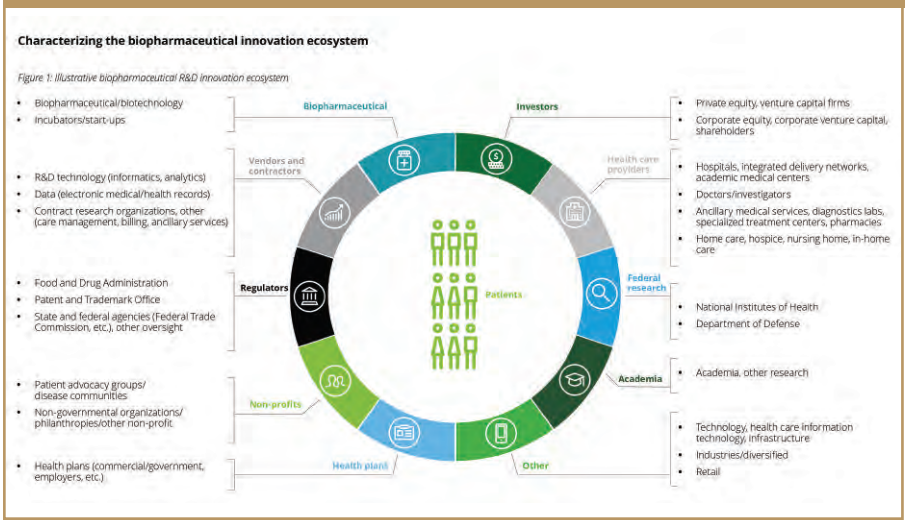
CHARACTERIZING THE BIOPHARMACEUTICAL INNOVATION ECOSYSTEM

An ecosystem model can be used as a lens through which to view the biopharmaceutical innovation landscape. Deloitte defines ecosystems as "symbiotic, cooperatively evolving communities composed of multiple diverse players."[3] The biopharmaceutical R&D ecosystem is composed of a range of stakeholders, including but not limited to: biopharmaceutical companies, investors, healthcare providers, federal research organizations, academic institutions, non-profits, services, regulators, health plans, and others.

This ecosystem enables a varied group of stakeholders to achieve together that which would be difficult for any individual participant by itself. Together, the highly specialized players contribute new perspectives, capabilities, and resources to drive new scientific advances and solutions. Both collaboration and competition are essential drivers of sustained ecosystem success. Stakeholders may be motivated to collaborate by their shared ambitions, objectives, and commitments, while inherent competition may bolster ecosystem activity and contribute to a more efficient and productive R&D process.

Innovative biopharmaceutical companies serve not just as partners, but often as integrators in this ecosystem, bringing together diverse players. They also provide scientific, regulatory, and delivery system insights, operational capabilities, and financial resources to help deliver critical new therapies to patients in need.

FIGURE 2



R&D PARTNERSHIP DATABASE FINDINGS: PARTNERING MODELS & TRENDS

Deloitte analyzed the types of biopharmaceutical R&D partnerships created from January 1980 through August 2015, building a comprehensive database of collaborations from EvaluatePharma Life Sciences partnership information, supplemented with non-duplicative data from FasterCures' Consortiapedia. To accommodate the diversity of partnership types and stakeholders investigated as part of this research, Deloitte conducted a manual scan of various PhRMA member company partnerships throughout the past 10 years (2005–2014) in October 2015, which resulted in the inclusion of additional unique, non-duplicative partnerships. Further, Deloitte interviewed 12 biopharmaceutical industry ecosystem executives, covering individual biopharmaceutical companies and consortia, academia, federal research, and other organizations.

The database identified two broad categories of partnerships – asset-based and non-asset-based. Asset-based partnerships include acquisitions and licensing of compounds, products, or technology. Non-asset-based partnerships include joint ventures (JVs), consortia, and others, such as those focused on education and awareness.

Traditional asset-based partnerships typically involve two parties (such as a pair of biopharmaceutical companies) that are focused on a particular asset (ie, investigational medicine), and use a structure (a "sponsor" and "partner" model) that distributes control, risks, and rewards. A common objective is to progress a single asset through the R&D process, obtain approval, and launch. Today's non-asset based partnerships diverge notably from that model — collaborative alliances may include three or more parties and are often composed of a mix of ecosystem stakeholders, including biopharmaceutical companies, academia, non-profits, and government entities. Importantly, these partnerships feature shared control and decision-making, thus spreading both the potential risks and rewards.

Non-asset-based partnership examples include:

- **Joint Ventures (JVs):** Two or more entities enter a collaboration wherein all involved parties agree to jointly contribute to R&D-related activities to achieve a specific objective. They typically involve joint governance and decision-making, and sharing of accompanying risks and rewards.

- **Consortium:** Three or more parties pool resources and work together to achieve a common goal, such as accelerating scientific discovery in a particular disease area or technology. Some consortia include "pre-competitive" arrangements in which all players work together to solve problems and develop capabilities in areas where they would typically compete with each other.

- **Other:** Parties provide financial resources and/or marketing, educational, and promotional programs (eg, company support of broader disease awareness efforts).

PARTNERSHIP GROWTH

Approximately 9,000 new biopharmaceutical R&D partnerships were formed between 2005 and 2014 at an annual growth rate of 4% during that 10-year period. The 9,000 new biopharmaceutical R&D partnerships formed between 2005 and 2014 are more than double the number formed (approximately 4,000) in the preceding decade (1995–2004). Consortia showed the strongest growth, increasing nine times over the prior decade, with 334 new R&D consortia in 2015. Additionally, early stage partnerships (ie, prior to a potential new therapy entering clinical trials) have more than doubled between 2005 (256) and 2014 (578).

IMPACT OF COLLABORATIVE PARTNERSHIPS

Deloitte conducted interviews that further explored consortia practices, learnings, and outputs. These collaborative partnerships have already expanded knowledge and made progress against some key health challenges and opportunities:

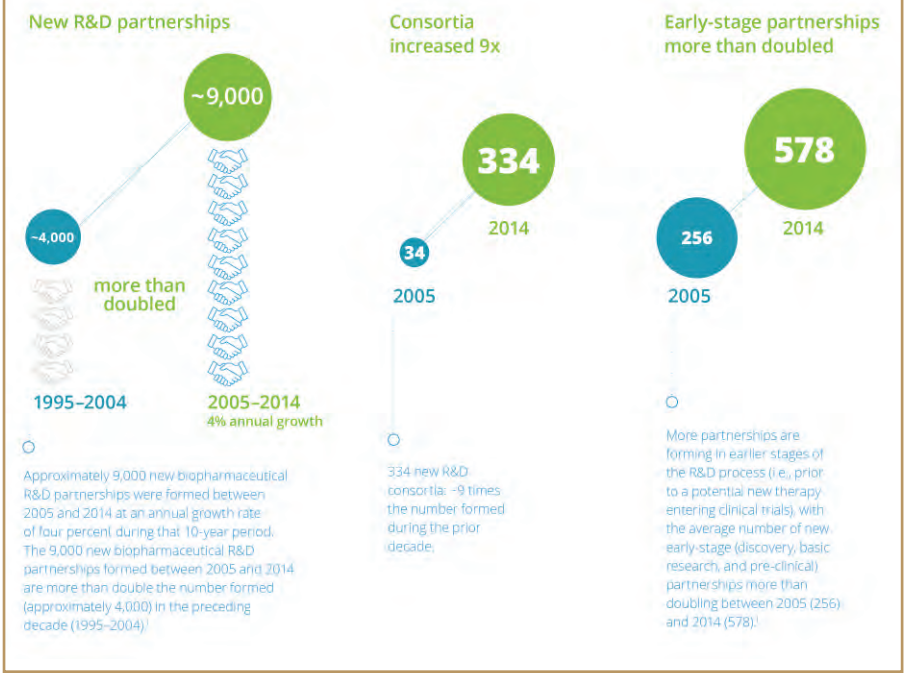
Understanding Difficult Diseases at the Molecular Level: Alzheimer's Disease Neuroimaging Initiative (ADNI)

Growing understanding of the inner workings of complex diseases is revealing important pathways for new research, but also unearthing new challenges. The ADNI was formed in 2004 to advance understanding of this devastating disease in order to develop new treatments to slow or stop Alzheimer's progression. The initiative, formed by the NIH, National Institute on Aging (NIA), FDA, and numerous industry, academic, and non-profit organizations, has made tremendous strides in Alzheimer's Disease (AD) detection, helping to elucidate the underlying pathways of AD progression, and improving the efficiency of clinical trials related to addressing AD.

Quickly & Effectively Diagnosing & Tracking Disease Progression: Cure Huntington's Disease Initiative (CHDI)

The non-profit CHDI Foundation was created in 2002 by several biopharmaceutical, academic, and contract research organizations (CROs) to focus on developing therapeutics to track and slow the progression of Huntington's Disease (HD).[4] One accomplishment includes developing an assay to measure the build-up of a protein that is known to be harmful for patients with HD.

FIGURE 3



Using Biomarkers to Monitor Patients Before, During & After Trials: Biomarkers Consortium

The Biomarkers Consortium, formed in 2006, is focused on identifying, developing, and qualifying biomarkers for cancer, inflammation and immunity, metabolic disorders, and neuroscience. The Biomarker Consortium includes 30 organizations, and is managed by the Foundation for the National Institutes of Health (FNIH) as a public-private partnership. Some notable achievements via the application of biomarkers to research include development of approaches to accelerate trials for breast cancer, defining sarcopenia (loss of muscle tissue) as a disease (versus simply an effect of the aging process), and predicting long-term results of statins used to treat patients with high cholesterol and/or risk of developing cardiovascular disease.

Developing New Ways of Conducting Clinical Trials to Take Advantage of Recent Technological & Operational Advances: Lung Master Protocol (Lung-MAP) Consortium

As we move toward an era of targeted and personalized treatment, the traditional randomized, controlled trial presents some significant challenges. New trial designs, which capitalize on the growing understanding of the underlying biology of disease, are beginning to present new paradigms for conducting clinical research. The Lung-MAP consortium is a public-private partnership formed in 2014 to develop a novel, multi-drug clinical trial for patients with a specific, difficult-to-treat form of advanced lung cancer (squamous cell carcinoma). The trial design leveraged genetic profiling to assign patients to one of the trial arms.[5] Applications of this type of study design have helped to advance precision medicine in oncology and generate interest from biopharmaceutical companies and others in tackling difficult cancers with a personalized approach.

Evaluating the Potential for Combination Treatments: Collaborative Novel-Novel Combination Therapies (CoNNCT)

Over time, researchers often identify additional benefits of medicines when used in novel combinations with other drugs. In many cases, the treatments may confer greater benefit together than when used individually. Recognizing the value of these expanded therapeutic options, academic centers, biopharmaceutical companies, and non-profits are collaborating through a partnership called CoNNCT to accelerate identification of effective drug combinations for cancers. The goals of this collaboration are to make it easier to test multiple combinations of new drugs, reduce the cost of investigational studies, shorten the time to demonstrate proof-of-concept and, ultimately, to accelerate the development of novel treatments in other diseases and conditions.[6]

Accelerating Translational Research: The California Institute for Biomedical Research (Calibr)

Translating early research findings into therapeutic advances is a challenging process that requires both in-depth understanding of the science as well as specific regulatory and development capabilities. Calibr is a not-for-profit collaborative that is bringing partners together to accelerate translational research in order to develop new medicines for patients with unmet needs across a broad range of disease areas.[7] Building on the success of early, open collaboration, Calibr also has a unique structure that enables commercial partnerships later in the development process.

FUTURE OUTLOOK

The Deloitte R&D partnership database research and interviews with key ecosystem leaders point to a growing recognition of the value and importance of collaboration across members of the R&D ecosystem. These collaborations address the most pressing scientific and technological challenges while harnessing complementary strengths to bring new treatments to patients. Notable achievements and lessons learned from existing pre-competitive collaborations will be used to enable more pre-competitive collaboration in additional research areas, increasing the potential for new breakthroughs.

In the coming years, we expect to see partnering earlier in the development lifecycle with a continued expansion in disease area-focused consortia, including growing emphasis on more "open" arrangements with respect to structure, control, risk sharing, and other business arrangements. Active innovators will seek to develop a portfolio of partners with a diverse mix of scientific and operational capabilities to support non-asset -based partnerships to propel innovation and bring new medicines to patients in need more quickly and safely. The eco-system is likely to expand its membership as regulators and the healthcare delivery system, particularly health plans, need an ever-larger evidence base (including patient-generated data, patient-reported outcomes, and "real-world evidence") to inform review and approval of drug applications. Additionally, evolving innovative coverage and payment models could fuel an even broader range of partnerships in the future.◆

REFERENCES

1. Food and Drug Administration, "Novel New Drugs 2016 Summary," January 2017.
2. Adis R&D Insight Database, February 2017.
3. Eamonn Kelly, "Business ecosystems come of age," Deloitte University Press, April 15, 2015.
4. CHDI Foundation website; accessed June 30, 2016.
5. "Ambitious Lung-MAP Trial Launched With Five Novel Drugs", Onclive.com, July 31, 2014.
6. "More than 40 Industry Visionaries Meet to Explore New Combination Cancer Drug Development Paradigm", BusinessWire, March 7, 2016.
7. Calibr website; accessed June 30, 2016.

BIOGRAPHIES

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NEXT-GENERATION SEQUENCING

Emerging Clinical Applications & Projections to 2022

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

INTRODUCTION

The growth curve for clinical applications of next-generation sequencing (NGS) is approaching an upward trajectory as existing applications gain traction and new ones begin to establish a foothold. BCC Research found that principal drivers of market growth in the clinical NGS industry include precision medicine and genomics initiatives; penetration into large market economies such as China; and the emergence of high-potential applications in average-risk noninvasive prenatal testing, preventive genetic screening, and early cancer detection.

Several unique aspects of NGS make it a desirable technology for clinical applications. Because NGS platforms can sequence entire genomic regions or even whole genomes, a single test can examine hundreds or thousands of clinically important genetic variations. An NGS platform also allows companies to expand their menu of disorders and diseases over time, after initial launch of a test. This strategy has been used in reproductive health applications, for example, launching a test to initially screen for aneuploidies and later expanding it to include screening for additional genetic variants.

The global clinical NGS market is estimated at approximately $3.2 billion in 2017 and is forecast to increase at a compound annual growth rate (CAGR) of 27% to reach $10.5 billion in 2022. Non-cancer applications accounted for an estimated $2.4 billion in 2017 and are projected to grow at a CAGR of 22.3% to reach $6.4 billion in 2022. Cancer applications, valued at roughly $839 million in 2017, have an anticipated CAGR of 37.3%, putting this segment at close to $4.1 billion in 2022. Important cancer applications include screening and early detection, diagnosis, therapy guidance, and monitoring.

TABLE 1

Global Clinical Next-Generation Sequencing Market, by Disease Class, Through 2022
($ Millions)

Disease Class	2015	2016	2017	2022	CAGR% 2017-2022
Non-cancer	1,576.6	1,979.8	2,352.8	6,441.0	22.3
Cancer	669.5	778.1	838.8	4,093.2	37.3
Total	2,246.1	2,757.9	3,191.6	10,534.2	27.0

Source: BCC Research

NGS is often more accurate and reliable than existing diagnostics. The following sections examine the main applications for NGS diagnostics that are commercially available or forecast to emerge in the next 5 years.

CANCER APPLICATIONS

The main applications of NGS diagnostics in cancer are tumor sequencing, familial screening, and monitoring for cancer recurrence. It is becoming increasingly apparent that cancer is a genetic disease. Knowing the genetic profile of a tumor can change the way that cancers are treated, eg, by determining which drug is given to a patient. There is a move toward classifying and treating cancers on the basis of their genetic makeup rather than their location in the body. For example, trastuzumab is effective for treating breast cancers in which the gene ERBB2 is present. However, some colon cancers also overexpress this gene and may also be treatable with trastuzumab. Cancer diagnostics that can genetically profile a tumor could thus be clinically valuable and influence a physician's treatment decision. This is a crit-

ical driving force behind NGS-based tumor sequencing diagnostics. The key issue for this application is establishing a clinical connection between the mutation profile of a given tumor and an effective therapy. It is believed, however, that many large-scale sequencing projects are addressing this issue and significant progress is being made.

Current applications of NGS in cancer are focused on discrete sets of genes. However, BCC Research believes that whole-exome and whole-genome sequencing will increasingly gain traction as sequencing costs fall and the value of testing for only a single gene (or several genes) declines. Longer term, it is expected that most tumors will be completely sequenced so that physicians can have a complete set of genetic information when treating patients.

The second application of NGS in cancer is familial screening offered to relatives of patients with cancer or individuals otherwise at risk. Relatives of patients with cancer could be at high risk of developing cancer, and genetic testing among a broader population such as this could reduce the mortality rate and overall costs of the disease. The key driving force for this application is a reduction in sequencing costs to the point where there are significant benefits versus costs for NGS tests.

Another driving force for familial screening is breakout into the general population. There is evidence that many people who have no history of cancer in their family can still carry cancer-risk mutations. It is unlikely that the general population of at-risk people will undergo NGS-based screening tests without insurance reimbursement. Therefore, both sides of the cost-to-benefit-ratio must be improved (ie, NGS costs must continue to decrease and clinical validity must be established).

The third application of NGS for cancer through 2022 is monitoring for cancer recurrence. This involves the capture and sequencing of low levels of circulating tumor cells in peripheral blood. There have recently been outstanding technical developments in this area, and continuing progress in this field will drive this application. BCC Research estimates that by combining state-of-the-art circulating tumor cell capture methods with whole-tumor NGS, cancer monitoring applications will reach commercial viability within the next 5 years.

MENDELIAN DISORDERS APPLICATIONS

Mendelian disorders (rare genetic disorders) are difficult to diagnose. Diagnostic odysseys occur when an individual has a rare genetic disorder and undergoes multiple expensive, invasive clinical procedures to determine the cause. These cases occur frequently in clinics that evaluate children for things such as cognitive impairment, neuromuscular disorders, or congenital anomalies. Diagnostic odysseys often include serial molecular testing of one or a few genes, running up the costs of diagnosis.

Many of these rare genetic diseases are due to a single-gene mutation in the genome. They are referred to as Mendelian disorders because they comport with the inheritance pattern first discovered by Gregor Mendel. BCC Research believes that there are as many as 25 million individuals in the US who have inherited Mendelian disorders. Some of these are well understood, including cystic fibrosis and muscular dystrophy, but others are much rarer. There are approximately 6,000 of these very rare disorders, and only half of them have been identified.

NGS is changing the diagnostic paradigm in these cases because it can produce a correct diagnosis faster and more cost effectively than conventional approaches. The key advantage of NGS is that it is highly multiplexed to cover many genes in one test format, including genes for which no commercial molecular test exists. One of the key challenges to implementing NGS for this application is demonstrating the clinical value of such test formats to the medical community. BCC Research believes that this challenge is being aggressively addressed by a number of leading institutions in this field, as well as by several high-profile initiatives.

REPRODUCTIVE HEALTH APPLICATIONS

The main applications of NGS diagnostics in reproductive health are prenatal, newborn, and preimplantation screening. The first NGS test for prenatal screening was introduced by Sequenom in October 2011, and by mid-2017, more than 13 companies were marketing such tests. The key to this market opportunity was the development of technology that could detect and genetically analyze very low concentrations of fetal DNA in the peripheral circulation of pregnant women. The fetal DNA had to be accurately analyzed for chromosomal abnormalities that may lead to birth defects. Once this hurdle was overcome, the clinical benefit was rapidly recognized by the medical community.

Since launch of the initial tests, providers have sought to expand their testing menus to detect additional chromosomal abnormalities. This is a key strategy to

"Current applications of NGS in cancer are focused on discrete sets of genes. However, BCC Research believes that whole-exome and whole-genome sequencing will increasingly gain traction as sequencing costs fall and the value of testing for only a single gene (or several genes) declines. Longer term, it is expected that most tumors will be completely sequenced so that physicians can have a complete set of genetic information when treating patients."

getting higher market share in the at-risk population. The main clinical benefits of using NGS-based tests is a reduction in the number of invasive procedures and earlier diagnosis of fetal aneuploidy. Currently, NGS testing is mostly used to screen women at high risk of carrying babies with chromosomal abnormalities. A key issue that will impact future market potential is whether NGS-based screening will be adopted by the average-risk patient population. For that to happen, insurance providers and other payers will need to recognize a clear clinical benefit to screening this segment.

For newborn screening applications, NGS offers much promise as the technology continues down the cost curve. Newborn screening entails sequencing a baby's genome at birth and keeping that information as a reference sequence throughout his or her life. The key driving force for this application is the decline in costs of sequencing and associated informatics, because mass screening is heavily dependent on costs. It is expected that sequencing costs will continue to decline; thus the future looks encouraging for this market application. The key hurdle that must be overcome for commercial success is demonstration of cost versus benefit and subsequent coverage of a screening test by insurance providers.

The first step is to show that NGS can duplicate the results of conventional newborn genetic tests, for which the current total cost is approximately $2,000. The next step is to demonstrate that NGS tests can provide more relevant clinical genetic information than conventional methods at a price point that is comparable or lower. If this can be done over the next few years, it is likely that insurance companies will come on board and a viable market will form.

Preimplantation screening using NGS is an emerging application. A key benefit is the potential to increase pregnancy success rates of in vitro fertilization. The main technological hurdle is being able to offer these tests at an attractive price point versus microarray methods and thereby increase the penetration of NGS. The tests do not rely on insurance coverage because they are offered with the option of cash payment. This feature has attracted the interest of a significant number of companies.

MICROBIOLOGY & INFECTIOUS DISEASE APPLICATIONS

The main applications of NGS diagnostics in microbiology and infectious diseases are 1) rapid pathogen detection and characterization, and 2) human immunodeficiency virus (HIV) tropism. Sequencing is playing an increasingly important role in the first market segment. The use of sequencing to diagnose patients who are hospitalized with food-borne infections is viewed as a near-term point of entry for NGS diagnostics. A key driving force for this particular application is the recent use of NGS to successfully manage disease outbreaks caused by food-borne pathogens (eg, Escherichia coli).

BCC Research envisions that the initial application of NGS for management of food-borne infection will be in hospitalized patients, representing only a small subset of individuals who become sick due to these infections. A main obstacle to commercialization will be education of clinicians on the benefits of using NGS to quickly identify pathogen strains so that effective treatments can be implemented. It will be important for developers to market the new tests appropriately to critical-care physicians and to contrast the benefits of NGS versus polymerase chain reaction (PCR) methods.

The comparison between NGS and PCR is a general issue in infectious disease testing. PCR is increasingly used in infectious disease diagnostics because it provides speed, accuracy, ease of use, and multiplex capabilities. Sanger sequencing, which is also used in some applications, provides highly accurate results too. NGS must compete with both technologies to meaningfully penetrate the infectious disease market.

The second application in which NGS has shown near-term commercial promise is HIV tropism testing, for which Sanger sequencing is the gold standard. However, NGS provides a better detection limit, such that mutations at lower allele frequencies can be detected. These lower-frequency mutations may be important in predicting drug resistance. It is thought that frequencies as low as 1% may influence drug sensitivity, and the present detection limit of Sanger sequencing is 20% frequency.

COMPLEX DISORDERS APPLICATIONS

The main applications of NGS diagnostics in this area include immune system, metabolic and mitochondrial, cardiovascular, and neurological disorders. Complex disorders are usually multifactorial, meaning there are many factors that determine who acquires the disease. These factors can be genetic or non-genetic (eg, environmental). Genetic factors may play only a minor role in some diseases, limiting the impact of NGS as a diagnostic. On the other hand, for many diseases, knowledge of their etiology remains incomplete and genetics may well play an important role. Thus, it is likely that as new knowledge is gained regarding the genetic basis of these diseases, the need for NGS diagnostics will increase.

For immune system disorders, main applications include immune system profiling, human leukocyte antigen (HLA) typing, rheumatoid arthritis (RA), and multiple sclerosis (MS). In the field of immune system profiling, NGS is making progress through both commercial assays and research. In addition, the Human Immunology Project Consortium is collecting all data generated by immune profiling techniques and putting it into a central, publicly accessible repository. This will help to accelerate this field.

Sanger sequencing is the current standard for high-resolution HLA typing. However, due to an increasing number of HLA alleles in the international ImMunoGeneTics database, histocompatibility testing is becoming more complex, even with Sanger sequencing. NSG assays provide rapid, high-resolution typing at a competitive cost. RA and MS are phenotypically complex, with underlying causes that are not well understood. Research into the genetic underpinnings of RA and MS is ongoing, and NGS technologies are useful in this effort. As this research progresses, it is expected that new molecular diagnostics will be developed, some of which will use NGS formats.

Mitochondrial disorders are difficult to diagnose because they have complex genetic causes and a wide range of phenotypes. These features make these diseases well suited for NGS diagnostics. Several laboratories have launched NGS-based clinical tests for mitochondrial disorders. Targeted panels are designed for cases in which a diagnosis is narrowed down to a small subset of mitochondrial diseases on the basis of phenotype, but further definition from a molecular diagnosis is needed. For this market segment, single-gene tests do not provide enough information, whereas whole-exome sequencing is too costly and overkill.

Cardiovascular and neurological disorders comprise a strong potential future market for NGS diagnostics. NGS tools have been used to demonstrate that breakdown in the control of gene expression may help to initiate or progress some of these diseases. A market for NGS diagnostics will coalesce when clinical research can correlate genetic changes with the risk of disease onset or progression. For example, it is important to determine if a patient with dilated cardiomyopathy has mutations in up to 40 genes that are associated with the disorder. NGS-based multigene tests are important diagnostic tools in the management of these patients. As a result, dilated cardiomyopathy is a focus for NGS test providers.

INTEGRATION OF CLINICAL NGS IN HEALTHCARE

NGS is playing an important role in the mission to transform cancer care, in particular. Examples include use of NGS in liquid biopsy pan-cancer panels; efforts to make gene sequencing and analysis services more accessible to physicians; and the emphasis on noninvasive liquid biopsy formats for early cancer detection, therapy selection, and monitoring. A high level of corporate deal-making illustrates the dynamic nature of the NGS market and reflects the promise of NGS in clinical applications. It also highlights the urgent need for companies to meet their goals toward delivering better clinical products and services to the healthcare industry. ◆

This article is based on the following market analysis report published by BCC Research: DNA Sequencing: Emerging Clinical Applications and Global Markets (BIO126C) by John Bergin.

BIOGRAPHIES

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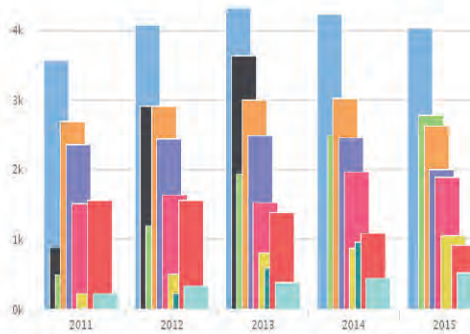

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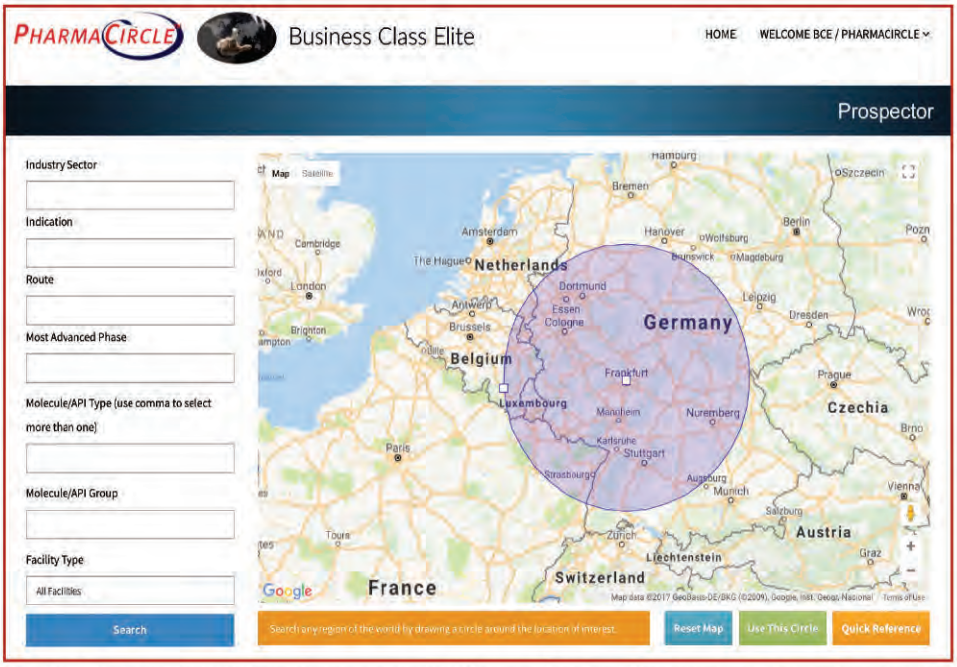

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By: Allan B. Haberman, PhD

INTRODUCTION

This new report builds on our 2014 Insight Pharma Report, Cancer Immunotherapy: Immune Checkpoint Inhibitors, Cancer Vaccines, and Adoptive T-Cell Therapies. In that report, we focused on the major classes of cancer immunotherapy drugs that were then emerging from academic and corporate research: immune checkpoint inhibitors, cancer vaccines, and adoptive T-cell therapies. This new report includes an updated discussion of approved and clinical-stage agents in immuno-oncology, including recently-approved agents. It also addresses how researchers and companies are attempting to build on prior achievements in immuno-oncology to improve outcomes for more patients. Some researchers and companies refer to this approach as "immuno-oncology 2.0." The American Society of Clinical Oncology (ASCO), in its 12th Annual Report on Progress Against Cancer (2017), named "Immunotherapy 2.0" as its Advance of the Year.

As discussed in our 2014 report and still true in early 2017, the most successful class of immunotherapeutics has been the checkpoint inhibitors (which are discussed in this report). Checkpoint inhibitors and other immuno-oncology agents represent a significant advance in cancer treatment beyond the traditional modalities of chemotherapy, radiation therapy, and surgery. Moreover, treatment of advanced melanoma (the cancer for which the largest amount of data on immunotherapy has been amassed) with checkpoint inhibitors has in some cases produced spectacular results. For example, data released at the May 2016 ASCO Annual Meeting indicate that 40% of metastatic melanoma patients who received pembrolizumab (Merck's Keytruda) in a large clinical trial are still alive 3 years later. This represents a substantial improvement over just a few years ago, when the average survival time for patients with advanced melanoma was measured in months.

As discussed in this report, researchers have found that checkpoint inhibitors produce tumor responses by reactivating TILs (tumor infiltrating lymphocytes) - especially CD8+ cytotoxic T-cells. This key observation is perhaps the most important factor driving development of second-wave immuno-oncology strategies. Thus, researchers have been developing biomarkers that distinguish inflamed (ie, TIL-containing) tumors, which are susceptible to checkpoint inhibitor therapy, from "cold" tumors, which are not. They have also been working to develop means to render "cold" tumors inflamed, via treatment with various conventional therapies and/or development of novel agents. These studies are the major theme of second-wave immuno-oncology, or immuno-oncology 2.0.

APPROVALS OF CHECKPOINT INHIBITORS

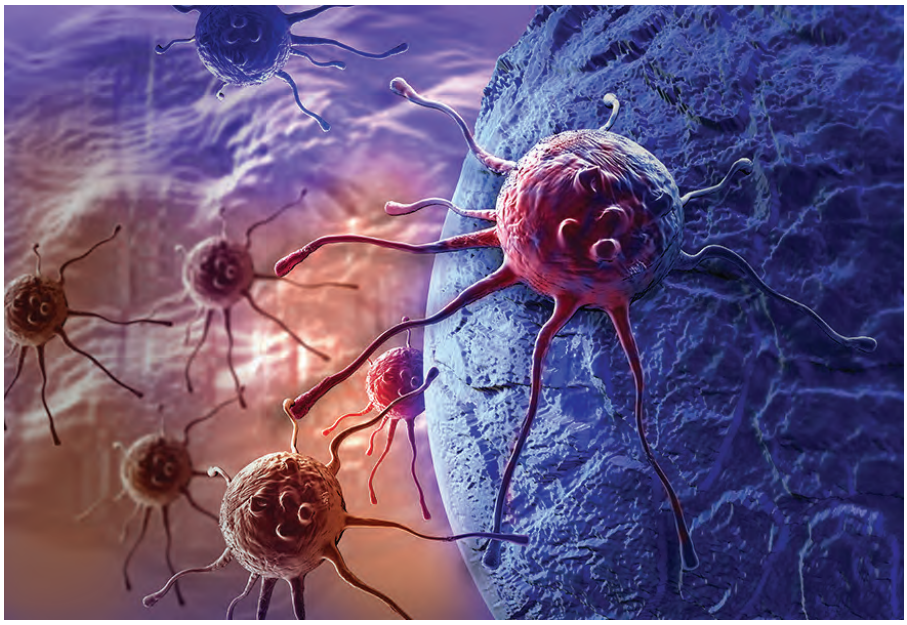
Researchers are continuing to conduct clinical trials designed to gain approval for new checkpoint inhibitors and for new indications for already approved agents. Notable recent developments include the 2016 approval of atezolizumab (Roche/Genentech's Tecentriq), the first PD-L1 (programmed death-ligand 1) inhibitor to be approved. On May 18, 2016, atezolizumab was approved by the FDA for treatment of advanced or metastatic urothelial carcinoma that has worsened during or following platinum-containing chemotherapy or within 12 months of receiving platinum-containing chemotherapy, either before or after surgical treatment. Later, on October 18, 2016, the FDA ap-

proved atezolizumab for use in patients with metastatic NSCLC (regardless of PD-L1 expression) who have progressed during or after treatment with a platinum-based chemotherapy or appropriate targeted therapy.

Also in October 2016, the FDA approved the PD-1 (programmed cell death protein 1) inhibitor pembrolizumab as a monotherapy for first-line treatment of patients with advanced NSCLC whose tumors expressed PD-L1 at ≥50%. This was after this agent met its primary endpoint of progression-free survival in patients with previously untreated advanced NSCLC whose tumors expressed PD-L1 at ≥50%. In contrast, monotherapy with the competing PD-1 inhibitor nivolumab (Bristol-Myers Squibb's Opdivo) did not meet its primary endpoint of progression-free survival in patients with previously untreated advanced NSCLC whose tumors expressed PD-L1 at ≥5%. This result is affecting the competition between BMS' nivolumab and Merck's pembrolizumab.

APPROVED & CLINICAL-STAGE IMMUNOTHERAPY BIOLOGICS OTHER THAN CHECKPOINT INHIBITORS

In addition to serving as an introduction to the report and discussing the early history of cancer immunotherapy, the beginning of the report focuses on cytokines as cancer immunotherapeutics. Interleukin-2, interferon-alpha-2a, and interferon alpha-2b have long been approved for treatment of various cancers. To this day, despite the introduction of newer immunotherapies, such as checkpoint inhibitors, high-dose recombinant IL-2 (Novartis/Prometheus Laboratories' Proleukin) is the only drug so far that has produced durable, long-term responses in patients with metastatic melanoma or metastatic renal cell carcinoma. According to Patrick Ott, MD, PhD, of the Dana-Farber Cancer Institute in Boston, MA, "High-dose IL-2 has a track record of patients who have been disease-free for 20 years, and we just don't know that yet with the new drugs [such as checkpoint inhibitors]." In the case of advanced melanoma, high-dose intravenous bolus IL-2 induces objective clinical responses in 15% to 20% of patients and durable complete responses in 5% to 7% of these patients. For metastatic RCC (mRCC), high-dose intravenous bolus IL-2 gives an objective clinical response rate of approximately 25% and a 7% durable complete response rate.



In addition to discussing approved and clinical-stage checkpoint inhibitors and their mechanisms of action, the report includes discussions of clinical-stage checkpoint inhibitor modulators, such as LAG-3 (lymphocyte-activation gene 3) inhibitors, TIM-3 (T-cell immunoglobulin and mucin-domain containing-3) inhibitors, small-molecule IDO (indoleamine 2,3-dioxygenase) pathway inhibitors, and a small-molecule PI3K (phosphoinositide 3-kinase gamma) inhibitor. These agents are in Phase 1 or Phase 2 development. In general, they work to overcome immunosuppression and/or T-cell exhaustion, and thus may overcome blocks to T-cell activation by checkpoint inhibitors.

IMMUNE AGONISTS

The report focuses on immune agonists. Immune agonist therapeutics - most of which are mAbs - target specific cell surface proteins on T-cells, resulting in stimulation of T-cell activity. This mechanism contrasts with that of checkpoint inhibitors, which are designed to overcome blockages to T-cell activity mediated by immune checkpoints. Companies are developing immune agonist immunotherapeutics principally for use in combination with checkpoint inhibitors (ie, as immuno-oncology 2.0 agents). All the agents discussed in this report are in early stage clinical trials.

FIGURE 1

Biomarker	Description
PD-L1	Target biomarker used to define patient populations that may be effectively treated with anti-PD-1 or anti-PD-L1 checkpoint inhibitors, especially in clinical trials and in approval decisions by regulatory agencies. Imperfectly discriminates between patients who can benefit from these therapeutics and those who cannot. It is of little use in designing improved therapies that build on current checkpoint inhibitor therapies to improve patient outcomes.
Mismatch repair (MMR) deficiency	Genetic biomarker used to determine the likelihood that a patient's tumors possess a sufficient somatic mutation load to support a large and diverse population of CD8+ TILs, which are specific for mutation-associated neoantigens. Treatment with checkpoint inhibitors may reactivate these TILs, resulting in effective antitumor immune responses.
Determination or estimation of mutation load.	Genetic biomarker used to evaluate somatic mutation load. A sufficiently large mutation load results in a large and diverse population of CD8+ TILs, supporting effective checkpoint inhibitor therapy.
Immunohistochemical determination of CD8 expression at the invasive margin of a tumor.	Immunological biomarker that correlates with numbers of CD8+ TILs present at the invasive margin of a tumor. Patients who respond to checkpoint inhibitor therapy show proliferation of intratumoral CD8+ TILs that directly correlates with reduction in tumor size.
Immunoscore	Immunological biomarker. The Immunoscore is a method of characterizing the nature and function of immune cell infiltrates into tumors based on measuring the densities of CD3+ and CD8+ in the tumor core and the invasive margin using IHC. Some researchers see the Immunoscore as the best predictor of survival in patients with colorectal cancer. The Immunoscore Colon test is available as a laboratory service from HalioDx as of July 2016 and is on track to be commercialized as a CE-IVD (in vitro diagnostic) solution by end of the year in Europe.

Biomarkers for Use in Clinical Studies of Checkpoint Inhibitors

BISPECIFIC ANTIBODIES

The report discusses bispecific antibody (bsAb) cancer immunotherapeutics, which are a type of mAb. bsAbs are designed with two different variable domains that enable the Ab to bind simultaneously to two different types of targets. bsAbs used in cancer immunotherapy usually bind one target on a tumor cell and another target on a cytotoxic immune system cell, bringing the two types of cells into proximity. This allows the immune system to act against the tumor cell.

ANTICANCER VACCINES

This section of the report focuses on therapeutic anticancer vaccines and oncolytic viruses. Efforts to develop therapeutic cancer vaccines began in the 1990s. However, the cancer vaccine field has been characterized by a long series of clinical failures, beginning in the 1990s and continuing to the present day. Researchers have been working to overcome these difficulties by using improved research methodologies and by employing advances in our understanding of immuno-oncology. In the current era, researchers have used their greater understanding of dendritic cell biology to attempt to improve the design of peptide and protein vaccines. Another important factor that has contributed to the failure of cancer vaccines is immune suppression in the tumor environment. Some researchers hypothesize that one way to overcome this immunosuppression is to administer vaccines in combination with checkpoint inhibitors.

In 2015, the FDA approved talimogene laherparepvec (Amgen's Imlygic, also known as T-Vec), an oncolytic herpes simplex virus that expresses granulocyte macrophage colony-stimulating factor (GM-CSF). It is approved for the treatment of melanoma lesions in the skin and lymph nodes. This oncolytic virus is injected into a single tumor, where it lyses tumor cells. It was postulated that upon lysis of tumor cells in the treated lesion, systemic immune responses are induced. There was evidence for induction of immune responses in distant tumor sites in a published Phase 1 study, and there was a trend toward improved overall survival in early results of a Phase 3 study presented at the 2013 ASCO Annual Meeting. However, as determined by completed results of the same Phase 3 study, the agent was not subsequently shown to improve overall survival or influence distant metastases.

Imuno-oncology 2.0 strategies now feature prominently in therapeutic cancer vaccine and oncolytic virus therapeutic de-

FIGURE 2

Targets	Agent	Description	Stage
EpCAM and CD3	Catumaxomab (Neovii Biotech's Removab)	A rat-mouse hybrid mAb that consists of one anti-EpCAM antibody moiety and one anti-CD3 antibody moiety, plus an Fc domain.	Marketed in Europe for treatment of malignant ascites in patients with EpCAM-positive cancer if a standard therapy is not available.
CD19 and CD3	Blinatumomab (Amgen's Blincyto)	A small, 55 kilodalton murine BiTE bsAb. Unstable with a short serum half-life. Must be administered as a continuous intravenous infusion over a minimum of 4 weeks, via a minipump system.	Approved by the FDA under the accelerated approval program in 2014 for treatment of Ph⁻ B-cell ALL. Granted conditional marketing authorization in the EU in 2015.
CD20 and CD3	XmAb13676 (Xencor/ Novartis)	A full-length bsAb with an Fc domain, based on Xencor's cross-linking monoclonal antibody (XmAb) bispecific platform technology.	Xencor expects to begin a Phase 1 trial of XmAb13676 in 2016 for treatment of B-cell malignancies.
CD123 (alpha-chain of the interleukin-3 receptor) and CD3	XmAb14045 (Xencor/Novartis)	A full-length bsAb with an Fc domain, based on Xencor's cross-linking monoclonal antibody (XmAb) bispecific platform technology.	Phase 1, AML and other CD123-expressing hematologic malignancies.
CD20 and CD3	REGN1979 (Regeneron)	A full-length bsAb with an Fc domain, based on Regeneron's native human Ig format bsAb technology.	Phase 1, CD20⁺ B-cell malignancies in patients who had been previously treated with an anti-CD20 mAb therapy.

Select Bispecific Antibody Agents for Cancer Immunotherapy

velopment. This is particularly true with neoantigen vaccines, which are designed to induce neoantigen-specific TILs within patients' tumors. The strategy is to use the vaccine to induce the TILs, rendering checkpoint inhibitors effective in inducing tumor regression. Based on this strategy, Neon's NEO-PV-01 vaccine is being combined with poly-ICLC adjuvant and Bristol-Myers Squibb's PD-1 immune checkpoint inhibitor nivolumab in collaborative clinical studies in advanced melanoma, smoking-associated NSCLC, and bladder cancer.

The immuno-oncology 2.0 strategy has become a general theme of cancer vaccine research and development beyond neonantigen vaccines - use cancer vaccines to render tumors inflamed, and use checkpoint inhibitors to induce regression of the inflamed tumors. Thus, there are several examples of trials of cancer vaccine/checkpoint inhibitor combinations discussed in this section of the report. In some cases, cancer vaccines are being tested in combination with checkpoint inhibitors in Phase 1 or Phase 2 clinical trials, rather than the "traditional" approach of first getting a vaccine approved and then conducting trials of the vaccine in combination with other agents. It is possible that testing a vaccine in combination with a checkpoint inhibitor in early stage clinical trials may reduce the number of failed cancer vaccines. However, whether this is true remains to be seen.

This report focuses on the use of adoptive T-cell immunotherapies for cancer. In this class of therapies, autologous or syngeneic activated T-cells (which may or may not be genetically modified) are infused into patients to attack their cancers. Adoptive immunotherapy is also known as adoptive cell transfer (ACT).

IMMUNOTHERAPY WITH TIL CELLS

ACT was pioneered by Dr. Steven A. Rosenberg of the National Cancer Institute (NCI). The major focus of the Rosenberg group has been TIL therapy, which involves isolation of TILs (which are tumor-infiltrating T-cells) from a patient's tumor, followed by ex vivo expansion of these cells with IL-2. The TILs and high-dose IL-2 are then infused intravenously into the patient. The infused T- cells traffic to tumors and can mediate their destruction. Clinical study of TIL therapy has continued to the present day. Moreover, attempts to overcome some of the limitations of TIL therapy have resulted in the development of other newer forms of ACT based on various types of genetically engineered T-cells.

Kite Pharma, which expects to complete its submission for marketing of KTE-

FIGURE 3

Target	Agent	Description	Stage
CD27	Varlilumab (CDX-1127)–fully human mAb that targets CD27 (Celldex Therapeutics/BMS)	Varlilumab can deliver a costimulatory signal to T cells with engaged TCRs, transforming a weak immune response into a strong, prolonged response. Varlilumab may also exert direct therapeutic effects against tumors that express CD27 at high levels, such as human B and T cell lymphomas.	Phase 1/2, in combination with the anti-CD-1 checkpoint inhibitor nivolumab.
OX40	MEDI0562–humanized anti-OX40 mAb (MedImmune/AZ)	OX40 is a costimulatory receptor that can potentiate TCR signaling in T cells, leading to the activation of these cells by antigens recognized by their TCRs. Engagement of OX40 by its natural ligands on dendritic cells or by anti-OX40 antibodies initiates a signal transduction cascade that enhances T cell survival, proliferation, and cytokine production, and can augment immune responses to tumors.	Phase 1, advanced solid tumors as a monotherapy or in combination with the checkpoint inhibitors tremelimumab (an anti-CTLA-4 checkpoint inhibitor) or durvalumab (an anti- PD-L1 checkpoint inhibitor).
OX40	MOXR0916–humanized effector-competent agonist IgG1 mAb that targets OX40 (Roche/Genentech)	OX40 is a costimulatory receptor that can potentiate TCR signaling in T cells, leading to the activation of these cells by antigens recognized by their TCRs. Engagement of OX40 by its natural ligands on dendritic cells or by anti-OX40 antibodies initiates a signal transduction cascade that enhances T cell survival, proliferation, and cytokine production, and can augment immune responses to tumors.	Phase 1b, advanced solid tumors as a monotherapy or in combination with the PD-L1 inhibitor atezolizumab.
CD122	NKTR-214–engineered cytokine related to IL-2 (Nektar Therapeutics/BMS)	A PEG-modified aldesleukin-2 protein with specificity for CD122 (IL2Rβ) and for activation of $CD8^+$ TILs.	Phase 1/2, as a monotherapy and in combination with checkpoint inhibitors.
Glucocorticoid-induced TNFR-related (GITR) protein	TRX518 (Leap Therapeutics)	A non-glycosylated, humanized, Fc-disabled agonist mAb that targets GITR.	Phase 1, advanced solid tumors.

Select Immune Agonists for Cancer Immunotherapy

C19 (axicabtagene ciloleucel) in the first quarter of 2017, opened a 43,500-sq-ft state-of-the-art T-cell therapy manufacturing facility near Los Angeles International Airport in June 2016. This manufacturing plant is designed to support production of engineered CAR and TCR cellular immunotherapies. The facility has been designed to produce CAR and TCR product candidates for clinical trials, as well as to produce KTE-C19 (axicabtagene ciloleucel) for its anticipated launch and commercialization in 2017.

ADOPTIVE IMMUNOTHERAPY VIA AUTOLOGOUS RECOMBINANT TCR TECHNOLOGY

Other researchers and companies are developing autologous T-cell therapies based on recombinant TCRs. Adaptimmune is the leader in this field. Adaptimmune has designed autologous T-cells engineered with an increased affinity recombinant TCR that targets the cancer testis antigen NY-ESO-1. Adaptimmune is developing its NY-ESO-1 recombinant TCR therapeutic candidate in partnership with GSK as the result of a 2014 strategic collaboration and licensing agreement between the two companies.

Phase 1/2 clinical trials for the anti-MAGE-A10 TCR therapy in advanced NSCLC were initiated in late 2015. In 2016, the company added a Phase 1 study of the MAGE-A10 TCR therapy in urothelial cancer, melanoma, and head and neck cancers. In both cases, patients selected for the trials must test positive for HLA-A*0201 and/or HLA-A*0206 protein (in accordance with the MHC restriction of the recombinant TCR), and their tumors must test positive for MAGE-A10 expression.

Another Adaptimmune recombinant TCR therapeutic is designed to target alpha fetoprotein (AFP), which is associated with hepatocellular carcinoma. The FDA accepted the company's investigational new drug (IND) application for this therapy in April 2016. Adaptimmune plans to evaluate this candidate in a Phase 1 study, and site selection activities are underway.

GENERAL CONCLUSIONS ON THE PROGRESS OF CELLULAR IMMUNOTHERAPY

There are two CAR T-cell therapies that are expected to reach the preregistration stage with the FDA in early 2017 - Novartis' CTL019 and Kite's KTE-C19/axicabtagene ciloleucel. Both of

these target CD19 and are indicated for treatment of B-cell leukemias and/or lymphomas. The approval and marketing of one or both therapies will represent a milestone in cancer immunotherapy and will enable cellular immunotherapy to take its place beside checkpoint inhibitor therapies as an important (and marketed) modality of immunotherapy for cancer. Both therapies were approved by the FDA later in 2017, after the publication of our report.

Another focus of cellular immunotherapy is the development of engineered improvements in CAR T cell therapy. Cellectis is using gene-editing technology to design "off-the-shelf" allogenic CAR T-cell therapies that do not require the patient-specific manufacturing protocols needed for conventional autologous CAR T-cell therapies. Like biologics, the production of Cellectis' CAR T-cell therapies can be industrialized and standardized with consistent pharmaceutical release criteria. Meanwhile, Bellicum is developing CAR T-cell therapies that incorporate inducible activation switches that allow for continuing anti-tumor surveillance or serve as safety switches to eliminate cells in the event of toxicity. Notably, Bellicum postulates that its proprietary cellular controls may enable successful treatment of solid tumors by CAR T-cell therapeutics.

OUTLOOK FOR CANCER IMMUNOTHERAPY

This report includes the results of a survey on immuno-oncology that Insight Pharma Reports conducted in conjunction with this report. It also includes the general conclusions of the report and a discussion of the outlook for cancer immunotherapy.

Regular use of immunotherapy for treatment of cancer, which has been an elusive dream for more than 100 years, has very recently come within the grasp of researchers, physicians, and patients. As of the early to mid 2010s, cancer immunotherapy has become a "hot" area, with intense competition between biotechnology and pharmaceutical companies to be the first to market the newest, most effective therapies.

Moreover, building on the initial successes of researchers and companies in development and marketing of cancer immunotherapies, researchers, companies, and oncologists have been moving toward immuno-oncology 2.0 strategies that can achieve improved outcomes for more patients. Thus, as mentioned earlier, ASCO's 12th Annual Report on Progress Against Cancer (2017) named Immunotherapy 2.0 as its Advance of the Year.

In August 2015, Forbes estimated that approximately 20% to 25% of Bristol-Myers Squibb's valuation was based on the expected growth of its cancer drugs, primarily ipilimumab and nivolumab. Forbes expected the sales of these two checkpoint inhibitors to grow from $1.3 billion in 2014 to almost $7.5 billion by 2022. The same article projected a market for immuno-oncology drugs (principally checkpoint inhibitors) over the same period that could reach $35 billion.

In conclusion, immuno-oncology has begun to fulfill its promise as a game-changing approach to treating cancer. It is likely to constitute a new mode of cancer treatment, alongside surgery, chemotherapy (including treatment with cytotoxic and/or targeted drugs), and radiation therapy. Immunotherapies may eventually be used in as many as 60% of cases of advanced cancer. Immuno-oncology 2.0 approaches - as well as the successful development and commercialization of TIL-based treatments and recombinant T-cell therapies - may enable improved cancer treatments that can produce greater numbers of remissions, and even cures, for cancers that have been uniformly fatal until very recently. Thus, immuno-oncology continues to be an important and rapidly emerging field that is deserving of the attention it has been receiving in recent years.◆

This article is based on the following market research report published by Insight Pharma Reports: Cancer Immunotherapy: Building on Initial Successes to Improve Clinical Outcomes by Allan Haberman, PhD. For more information, visit http://www.insightpharmareports.com/Cancer-Immunotherapy-2017-Report/.

BIOGRAPHY

Dr. Allan B. Haberman is Principal of Haberman Associates and a Founder and Principal of the Biopharmaceutical Consortium. Dr. Haberman's consulting activities include work in new product development and technology strategy, opportunity assessment, assessment of drug pipelines, and due diligence on established and emerging biotechnology companies. He is also the author of numerous books, reports, and articles on the pharmaceutical and biotechnology industry, R&D strategy, therapeutic area and pipeline strategy, and technology assessment. Dr. Haberman also speaks at national and international conferences on the pharmaceutical and biotechnology industry and on drug discovery and development. Prior to forming Haberman Associates, Dr. Haberman was the Associate Director of the Biotechnology Engineering Center at Tufts University. He earned his PhD in Biochemistry and Molecular Biology from Harvard University.

CENTRALIZED BIOMETRICS

The Backbone of a Global Clinical Data Strategy

By: Paul Fardy

INTRODUCTION

Clinical trial data can be overwhelming and quite challenging for sponsors and participants alike. With reams of data spread across disparate systems – and more information being accumulated every minute, every day – clinicians would be wise to remember that more data doesn't always mean more insight. Sometimes more data is just that – more data.

So how do we control the management and delivery of this vast amount of data? Continuity between the biometrics team and the sponsor is essential to design a template that includes better integration of studies across all phases with common assessment methods and data standards. There needs to be agreement on the traceability of data and having one set of operating procedures. Agreement on centralization of study metrics and performance is also critical as is the use and re-use of global libraries – which elevates efficiencies and may lead to significant cost reductions.

This following will detail the steps needed to implement a successful global clinical data strategy and how to approach developing a centralized process that results in transparency, traceability, accuracy, and collaboration. Using one set of SOPs (standard operating procedures) and standard data formats will make it easier, more transparent, and more efficient in meeting the expectations of a regulatory body and/or the potential purchaser of a product license.

WHY IS CENTRALIZED BIOMETRICS THE BACKBONE OF A GLOBAL CLINICAL DATA STRATEGY?

Centralized biometrics is an alternative outsourcing approach that is appropriate for any size organization and may be especially helpful for small- and medium-size companies that are not heavily staffed to meet the challenges associated with managing the huge amount of data involved in a clinical trial. In the centralized biometrics model, sponsors keep clinical data functions - biostatistics and programming, data management, medical writing, and an EDC system – all with one specialized vendor. The main driver for implementing centralized biometrics is data standardization that promotes efficiencies and leads to cost savings, which is not found in other models.

There is no manual available describing just how to produce a global clinical data strategy; however, regulations and guidelines are forcing us in that direction. The EU clinical data transparency legislation is demanding that Sponsors produce traceable and transparent data, while the new ICH GCP E6 (R2) guidelines are forcing Sponsors to look at how they collect and report data. A centralized biometrics approach gets Sponsors moving in the direction of a coherent strategy. It can also help to

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deliver a rich repository of disparate data from multiple sources that is verifiable, traceable, and meets complex regulatory requirements. This can avoid delay and expense thereby optimizing the journey from Phase 1 right through to post-marketing.

GETTING STARTED – EARLY IS BETTER

Without a doubt, a global clinical data strategy is complicated and highly complex, which obviously leads to the question – where and when to start? The short answer is the earlier the better. There will be a variety of teams associated with developing a global clinical data strategy, eg, clinical development and regulatory marketing teams, external teams, third-party vendors, labs, all of the entities that provide different niche deliverables need to be onboard.

Continuity between the biometrics team and the sponsor is essential to design a template that includes better integration of studies across all phases with common assessment methods and data standards. There needs to be agreement on the traceability of data and one set of operating procedures. Agreement on consistent study metrics and performance to measure data quality is also critical.

When thinking about developing a strategy, there are several questions to ask:

- Is the data our greatest asset?
- What's our outsourcing strategy?
- How can we best utilize our data and make sense of it to assure appropriate decision-making?
- Is our company prepared for clinical data transparency?
- Are we aware of the regulator's recommendations for a risk-based monitoring approach and what does that mean?
- Have we considered the regulatory requirements that will factor into our strategy?

These are topics that have come up in our experience and have different definitions depending on where you sit. You can be a program manager, a data manager, or a statistical programmer. Perspective differs depending on the function, and it's often difficult to have an overarching vision and understanding of where you need to be and how to get there. It's complicated and complex to be sure!

THE IMPACT OF ICH E6 (R2)

The intention of ICH E6 (R2) is to "provide increased clarity and encourage implementation of improved and more efficient

approaches to clinical trial design, conduct, oversight, recording, and reporting."

Fundamental to this is a risk-based approach to the Quality Management System and a risk-based approach to study conduct. The storage system (irrespective of the media used) should provide for document identification, search and retrieval. If subcontractors are to be used by CROs, then there will need to be clauses in contracts to take into account sub-contracted third-party agreements.

The Investigator should have control of and continuous access to the CRF (case report form) data reported to the Sponsor. Keep in mind that responsibility for any non-compliance issues falls under the Sponsor, and when an issue occurs, the Sponsor needs to perform a root cause analysis and corrective action.

All of these elements are more predictable and easier to handle when a centralized strategy is adopted and will reassure the regulatory agencies that due care and attention is being given to the handling of the data.

CORPORATE GOVERNANCE COMMITTEE: KEYS TO A SUCCESSFUL GLOBAL STRATEGY

Designing and implementing a global standards governance committee serves as the foundation for both standardization and centralization of clinical trial data. With the variety of different standards implicit in the many disparate documents involved in a trial, compounded by the fact that each have their own individual standards applied to them, it's important to identify, create, and utilize global, cross-therapeutic and therapeutic standards within the entire clinical development process.

Also important is the centralization of study metrics and reporting. Centralization creates a platform in which the message is understood and clearly defined. This ensures the validity of the data and provides an understanding of exactly what the data is "saying" and can be understood and clearly defined. While this is a difficult task with separate sources, it's much easier when the data is centralized. And, even better, there is a cost-reduction element. The centralization approach means that through re-usage and efficiencies of process, those reductions should be immediately realized.

STEPS TO IMPLEMENTING A GLOBAL CLINICAL DATA STRATEGY

In short, a CRO with deep experience in leading sponsors to develop a global clinical data strategy will help create a path to:

- Design and implement a global standards governance committee
- Identify, create and utilize global cross-therapeutic and therapeutic standards
- Institutionalize and harmonize standards within the clinical development process
- Create due-diligence ready data sets
- Comply with regulatory requirements and industry standards

An experienced, data-driven full-service CRO can provide a cost-effective and efficient centralized clinical data package by providing data management, statistical analysis, programming, and medical writing services coupled with excellent clinical project management, regulatory consultancy, and accompanying eClinical solutions.

This centralized biometrics approach, when applied appropriately, converts a mass of processes and data into a coherent, information-driven pathway from which the vision can be achieved and success is more certain. ◆

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BIOGRAPHY

Paul Fardy is VP of Data Services for CROS NT (www.crosnt.com). He carries over 27 years of experience in biometrics team management with particular expertise in Clinical Data Management procedures and processes. Most of his career was spent in large pharmaceutical companies managing functional teams in Data Management, Statistics, Statistical Programming, and Medical Writing, where he recruited the necessary resources and developed metrics and resource planning for clinical studies. He also has experience in leading operations in the CRO sector prior to joining CROS NT and has earned a reputation for quickly developing productive, cohesive, and motivated teams. Mr. Fardy earned his degree in Microbiology from the University of Surrey and is based in the United Kingdom. He can be reached at: paul.fardy@crosnt.com.

ONCOLOGY DIAGNOSTICS

Advancements Paving the Way for More Tailored Drugs

By: Divyaa Ravishankar, MS

INTRODUCTION

Pharmaceutical companies have been subjected to a wide variety of external forces compelling them to get innovative about development of new platforms, liaise with new partners, leverage big data toward precision and predictive diagnosis, and identify new markers. This following describes some of the recent trends observed in the diagnostics industry that are creating opportunities for companies to partner in unconventional ways.

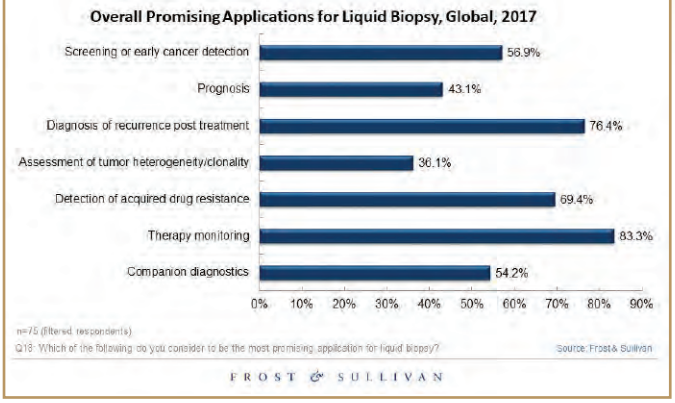
NEW INDUSTRY TRENDS

Liquid Biopsy Attracting Funds From Drug Developers

Clinicians have suggested that screening (early detection) and therapy selection, and monitoring are the short-term promising applications of liquid biopsies. Several In Vitro Diagnostics (IVD) and pharmaceutical companies are expanding their product portfolio to include liquid biopsy and companion diagnostic (CDx) in their long-term strategy. Figure 1 shows a Frost & Sullivan survey conducted with almost 100 clinicians is a key indicator of the promising applications of liquid biopsy. There are already a handful of companies marketing tests, but many of its applications are restricted toward improvement of late stage. Investments are flowing into the space where there is potential to develop technologies for early cancer detection and as well as post-cancer monitoring.

In March 2017, a slew of investors, including Amazon and some prominent pharmaceutical companies like Johnson & Johnson and Bristol Myers Squibb, financed a biotech firm called

FIGURE 1



Grail (a spin-off from Illumina). Grail plans to implement large-scale clinical trials to verify the technology's ability to detect early stage cancer. Another pharma-diagnostic partnership worth a mention is between BioCept and Catalyst Pharmaceuticals. BioCept's liquid biopsy tests will be offered to all patients enrolled in its Phase III clinical trial of Firdapse for treatment of Lambert-Eaton myasthenic syndrome(LEMS), a very rare autoimmune disorder. BioCartis and Merck launched their second liquid biopsy test Idylla™ ctNRAS-BRAF-EGFR S492R Mutation Assay. Some of the other ideal members to partner and to watch over for their CDx portfolio include the companies shown in Figure 2.

Overall, it can be said that technological advances have changed recent sentiments toward circulating tumor cells (CTCs) as valuable predictive or prognostic biomarkers, as evidenced by the growth in comparative studies of genomic mutation analysis in solid tumors and CTCs. Advances such as highly sensitive microfluidic biosensors, single cell analysis, and deep sequencing of circulating cell-free tumor DNA are making the concept of the

FIGURE 2

Liquid Biopsy Companies, US, 2017

FOCUS AREAS	PROGNOSIS	DIAGNOSIS	CDx	RECURRENCE MONITORING
myriad	X			
ASPIRA LABS		X		
ONCOCYTE		X		X
Genomic Health			X	X
Biocept			X	
FOUNDATION			X	
veracyte		X		
QIAGEN			X	
MDxHealth	X			
GUARDANT HEALTH			X	
admera			X	X

liquid biopsy, or the ability to monitor a tumor noninvasively, a near-term reality.

Growing Favor of CDx Tests by the FDA

The FDA is going so far as to reject drugs that require CDx for eventual patient selection, such as in the rejection of the Australian company ChemaGenex's leukemia drug candidate because it did not have a companion diagnostic to select patients. This example signals the FDA's favorable view of CDx. In December 2016, the FDA also offered an accelerated approval to the first next-generation sequencing–based companion diagnostic test for Rubraca™ (rucaparib) developed by FoundationFocus CDxBRCA. Similarly in June 2016, the FDA offered approval to the first-ever liquid biopsy companion diagnostic test from Roche that goes hand in hand with Tarceva developed by Astellas Pharma in the US.

New Clinical Biomarker Classes

Epigenetic regulators are emerging targets for cancer therapy and as future clinical biomarkers. The growing clinical research may lead to novel epigenetic-based companion diagnostics in the future.

Using Big Data From Diagnostic Companies to Tailor Drugs

On March 12, 2015, 23andMe, a consumer genetic testing company announced that it will no longer just sell tests to consumers or genetic data to pharmaceutical companies, but instead, they will start to produce medicine itself. The company has also hired Richard Scheller, who led drug discovery at biotech icon Genentech for 14 years. 23andme has collected DNA information from over 1.2 million people, and it is said the company has sold access to information to over 13 pharmaceutical companies whose names were not revealed except Genentech. This provides evidence that big data can truly revolutionize the pharmaceutical research and development (R&D) industry, as data will help identify new potential drug biomarkers that can be tailored to the genetic make-up of the patient. Based on the big data, patients can be identified for clinical trials with much more ease.

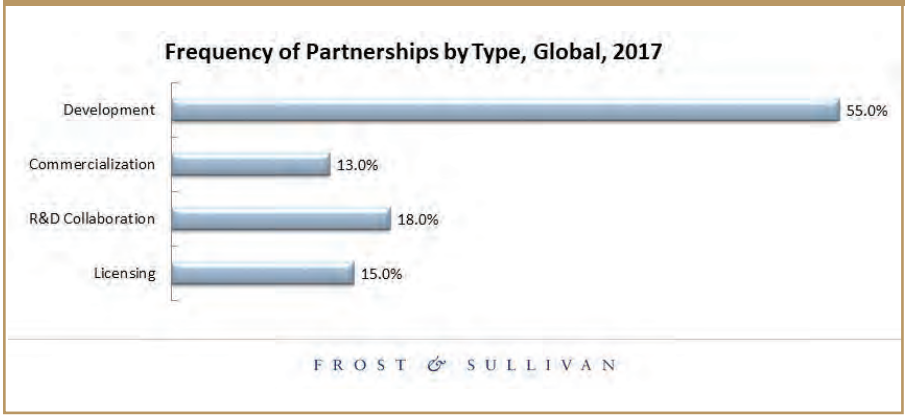
With the ResearchKit, a software framework for apps from Apple, the aim is to collect a myriad of physiological parameters formats, such as blood pressure, heart rate, pulse, between others. A combination of these two datasets both genetic (from 23andMe) and physiological parameters (from Apple) can lead to a breakthrough in analyzing different parameters and provide a 360-degree view to the bits and pieces of data from different corners of the medical research spectrum.

TYPES OF COMPANION DIAGNOSTIC PARTNERSHIPS

Most pharmaceutical companies developing targeted therapies choose a companion diagnostic partner to access technology and IVD expertise. More than 300 company press releases about CDx relationships from 2011 to 2017 (Figure 3) were analyzed for this research. Partnership types included the following:

- Development: Developing a CDx for a company's pre-existing drug candidate.
- Licensing: exclusive license between two companies on CDx development and commercialization.
- Commercialization: agreement on Rx-Dx co-commercialization in various market regions.

FIGURE 3



- R&D Collaboration: permission to use a diagnostic test for drug candidates or funding from the pharmaceutical company for R&D on a CDx.

VARIOUS CO-DEVELOPMENT MODELS EXIST

Approach 1: Leveraging Internal Expertise (eg, Roche and Johnson & Johnson) - The advantages include leveraging existing infrastructure facilitates collaboration and faster release of products. The disadvantages include appropriateness of the diagnostic platform, organizational challenges, and value sharing.

Approach 2: Using an External Diagnostic Partner (eg, Pfizer, Bristol Meyers, Merck, and Amgen) - This is the most common type of partnership and co development model. This type of partnership provides access to new and appropriate technology through license or fee-for-service arrangement. The disadvantages include negotiating balanced licensing, intellectual property, and partnering agreements.

Approach 3: Acquiring Diagnostic Capability (eg, Eli Lilly, Novartis/Genoptix) - The advantages include access to new technology. The disadvantages include integration challenges between organizations, diagnostic platform may not be appropriate for future compounds.

NEW MARKET OPPORTUNITIES

Critical Unmet Need 1: Even More Clinically Useful CDx Needed to Realize Personalized Medicine

Potential Game Changing Strategy - Biomarker development for future companion diagnostics should incorporate the following functions:

- Patient stratification, eg, a KRAS mutation test to determine eligibility for Eribitux
- Dose determination, eg, CYP2C9 variants to guide Warfarin dosage
- Treatment monitoring, eg, a BCR/ABL PCR analysis that measures response to therapy
- Prognostics, eg, a BRAF mutation test that predicts NSCLC patient survival

CDx developers can follow the above guidance to improve clinical utility.

Critical Unmet Need 2: Unsustainable Drug Development Model

Potential Game Changing Strategy - Biomarker testing in drug development offers the following additional benefits:

- Improving drug efficacy through patient enrichment
- Preventing patient exposure to ineffective medicines and side effects
- Shortening drug development time
- Possibly reducing costs
- Reducing regulatory risk
- Accelerating market adoption of the drug and the speed of commercialization.

CDx developers can convey these benefits to strengthen or increase co-development partnerships with pharmaceutical companies.

Critial Unmet Need 3: Drug Diagnostic Partnerships Are Unfavorable for CDx Developers

Potential Game Changing Strategy - Alternative business models that benefit CDx developers in early partnering deals can include the following:

- Joint R&D investment in CDx development
- Upfront payments from pharmaceutical companies for reaching milestones
- Royalties from future sales

SIGNIFICANCE OF THE CANCER MOONSHOT PROGRAM

Build a National Cancer Data Ecosystem

The objective of the cancer moonshot program is to create a national ecosystem

for sharing and analyzing cancer data so that researchers, clinicians, and patients will be able to contribute data, which will be an incentive to invest in artificial intelligence (AI) and data analytics. Companies participating in the working groups are Amazon, Google, Microsoft, and MIT Cancer Center.

Minimize Cancer Treatment's Debilitating Side Effects

The program also helps with accelerating the development of guidelines for routine monitoring and management of patient-reported symptoms, which will fuel liquid biopsy assay development. Among the institutions participating are the American Cancer Society, Kaiser Foundation Research Institute, UC San Diego Moores Cancer Center, and Louisiana State University.

Expand Use of Proven Cancer Prevention & Early Detection Strategies

Reduce cancer risk and cancer health disparities through approaches in development, testing, and broad adoption of proven prevention strategies will focus investments on screening technologies. Among the companies participating are Huntsman Cancer Institute, Vanderbilt-Ingram Cancer Center, Dana-Farber Cancer Institute, and Janssen Pharmaceutical.

Mine Past Patient Data to Predict Future Patient Outcomes

Predict response to standard treatments through retrospective analysis of patient specimens with AI algorithms. Among the institutions are Oregon Health & Science University, US Department of Veterans Affairs, National Cancer Institute, and Harvard Medical School.

FUTURE OUTLOOK FOR CANCER DIAGNOSTICS MARKET

Changes to Clinical Workflow

Move from disease treatment, to its full potential of preventive medicine. The technology to put Next-Generation Sequencing (NGS) available in every laboratory across the US to the use of improving clinical outcomes for patients and the benefit of their families is available today. We have companies that use a multi-marker approach with ease of use. They provide a panel for 28 of the most utilized gene markers for the high-volume disease. If the physician wants to focus on non-small cell lung cancer or colon cancer then the physician can just use the results for the appropriate gene combinations, usually between one to three markers. The technology allows for mRNA, cell free DNA, and CTC to be measured from blood samples and other body fluids, making it desirable for the screening and monitoring segment. These are the segments of growth in most of the cancers.

Shift in Care From Treatment to Screening

Provide physicians with improved diagnostic accuracy to guide medical decisions in the very early stages of the disease so that the correct therapy can have the effect of suppression therapy and the confidence that their decisions are factual to protect their integrity and that of their practice and hospitals, or healthcare delivery networks by moving the needle from treatment to prevention. For patients and their family with hereditary predisposition to cancer disease, they can undergo regular screening for any signs of early development.

Liquid Biopsy

There is a big limitation in the prognosis and therapy selection segments of the molecular pathology; the space where most companies are today and for which, the FDA has granted approvals for use; the specimen used is biopsies. Biopsies are a surveillance procedure and must be reported centrally and published by the Centers for Disease Control and Prevention (CDC). Physicians and professional medical associations want to decrease the number of annual biopsies. In most of the cancer types, such as colorectal and prostate, the total number of annual biopsies has trended down.

Molecular diagnostics and gene sequencing have proven that with the correct identification of a gene sequence, disease can be identified. But gene expressions are a very complicated science. A single mutated gene can have downstream effects on the activation of another gene or protein expression. The technology is available today for targeting and identifying different markers. Understanding these downstream ramifications and the methodology to measure them will be the proprietary technology for new assays. ◆

Divyaa Ravishankar has over 12 years of experience in market research and management consulting. In addition to authoring numerous reports in the area of In Vitro Diagnostics, she has advised clients on market trends, implications, and strategies on diverse topics as next-generation technologies, end-user and product/feature/pricing analysis, merger and acquisition target analysis, international market expansion strategies, detailed demand modeling, and competitive analysis. Ms. Ravishankar earned her Master's Degree in Biological Sciences from Birla Institute of Technology.

Drug Development
EXECUTIVE

Gordon Bates
Head of Chemical Division
Lonza Pharma & Biotech

Lonza

Lonza Pharma & Biotech: Taking on the Next Challenges in Small Molecules

The small molecule medicine market which accounts for two-thirds of the therapeutics in today's pharmaceutical market has entered a transition phase.[1] Drug candidates in the development pipeline are increasingly complex and specialized. Drug companies continue to evolve in terms of focus, capabilities, and outsourcing needs. Gordon Bates, Head of Chemical Division at Lonza Pharma & Biotech, shares his perspective with *Drug Development & Delivery* about industry needs and how strategic acquisitions are enhancing Lonza's position as a development and manufacturing partner of choice.

Q: We hear a lot about the need for integration in drug development – why is this important to the future of the industry especially as it relates to small molecules?

A: Increasingly, pharmaceutical companies are looking for a partner who not only manufactures the drug substance, but can optimize the formulation to meet the targeted product profile and client's objectives. Additionally, flexibility and scalability are sought after in order to satisfy the demands at each clinical phase through to commercial manufacturing. We believe an integrated approach can ensure a strong alignment and balance between our clients' short and long-term program goals, particularly where we recognize that speed to market is critical for new products. At Lonza, integration means offering clients the services - and appropriate business model - to fit their specific needs from product concept through commercial manufacturing. There are several factors

driving our strategy to offer our clients a premier integrated product development model.

First, big pharma continues to downsize. The emergence of virtual, small, and specialty companies are increasingly driving early stage pipelines. These companies need the support of high-quality experienced contract development service partners.

Second, bioavailability is a continuing challenge and the increase in highly potent medicines under development is further driving a need for specialized formulation and processing requirements. These challenges are not trivial and require specialized expertise. Development partners must have an extensive chemistry and formulation toolkit as well as the know-how and expertise to apply these tools effectively to meet target product profiles and the commercial objectives of clients. Equally, development partners have to be equipped and staffed to support all aspects of a development program, inclusive of robust feasibility studies, process development, process characterization, CTM services, scale up, and technology transfer. We listened and are responding to the feedback from our existing clients, as well as potential clients, by investing to strengthen our comprehensive capabilities across all of our product options – drug substance intermediates, drug substance, drug product intermediates, and finished drug products.

Third, and I mentioned this earlier, speed to market for new products is critical. Accelerated timelines are becoming the norm. We have been a trusted partner in more than a third of all small molecule product approvals with breakthrough therapy designations. We see many more breakthrough designations in our pipeline, as well as an increasing number of clients pursuing the 505(b)2 regulatory pathway or equivalent in Europe or elsewhere in the world. Capacity and flexibility is critical in meeting these needs. We have, therefore, focused on tools and best practices for optimizing timelines at each stage of development. For example, we have utilized our core engineering strengths and science-of-scale studies to design and develop specialized, phase-appropriate processing equipment to support proof-of-concept studies that are readily scaled to clinical and commercial manufacture.

Finally, security of supply has never been more important for today's medicines. We manufacture for nearly 300 commercial products across our product options. We have a proven track record of providing security of supply with a clear commitment to quality.

Q: What are the most pressing challenges for the CDMO market as it relates to small molecule-based drug development and manufacturing, and how is Lonza fulfilling these future needs?

A: Designing a compound or formulation that is optimized for meeting the therapeutic window with future reproducibility and manufacturability is considered in the proof-of-concept stage. To accomplish this objective, a partner should have depth in addressing chemistry or formulation challenges. This includes multiple technology options, know-how, and expertise for specific problem statements, and specialized processing equipment with a history of tackling these challenges. We have advanced thousands of compounds across a myriad of parameters and challenges – and this experience has led to innovative approaches in product and process design, development and manufacture.

Lonza's investments are in-sync with the key industry problem statements and responsive to challenges faced by our clients today. For example:

Highly Potent Active Ingredients – Driven by the oncology development pipeline, HPAPI demand continues to increase. Lonza specializes in custom HPAPI development. We have the largest commercial production capacity in the world at Visp (CH). Our formulation labs are all equipped to handle highly potent and other challenging compounds as are our manufacturing sites for drug product intermediates and finished dosage forms.

Bioavailability Enhancement – The majority of compounds have either dissolution rate or solubility issues. We have a full portfolio of enabling technologies combined with selection methodologies and formulation expertise to match the optimal approach to the specific challenge.

Modifying Pharmacokinetics – Tailoring drug delivery profiles to increasingly specialized target product profiles is often required. Our acquisition of Capsugel has given us a full range of technologies and expertise for meeting any delivery profile required.

Q: With the recent acquisitions of Capsugel and Micro-Macinazione, can you speak to the key synergies you see with Lonza's core drug substance business?

A: We are excited to integrate our custom drug substance capability with the particle engineering expertise we now have through these acquisitions. Capsugel and Micro-Macinazione have a combined 65 years of experience in micronization from developmental studies to commercial supply. We have capacity of more than 2000 MT and a geographic presence that spans North America and Europe. Capsugel has also brought premier depth in spray drying, pioneered by Bend Research, another key approach for engineering optimal particle size distributions.

This combination gives us the opportunity to further optimize and tailor drug substance and drug product intermediate to meet a client's specific compound and formulation requirements. These acquisitions of industry leaders in particle engineering give Lonza premier expertise, technology options, and flexibility through spray drying, jet milling, nano-milling, cryogenic milling or combination approaches. Specialized capabilities are in place for HPAPI, controlled substances, hormones, steroids and other challenging compounds. Nano-milling is in place for sub-micron applications, as is cryogenic milling for optimizing particle size for elastic/semi-solid compounds. The choice of technology and approach is always dependent upon a client's specific problem statements, and we now have a full range of particle engineering approaches.

Given our global capability, capacity, and technology options – and the quality and security of supply that Lonza stands for – we offer clients a best-in-class partnership throughout the development and commercialization process.

Q: What is the approach Lonza is taking to integrate its new drug product intermediate and drug product offerings?

A: We are integrating our small molecule offering from concept to commercial scale manufacturing. We already have in place the capability to support the full range of products – from drug substance to finished forms – throughout the development cycle to commercialization.

Our site leaders and product development teams are interacting well. They are very keen and quick to share best practices and exhibit a strong desire to learn from each other to further advance our capabilities. The R&D teams have been integrated with many new ideas and applications leading to a number of priority actions to be pursued in the short- to mid-term.

Ensuring common technology selection methodologies is key to offering clients an unbiased approach to problem-solving and the most appropriate formulation development. This can be a challenge when integrating technology leaders in the industry – spray drying, micronization, lipid-based formulations, and liquid filled hard capsules to name a few. Nevertheless, I am encouraged by how a dedication to science and engineering principles is guiding our team's decision-making.

Q: What's ahead for Lonza in terms of the next innovation or technology development in small molecules?

A: We listen to our clients and invest in innovative capabilities to meet their needs. We always look to leverage our core strengths in engineering and science to facilitate continued advances.

As mentioned earlier, we have advanced thousands of compounds and continue to identify and model the barriers to effective drug absorption. Each year, we advance our predictive modeling capability, and will continue to do so with additional data and the experience brought by our acquired companies.

We will continue to improve our approaches for optimizing the efficiency and productivity of our drug substance and drug product intermediate manufacture, expand the application space of our technologies, and seek new applications for our specialized technologies.

Our team has been sharing ideas and brainstorming new areas to explore, and I don't expect we will be short of projects to keep our R&D experts occupied. We remain focused on investing for the future and partnering with clients to tackle the next challenge together. ◆

REFERENCE

1. Miller J. Small-molecule API CMOs are thriving. BioPharm International. October 1, 2015. Website visited: http://www.biopharminternational.com/small-molecule-api-cmos-are-thriving-0.

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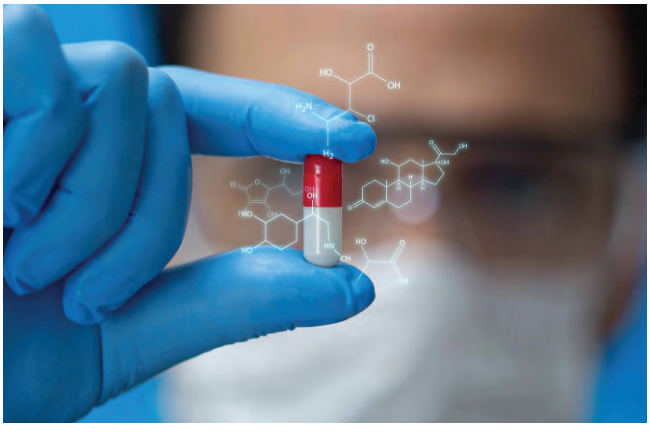

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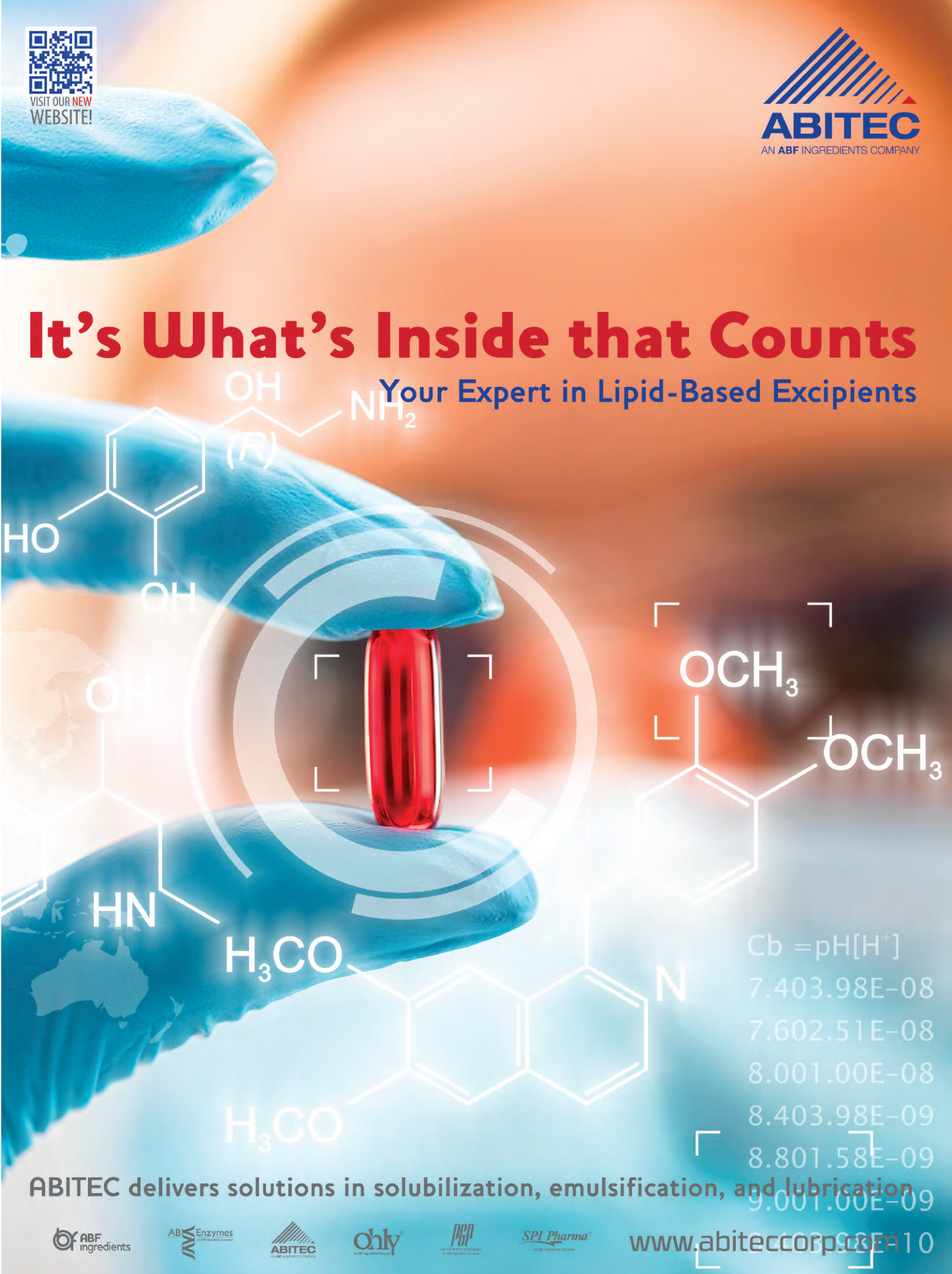

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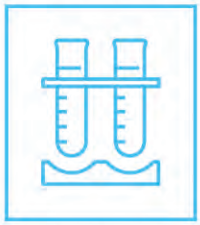

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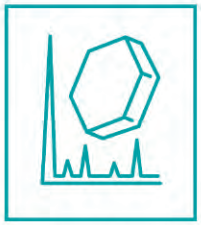
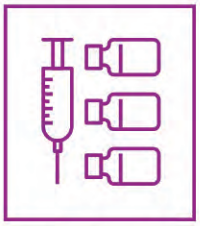


Analytical and Solid State Services

API Manufacturing



Drug Product

Explore our expert solutions at amriglobal.com

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Setting the Standard for the Drug Delivery Industry for Decades

Aptar Pharma is a leading provider of innovative drug delivery systems to pharmaceutical, consumer healthcare, and biotech customers worldwide, enabling safe, convenient, and compliant medication delivery.

Every year, over 1 billion people use 6 billion Aptar Pharma systems safely, helping to improve their lives. In fact, every second, thousands of patients receive their medication due to Aptar Pharma's technology.

We specialize in innovative and proven injection and spray drug delivery systems for the world's biggest pharmaceutical brands, representing over $50 billion in pharma products. Our drug delivery systems provide strategic competitive advantages to help our customers succeed.

Aptar Pharma has an extensive product portfolio reflecting our broad therapeutic expertise in Nasal, Pulmonary, Injectables, Eye Care, and Dermal delivery routes, among others.

Our global manufacturing footprint of sites in Argentina, China, France, Germany, India, Switzerland, and the United States provide security of supply and local support to our customers.

Continuing to Break New Ground in Innovative Healthcare Technologies

Aptar Pharma has products and solutions addressing key megatrends in the drug delivery industry, reflecting the evolving Pharma market, customer, patient, and consumer needs. Aptar Pharma is aligned with key industry trends such as security and safety, convenience and ergonomics, and patient adherence.

Delivering Connected, Intuitive Devices to Improve Patient Health Outcomes

As the leader in respiratory drug delivery systems, Aptar Pharma is focused on supporting customers and patients to effectively treat respiratory diseases, including asthma & COPD. Today 60% of patients fail to comply with their medication regimen.

At Aptar Pharma, we strongly believe that patient behavior can be changed through connected and intuitive, user-friendly devices. Connected devices provide objective monitoring and real-time data with digital solutions. This can improve patient engagement, significantly increase dose adherence, and improve patient health outcomes, as patients manage their treatments more effectively. This also creates value in the healthcare system as improved adherence reduces the number of hospitalization events in chronic diseases, resulting in lower healthcare costs to the payers.

Aptar Pharma offers a range of drug delivery devices that can bring in the full connected functionality and integrate them with software solutions that are accessible to patients and consumers. We have partnered with several digital health solution providers to develop a portfolio of connected devices, such as MDIs and DPIs. We can provide add-on devices as well as integrated devices. Depending on your data stream objectives, such as monitoring adherence and compliance, we can develop the right connected solution for you.

Aptar Pharma...delivering solutions, shaping the future

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France
Media Contact: Carolyn Penot, Director, Operational Marketing
T: +33 1 39 17 20 38 W: www.aptar.com/pharma

Together, we can tackle patient adherence. Let's connect.

Aptar Pharma – delivering connected, intuitive devices to improve patient health outcomes

As the leader in respiratory drug delivery systems, Aptar Pharma is focused on supporting customers and patients to effectively treat respiratory diseases including asthma & COPD.

Today, 60% of patients fail to comply with their medication regimen. At Aptar Pharma, we strongly believe that patient behavior can be changed through connected and intuitive, user-friendly devices. This can significantly increase dose adherence and improve patient health outcomes. That's why we are partnering with digital health solution providers to develop a portfolio of connected devices such as MDIs and DPIs.

To find out more about how we can help you deliver better patient health outcomes via connectivity, call **Chris Baron**, Associate Director, Business Development, at Aptar Pharma on **+33 6 3095 5331** or email **chris.baron@aptar.com**

Delivering solutions, shaping the future.

Aptar pharma

AVOMEEN
ANALYTICAL SERVICES

Avomeen Analytical Services
Toll-Free: (800) 930-5450 • Fax: (800) 930-5479
Email: scientist@avomeen.com
Web: www.avomeen.com/pharma

Full-Service cGMP Analytical Testing & Formulation Development Services

From method development to after-market support, Avomeen's experienced chemists support all segments of your drug development pipeline. As a full-service CMC/CRO laboratory we provide customized services that aid pharmaceutical researchers, developers, and manufacturers.

You'll be in good hands with our reliance on a Quality by Design (QBD) approach and rejection of the typical "list price testing". We recognize that every project is unique, which drives us to spend the time to find out the true nature of our clients' needs and develop a personalized plan just for you.

Our multi-disciplinary scientists and state-of-the-art facilities make us the perfect laboratory to meet your product development needs. Avomeen's scientists are current with the most sophisticated instrumentation, methods, and technical developments in the industry. Our leading scientists have years of experience with multiple dosage forms including creams & ointments, tablets & capsules, solutions and drug-device combination products.

As one of America's fastest growing independent contract laboratories we hope to grow with you as your full-service partner, not just your testing lab. Avomeen is FDA Registered & Inspected, GLP/cGMP Compliant, DEA-Licensed, and ISO 17025-Accredited.

Contact Us Today for a Complementary Initial Consultation with one of our Skilled Chemists

Why Turn to Avomeen for Your Pharmaceutical Development Needs?

- Direct Consultation with Experienced Chemist
- Rapid Turnaround on Requests for Proposals (RFP)
- Project Customization (No Cookie Cutter Quotes)
- Wealth of Knowledge & Technical Expertise
- Responsive Staff who are Flexible to Your Needs
- Non-Routine Investigative Problem Solvers - 65% of our Technical Staff Members are Ph.D. Chemists
- Rush Services Available – We Can Work Within Even the Tightest Deadlines

Services Offered

Pre-Formulation/Formulation Development

- API, Excipient, Impurities, & Drug Product R&D
- Clinical Trial Material Manufacturing (Phase I-IIa)

cGMP Analytical Testing & Development

- Method Development, Validation & Transfer
- Raw Material & Compendial (Pharmacopoeia) Testing
- ICH Stability & Degradation Studies
- Analytical Characterization & Monograph Testing (USP, EP, BP, JP, FCC, ACS, AOAC, AOCS)
- Residual Solvents, Trace Metals, & Contaminants
- Q1/Q2 (Q3) Determination & Deformulation Analysis
- Solid State Characterization
- Dissolution, Elution, & Drug Product Release Profiles
- Proteomics - Protein (Therapeutic Biologics) Analysis
- USP 232/233 - Elemental Impurities

Packaging

- Extractables & Leachables

Litigation Support Services

- Counterfeit Identification
- Patent Infringement

PRODUCT DEVELOPMENT • PHASE I-IIa CLINICAL TRIAL MATERIALS MANUFACTURING

AVOMEEN
Pharmaceutical Services

Avomeen is the premier laboratory for product development, analytical testing, and Phase I-IIa clinical trial material manufacturing services. We work closely with our clients to develop a custom program designed to get their API into clinic as quickly as reliably possible.

We work with Oral (Solid, Semi-Solid, and Liquid), Biologics, and Topical Products. Our multi-disciplinary expert scientists and state-of-the-art analytical facilities make us the perfect laboratory to meet your product development needs.

- Preformulation/Formulation
- Method Development & Validation
- ICH Stability & Release Testing
- Extractables & Leachables Analysis
- Clinical Trial Material Manufacturing

FDA REGISTERED GLP/GMP COMPLIANT

DEA LICENSED ISO 17025 ACCREDITED

API to Clinic
The Fastest Route

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scientist@avomeen.com
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65% of our Technical Staff are Ph.D. Chemists
Rush Services Available
We Specialize in Product Development Services

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 nanoparticle 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 nanoparticle engineering (milled crystals and solid-lipid particles), stable oil-in-water nanoemulsions (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 in our ISO7/8 cleanrooms, and can process aseptically and/or handle potent compounds using our Compound Aseptic Isolator capability.

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 nanoemulsion form of cyclosporin for dry-eye syndrome. Ascendia has a state-of-the-art pharmaceutical research center located in North Brunswick, NJ, and also operates a formulation research and development facility in Xiamen, China.

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

BASF creates chemistry for a sustainable future offering intelligent solutions to the pharmaceutical industry. With our expertise in polymer chemistry, R&D-capabilities, and commitment to developing excipients, BASF creates solutions for Instant & Modified Release, Solubilization, Softgels, Skin Delivery, and Biologic applications. We also are a leading supplier of selected APIs, such as ibuprofen and omega-3. Our team of experienced industry specialists are here to support you in developing effective, reliable solutions to the formulation challenges you face today and tomorrow.

It is often the simple solution that sorts out a complex problem. At BASF, we know that innovation, speed-to-market, and cost-effectiveness are crucial to pharmaceutical companies. With expertise across the entire pharmaceutical value chain, we deliver on all three accounts, from lab to launch.

Equipped with an in-depth understanding of multiple industries, technologies, and applications, we have the skills and resources to make drug manufacturing more efficient, robust, and cost-effective. Whether you want to make your medicine more effective, safer, or more patient-friendly, we will help you find the solution to your formulation challenges.

Our ***Instant & Modified*** release solutions offer an unprecedented range of functionality, which means we can help you formulate pharmaceuticals with the exact release properties you desire. This ensures the precision you need every time.

Our ***Skin Delivery*** platform provides a portfolio of excipients spanning a wide range of solubility parameters for use in semi-solids, gels, liquids, and transdermal patches to increase drug penetration through the skin. What's more, our excipients are proven to be mild and non-irritating in highly sensitive clinical studies.

Our ***Softgel*** portfolio offers leading-edge functional excipients to help achieve the best possible results for each element of a softgel – whether coating, shell, or fill. Moreover, all ingredients have been tested according to the highest quality standards to minimize the possibility of crosslinking.

We offer a comprehensive range of cutting-edge ***Solubilization*** polymers, and have an unparalleled understanding of the corresponding process technologies. This unique combination means that we can make sure you achieve effective solubilization across a range of dosage forms – particularly in solid dispersions. And because we are a pioneer in the application of hot-melt extrusion technology in pharmaceutical production, we can help you combine effectiveness with cost efficiency.

With over 50 years of experience in EO/PO chemistry, the anchor of our ***Biologics*** platform is Kolliphor® P 188 Bio, specifically designed to meet the stringent requirements of biologics manufacturers for purity, consistency and performance in protecting cells from shear stress in mammalian cell culture systems.

Rely on us to help solve your drug development challenges.

BASF Corporation
100 Park Avenue
Florham Park, NJ 07932
T: (800) 469-7541
E: pharma-solutions@basf.com W: www.pharma.basf.com

BIODURO

In Pursuit of Your Success

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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11011 Torreyana Road
San Diego, CA 92121
T: (858) 529-6600
E: hello@bioduro.com W: www.bioduro.com

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BioScreen Testing Service is a full service GMP contract laboratory specializing in Analytical Chemistry, Microbiology, and Stability services. BioScreen is an ideal partner for R&D phase I-III, as well as GLP and GMP studies. All testing conforms to ISO 9001:2008. BioScreen is DEA Registered for handling class II-V controlled substances.

Analytical Chemistry

BioScreen has over 20 years of analytical experience. Specializing in method development and validation for in HPLC, GC, GC-MS, ICP and ICP-MS. All validation packages are delivered to the client ready for FDA review or submission.

Pharmacopoeia Testing per USP, EP, BP, JP, FCC, ACS, AOAC, and other Monographs
Active Pharmaceutical Ingredient (API) - Drug Substance
Excipient
Bulk Release
Drug Product/Finished Product
Water Testing
Total Organic Carbon Determination, USP, EP (2.2.44)
Conductivity Measurement, USP
Heavy Metals Testing, USP
Elemental Impurities - Limits, USP
Elemental Impurities - Procedures, USP
Cleaning Validation Studies
Leachables & Extractables, USP, EP (3.2.2)
Residual Solvents, USP
Container Closure Integrity/Dye Immersion
Content Uniformity
Dissolution Testing, USP
Physical Testing

Stability

Long & Short-Term Stability
Drug Substance or Drug Product Stability
IND, NDA, ANDA, Stability
Photostability
Protocol Design for R&D Stability & Formulation Evaluations

Stability Storage

All ICH Conditions
Ultra Low Freezer at -84°C to -66°C
Freezer at -20°C to -10°C
Freezer at -25°C to -15°C
Refrigerated at 2°C to 8°C
Photostability Chamber
Custom Conditions Available Upon Request

Microbiology Services

BioScreen has 30 years of experience in microbiology testing for pharmaceutical, biotechnology, and medical devices.

Microbiological Examination of Nonsterile Products: MLT per USP and BP/EP, JP, US
Antimicrobial Effectiveness Tests: USP, EP, JP, ISO
Minimum Inhibitory Concentration
Bacterial Endotoxin Tests: USP, BP/EP
- Gel Clot
- Kinetic
  - Chromogenic
  - Turbidimetric

Sterility Test: BP/EP, USP
- Direct Immersion
- Bacteriostasis/Fungistasis
- Membrane Filtration
  - Close (Steri Test)
  - Open

Particulate Matter: USP, BP/EP
- Light Obscuration
- Microscopic

Container Closure Study (Microbial Ingress)
Microbial Reconstitution
AMES Test (Mutagencity Test)
- OECD # 471

Susceptibility Tests
- Minimum Bactericidal Concentration (MBC)
- Log Reduction (Time Kill Study)

Heterotrophic Plate Count
Microorganism Identification
- Vitek
- Analytical Profile Index (API)
- DNA

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.

CREDENCE MEDSYSTEMS, INC.
1600 Adams Drive, Suite 235
Menlo Park, CA 94025
T: 1- 844-263-3797 (1- 844-CMEDSYS)
E: info@CredenceMed.com W: www.CredenceMed.com

Note: This product has not been evaluated by FDA.

CAPTISOL®
A Ligand TECHNOLOGY

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. Ten 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.

For a complimentary 20g sample, please visit www.captisol.com.

CAPTISOL, A LIGAND TECHNOLOGY
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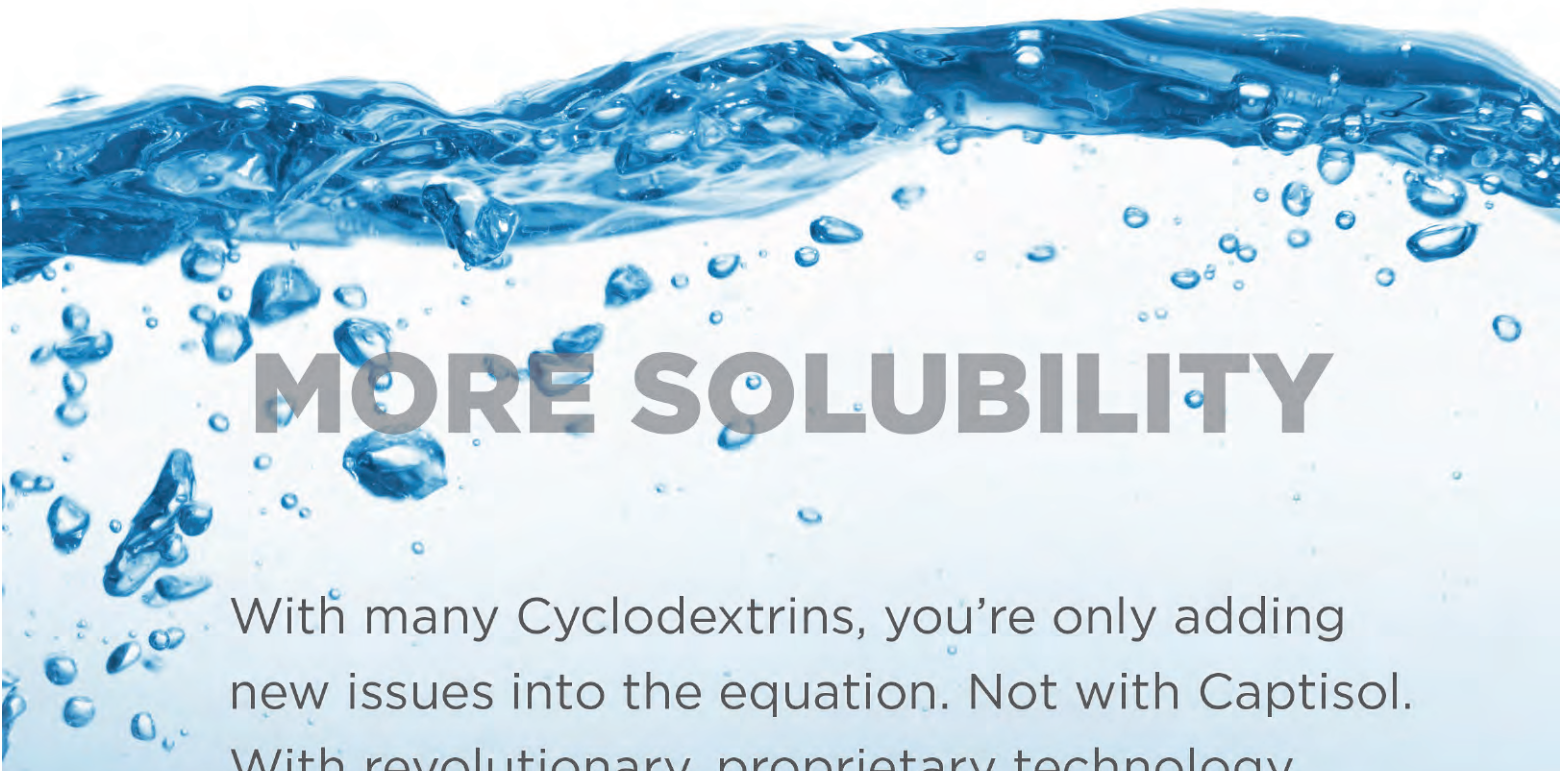
San Diego, CA 92121
E: orders@captisol.com W: www.captisol.com

MORE TECHNOLOGY.



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.

SOLVE PROBLEMS WITH CAPTISOL SOLUTIONS.

CAPTISOL®
A Ligand TECHNOLOGY

CAPTISOL.com

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 80 years serving the industry, we have proven expertise in bringing more customer products to market faster, enhancing product performance, and ensuring reliable product supply.

We serve over 1,000 innovator customers - both established and emerging - in over 80 markets, including 85 of the top 100 branded drug marketers, 23 of the top 25 generics marketers, 23 of the top 25 biologics marketers, and 22 of the top 25 consumer health marketers globally. Each year, Catalent manufactures more than 72 billion units 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 1,100 patents and patent applications, and our team of 1,400 talented scientists helped introduce 183 new products onto the market in 2016/7. 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 NCE softgel approvals by the FDA over the last 25 years have been developed and supplied by us.

CATALENT PHARMA SOLUTIONS
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E: solutions@catalent.com W: www.catalent.com

Catalent®

better treatments by design.™

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.

DEVELOPMENT DELIVERY SUPPLY

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Capsugel®

Now a **Lonza** Company

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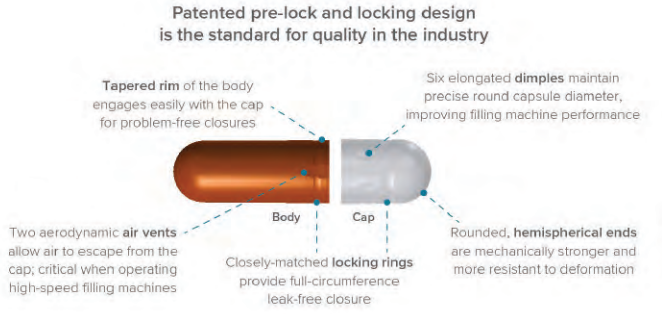
W: www.capsugel.com

Capsugel – now a Lonza company – designs, develops, and manufactures a wide range of innovative dosage forms for the biopharmaceutical and consumer health and nutrition industries. Our unique combination of science, engineering, formulation and capsule expertise enables our customers to optimize the bioavailability, targeted delivery and overall performance of their biopharmaceutical and consumer health and nutrition products. We partner with more than 4,000 customers in over 100 countries to create novel, high-quality and customized solutions that align with our customers' evolving needs and benefit patients and consumers. For more information, visit www.capsugel.com and follow us on Twitter, LinkedIn and YouTube.

GROUND BREAKING CAPSULE DESIGN: Building on our history of innovation in polymer science and capsule engineering, Capsugel 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, Capsugel has the right capsule to help you bring improved products to market faster. With a diverse portfolio including HPMC, liquid filled hard 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.

RELIABLE GLOBAL MANUFACTURING NETWORK: Producing 200 billion empty capsules per year requires a reliable, highly efficient and integrated global network of manufacturing sites in the Americas, Europe, India, China, Japan and Indonesia, all performing to the same identical specifications. This level of product and process control provides an assurance of supply to the largest and smallest of biopharmaceutical and consumer health and nutrition companies.



PRODUCT DEVELOPMENT SUPPORT: We supply an array of services supporting our capsule and encapsulation offering that can efficiently and effectively reduce product development timelines. These include:

- Fast track R&D capsule offering, including a full library of R&D capsule samples and fast-track manufacturing of customized capsules for R&D stability trials.
- Customized color selection assistance and a global Color Selector tool called Build Your Own Capsule
- Documentation immediately available on a customer portal
- Proprietary laboratory scale equipment for both powder and liquid formulations.

Vcaps® Plus Capsules

Not all capsules are created equal.

The new standard in HPMC capsules: Immediate release *in-vivo* performance bioequivalent to gelatin and consistent dissolution across changing pH and ionic strength.

Vcaps® Plus capsules can optimize capsule disintegration for pharmaceutical products with the ability to release contents independent of pH and ionic strength of the test media. An *in-vivo* study demonstrates that Vcaps Plus capsules are equivalent to gelatin in terms of human pharmacokinetics profile.

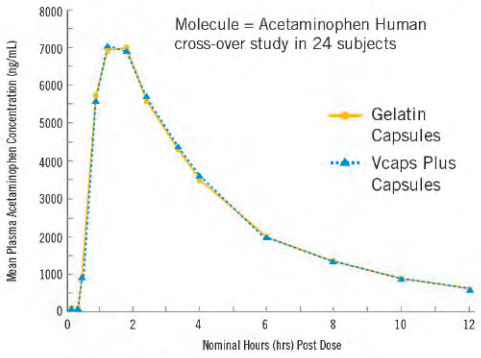
Finally, a superior specialty polymer capsule with proven gelatin-like performance without cross-linking potential, Vcaps Plus is the new capsule standard with benefits of narrow weight variability, impressive resistance to heat and humidity, and validated manufacturing experience. By reducing variability, Vcaps Plus capsules are quickly becoming a powerful tool to reduce timelines in drug product development.

Contact us at 800-845-6973 for our full technical package and samples for your development review.

***In-vivo* results** comparing Vcaps Plus HPMC Capsules and gelatin capsules demonstrate bioequivalency of HPMC in multiple dissolution profiles.

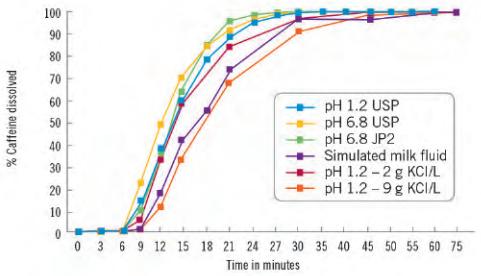
Read the full report at **VcapsPlus.com**.

Proven Bioequivalence to Gelatin



Mean *in-vivo* acetaminophen plasma concentration profiles over 12 hours.

True pH and Ionic Media Independence



In-vitro dissolution of caffeine in Vcaps Plus capsules

Capsugel®

Now a **Lonza** Company

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 & Oligonucleotides, Injectables, Highly Potent & Oncology, Small Molecules, Antibiotics** - CordenPharma experts translate complex ideas at any stage of development into high-value products.

Peptides, Lipids, Carbohydrates & Oligonucleotides

- Peptide API Production
  - Solid-phase, Liquid-phase, Hybrid Synthesis
  - cGMP & non-cGMP: Process & Analytical Development, Scale-up, Clinical & Commercial Supply
- Oligonucleotides
  - Process & Analytical Development, Clinical & Commercial Supply
  - Quality & Regulatory Support
- Lipids
- Carbohydrates

Sterile Injectables

- Aseptic Filling & Terminal Sterilization Capabilities (Sterile Solutions, Lyophilization, Pre-filled Syringes, Ampoules)
- Sterile Drug Product Formulation & Analytical Development, Clinical & Commercial Manufacturing
- Packaging & Labeling Services
- Sterile Emulsion Technology
- Large Pre-Filled Syringes
- Clinical Trial Services

Highly Potent & Oncology

- API Development & Commercial Manufacturing (SafeBridge Category 4, OEL ≤1 ng/m^3)
  - Development & Scale-up Capacity for Phase I/II Supply
- Drug Product Development & Manufacturing
  - New Development Suite (CTD2) for Mid-scale (up to 20 kg) Oral Dosage Forms
  - Sterile Liquid & Lyophilization
  - Primary & Secondary Packaging

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
  - Cephalosporins & Penicillins
  - Monobactams
  - Primary & Secondary Packaging

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CORDENPHARMA

EXPERTS TAKING CARE

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.

www.cordenpharma.com

TECHNOLOGY PLATFORMS

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

VISIT US AT

AAPS > Stand 1110
November 12–16, 2017
San Diego, CA USA

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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Meeting the Rising Need in Delivering Biological Treatments

Enable Injections' technology is designed to meet the delivery needs of biologics treatments that comprise an increasing focus in product development. The Enable Injections enFuse™ (wearable infuser) can address the new set of challenges and deliver these high-volume, often highly viscous therapeutics to the patient in an effective, safe, and affordable means that cannot be addressed by legacy injection systems. Enable Injections is introducing their wearable infusers to deliver these drugs subcutaneously, by patients at home, with the potential to help revolutionize treatment of cancer, autoimmune deficiencies, blood disorders, and a range of other conditions. Enable Injections intends to create market-leading biologics delivery devices to support patient-centric self-administration.

The Enable On-Body Delivery System

Now manufacturing devices for clinical studies, Enable Injections develops and manufactures medical devices for convenient self-administration of high-volume subcutaneous injectable drugs. The Enable on-body delivery system (OBDS) consists of a range of infusers capable of delivering up to 50 ml - with associated transfer systems (Syringe, Vial, or Fully-Automated Reconstitution) - that intuitively transfer drug from the original primary container closure to the enFuse™. Therefore, the system does not require any change to the primary container, ensuring further drug stability studies and new product or assembly lines are not required.

Enable's Solution for Patient Centricity & Differentiation

The Enable OBDS provides the potential solution for delivery of high-volume subcutaneous products to enable, enhance, and differentiate the biopharmaceutical portfolio. The flexible platform technology supports early clinical experience and patient adherence/acceptance to therapy. Early partnership provides Pharmaceutical companies with the opportunity to get new innovative pipeline products to market quickly and iterate design features with user feedback. For relevant products life cycle management opportunities supported by use of the Enable system include facilitating the delivery of intravenous formulations to subcutaneous delivery or by reducing the dose frequency of current subcutaneous formulations through increasing the dose volume.

Enable's Solution for Patients & Healthcare

The Enable enFuse™ is designed for the patient to self-administer at home, potentially replacing infusions at a health facility and improving cost effectiveness of biological therapies. Additionally, the infuser is designed to have a friendly looking appeal to reduce anxiety; provide the smallest profile and size for highest delivery volume; promote user mobility; and be simple/intuitive to use.

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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

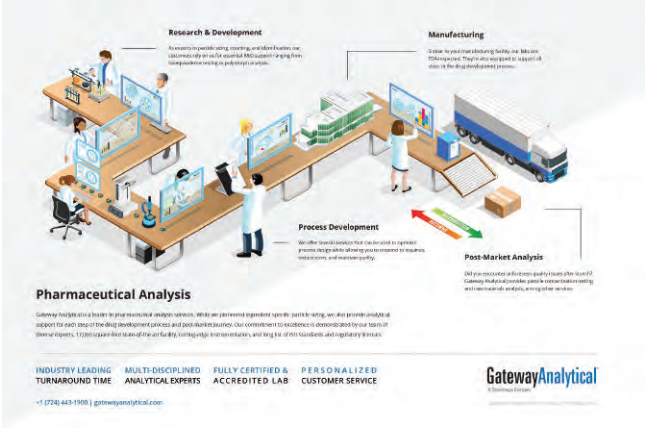
Specialized Testing Services

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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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
YOUR DRUG DEVELOPMENT PARTNER

AT FRONTAGE, PARTNERSHIP IS WHAT TURNS SERVICES INTO SOLUTIONS

At Frontage, we closely collaborate with pharmaceutical and biotech companies to help them bring promising drug candidates to market. With 14 locations in the US and China, Frontage has been assisting clients in their drug development efforts since 2001. We are committed to providing rigorous scientific expertise to ensure the highest quality and compliance on each project.

Spanning from preclinical through late-stage development, our full-service offerings include DMPK, bioanalysis using 60+ LC-MS/MS instruments, analytical testing, product development, and full biometrics support. Frontage also provides turnkey product development services to generic, innovator and consumer health companies to support IND, NDA, ANDA, and 505(b)(2) submissions.

- **Technical Expertise:** With 70% of our scientists holding advanced degrees and our depth & breadth of experience, we can solve complex problems
- **Highest Standards:** We have an unparalleled compliance and quality track record with 32 FDA Inspections across GXP
- **Flexibility:** We value agile project management, & a commitment to completing projects on time and on budget
- **Innovation:** Our $40M facility investment and 500+ FTE in USA & China give us the latest equipment and unparalleled access to China

ABOUT OUR CMC (CHEMISTRY, MANUFACTURING & CONTROL) SERVICES

With an outstanding compliance history, the CMC team at Frontage operates under strict adherence to ICH and US FDA GMP guidelines. Our facilities and processes undergo routine audits and inspections from sponsors and regulatory authorities.

Frontage's CMC portfolio of services spans the entire drug product development of oral solids, topical, and sterile, from proof-of-concept, preclinical through clinical trials and commercialization support. 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 Method Development/Validation & Sample Testing
- Formulation Development for IND, NDA & ANDA
- GMP Manufacturing of CTM (Oral Solids, Topical, Sterile)
- Commercial Product Release & Stability Testing

VALUE TO OUR CLIENTS

- **Integrated:** One-stop shop for product development
- **Customer Focused:** Flexible set up to meet client requirements
- **Quick & Responsive:** Keep client engaged and timely updates of project status
- **Strong Problem-Solving Skills:** Help client overcome challenging technical hurdles
- **Strong Quality & Compliance Track Record**

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Quality > It's how you get from formulation to the pharmacy.

At Frontage, our CMC service team has an unparalleled compliance and quality track record. 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. With proven success in developing drug products for novel, generic and consumer products, we focus our efforts on clients' specific needs.

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

FRONTAGE
YOUR DRUG DEVELOPMENT PARTNER

CONTACT US TODAY: *sales@frontagelab.com*
OR VISIT US AT: *frontagelab.com*

Fuji Chemical Industries USA, Inc.

The Company

Fuji Chemical Japan, founded in 1946, is a leading provider of contract spray drying service and a manufacturer of highly functional pharmaceutical excipients. Fuji Chemical USA is a sales and marketing company servicing the North American market. Fuji's primary mission is to provide high quality, unique ingredients and excellent service to the pharmaceutical and dietary supplement industries.

The Pioneer in Spray Drying

Fuji is a pioneer in both open-loop and closed-loop spray drying with over 50 years of experience. Over the years, we have helped customers to address various issues via our spray dry technologies.

Contract Spray Drying Service

Fuji is fully equipped from lab to cGMP commercial scale spray dryers to assist your project form early-stage development through commercial production. We provide our spray drying expertise and formulation services to solve solubility issues such as by amorphous solid dispersion which improves API properties, to produce high value APIs.

In addition, in responding to customer demand, Fuji installed a new High Containment Spray Drying Facility for Highly Potent Compounds, which implements stringent containment measures corresponding to chemical hazards. Due to recent capacity expansion, we are able to meet customers' tight project timelines.

Multi-Functional Spray Dried Excipients

Fuji has utilized the proprietary spray drying technology to develop multi-functional spray dried excipients to help formulators address various formulation challenges. Three of these high performance excipients, Fujicalin®, Neusilin®, and F-MELT® are being offered by Fuji to our customers:

- **Fujicalin** (porous Dibasic Calcium Phosphate Anhydrous) Fujicalin is the perfect sphere for direct compression and granulation with improved blend uniformity, rapid disintegration and less abrasive to the press.

- **Neusilin** (amorphous mesoporous Magnesium Aluminometasilicate) Neusilin is a multi-functional material that has made solid dispersion a viable technology and a competent adsorbent for liquid and SMEDDS.

- **F-MELT** (ODT base) F-MELT is a directly compressible ready-to-use excipient based for ODTs. F-MELT offers smooth mouth feel and good tablet stability.

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iCeutica works with pharmaceutical partners to create new branded medicines by combining our proprietary SoluMatrix™ Fine Particle Technology with our partners' product experience and commercial insights.

SOLUMATRIX™ FINE PARTICLE TECHNOLOGY

The SoluMatrix technology is a scalable and cost-effective manufacturing process that can produce submicron-sized drug particles that are 10 to 200 times smaller than conventional drug particles. The technology both grinds the drug particles into a superfine powder and protects those submicron particles from subsequent agglomeration. The resulting powder can be manufactured into tablets, capsules, and other dosage forms using standard pharmaceutical unit operations.

The SoluMatrix technology has been applied at commercial-scale and three products utilizing the technology have been approved by FDA.

How SoluMatrix Works

The SoluMatrix technology improves the performance of lipophilic and poorly water soluble pharmaceuticals by dramatically increasing the rate of drug dissolution and improving oral absorption. By making submicron-sized particles of a drug, it is possible to:

- Improve the bioavailability and reduce the pharmacokinetic variability of a drug
- Reduce the time to onset of therapeutic efficacy
- Reduce the amount of drug required to achieve a desired plasma level
- Reduce or eliminate food effects
- Change the mode of administration of a drug

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What SoluMatrix Can Do For Your Product

Using the SoluMatrix technology, iCeutica can transform development-stage or marketed pharmaceutical products in a number of clinically relevant and commercially important ways. For poorly soluble or highly variable products in development, we can ensure the product successfully progresses through clinical development and that the patient receives a consistent dose of the drug, with potentially less drug required and fewer side effects experienced. For marketed products, we can unleash improved performance and new intellectual property protection that extends the product lifecycle and profitability of the product.

SERVICES

iCeutica also provides companies development services, leveraging our staff of experienced industry professionals.

We offer the ability to be your single service provider to manage all steps of drug development from Phase 1 to NDA submission. Our development services include:

- Dosage Form Development
- Regulatory Submissions
- GMP Manufacturing Management
- Clinical Study Management

Our teams are led and staffed by experienced industry professionals and we can rapidly move from concept to clinical trial material to advance your drug development program.

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 USA, Canada, and Mexico.

Products

Creating sophisticated and innovative lipid excipients is a core specialty of the Gattefossé Group. Each excipient is designed to meet a unique set of formulation and functionality objectives while conforming to the highest safety, quality, and regulatory standards. The product offering includes solubilizers, emulsifiers, bioavailability enhancers, sustained release matrix formers, and skin penetration enhancers for all routes of administration.

Formulation Development Support

With the inauguration of the Gattefossé Technical Center of Excellence (TCE) in the USA, we are closer to the customers in North America, addressing their product formulation needs, helping advance their projects, and to shorten the time to successful drug development.

Additionally, guidance documents for excipient selection and formulation design for preclinical as well as late development stages are available upon request.

Investing in the USA

With the construction of a new, state of the art application laboratory, and expansion of office space at the current location in Paramus NJ, the Gattefossé group continues its investments in the region.

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 1990's are examples of such initiatives.

Safety, Regulatory & Quality Support

Gattefossé characterizes each excipient for 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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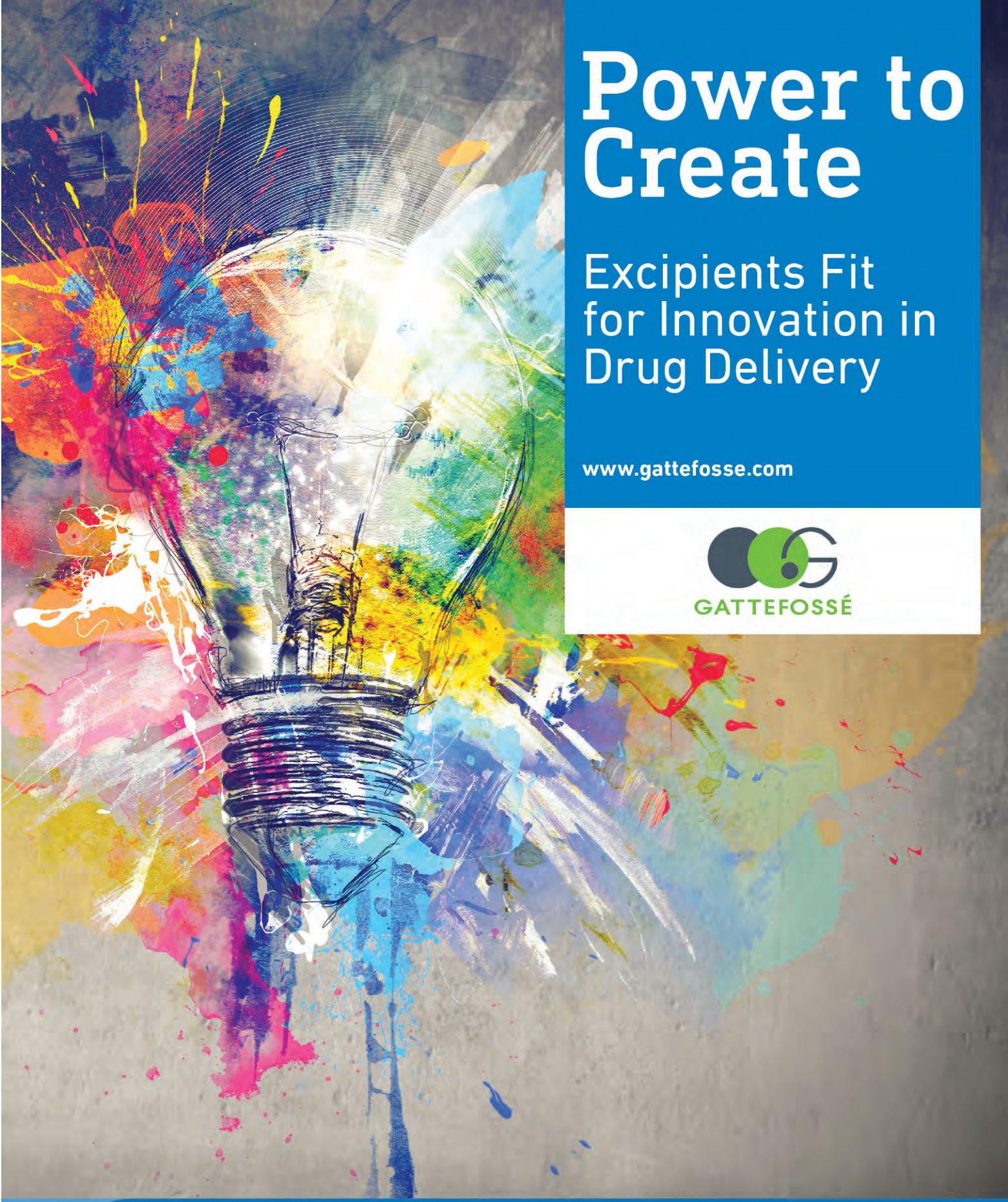

Power to Create

Excipients Fit for Innovation in Drug Delivery

www.gattefosse.com

GATTEFOSSÉ

People make our name

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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LATITUDE Pharmaceuticals Inc. is a leading-edge research boutique that provides innovative drug formulation development services to the human and animal health biotech/pharmaceutical industries. Since our founding in 2003, we have completed more than 750 client projects and established a reputation for successfully formulating highly insoluble compounds – a problem attributable to 40% of new drug development failures.

Expertise

We are formulation specialists who overcome the tough formulation challenges of problematic compounds, and we have built our reputation on a track record of creative approaches, reliability, rapid turnaround, and client satisfaction. LATITUDE's extensive experience and technical strengths in a wide range of dosage forms are applied to help our clients successfully address even the most difficult formulation challenges.

LATITUDE's background, experience, and unique internally developed technologies are applied to solve problematic formulation issues, such as insolubility, poor absorption, poor taste, and/or vein irritation that are often encountered.

In addition, LATITUDE develops its own proprietary drug products by re-formulating existing drugs, thereby improving efficacy, safety, and overall therapeutic value. We are proactive in forming strategic alliances and out-licensing new reformulated drug products.

Drug Delivery Platforms

Nano-E (Nanoemulsion)

- A versatile solubility-enhancing platform for oral/injectable liquid formulations, ideal for highly insoluble APIs or "brickdusts"

PG Depot (Phospholipid Gel Depot)

- Allows a customizable release profile of a subcutaneously-administered drug over 1-7 days
- Injectable through fine (up to 28 G) needles for easy subQ administration

ARTSS (Aqueous Room Temperature-Stable Solutions)

- A platform for the transformation of lyophilized powders or 2-8°C solutions into RT-stable aqueous solutions

RFAP (Rapidly-Dissolving Amorphous Powders)

- Creates a stable, amorphous, water-soluble powder that keeps the API from reverting to the crystalline state

24H (All-Day 24-hr ER Tablets)

- An oral tablet platform for increased dosage and linear, sustained release of drugs for up to 24 hours

MiniSpheres

- Novel delivery format for high/bulky dose oral drugs and/or sustained release

GelPatch

- Novel transdermal spray/rub-on gel that dries as durable patch to provide multiday drug delivery

Feedlets (Animal Health)

- Controlled-release, taste-masked pellets or chewables that can be easily administered in animal feed

Contact us for more information and to discuss how LATITUDE can address your formulation needs.

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.

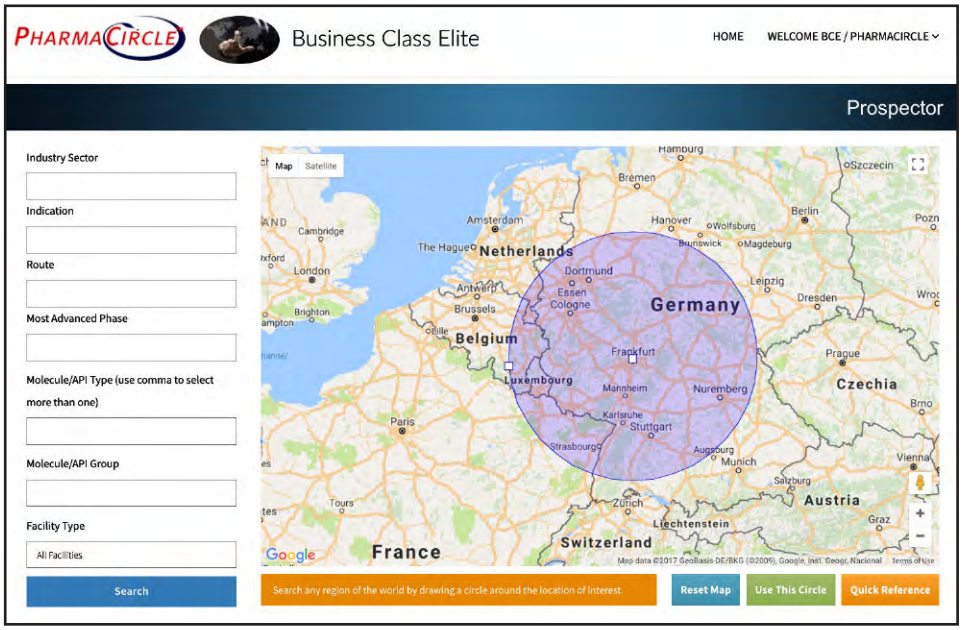
PharmaCircle's premier database tracks drugs, biologics and combination products in all stages of development, connecting pipeline and product information with formulation and component details. The database delivers seamless integration of scientific, clinical, safety, regulatory, manufacturing and 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 30 & 31 and visit our website www.pharmacircle.com.



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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. Construction of the new 126,000 sq ft, oral dose commercial manufacturing facility is now complete, with production beginning in January 2018. The facility quadruples the company's US manufacturing capacity, and the repurposing of existing space creates 10+ new analytical laboratories and formulation development suites.

The new facility means Metrics Contract Services can offer a more 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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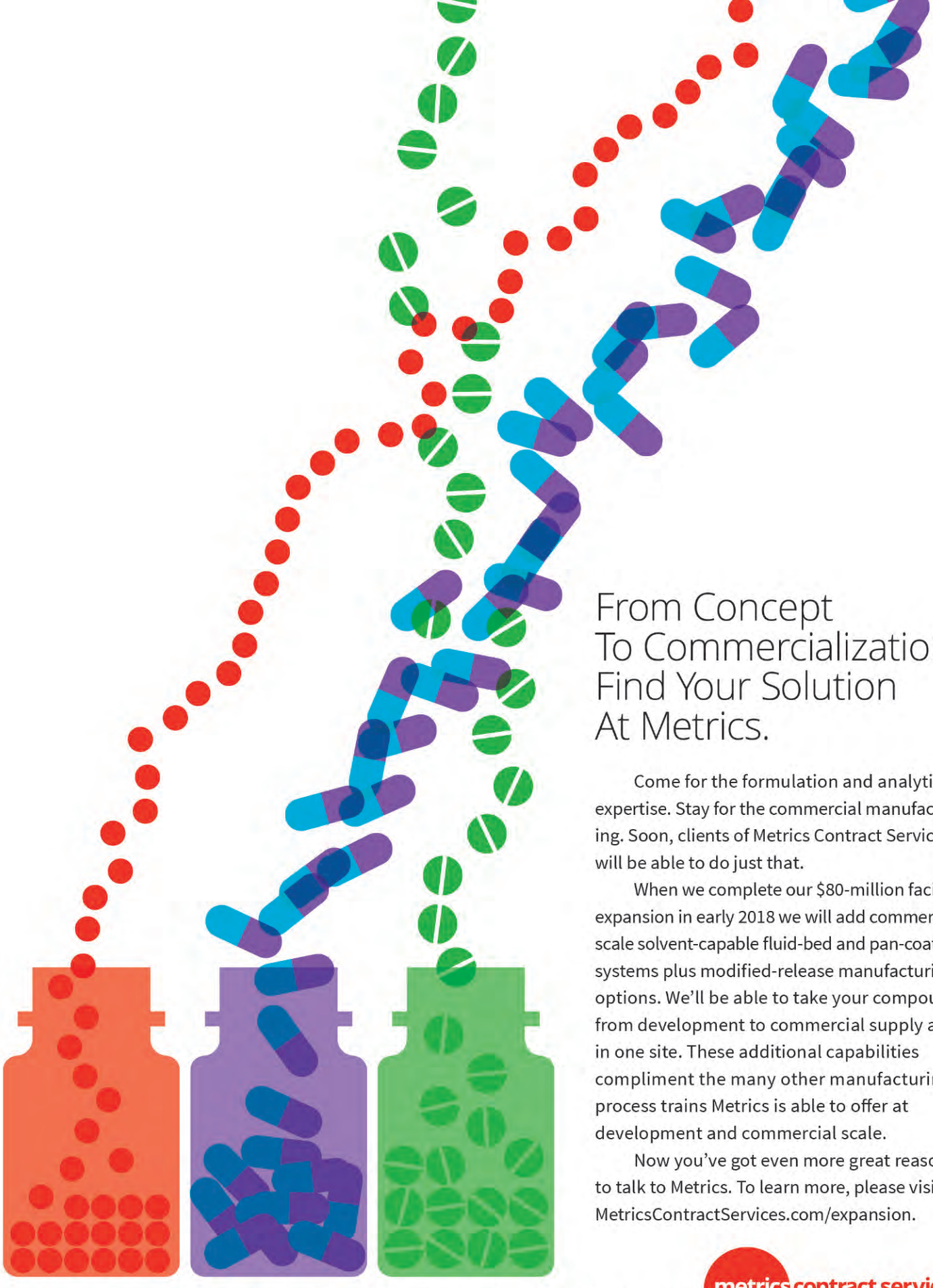

From Concept To Commercialization. Find Your Solution At Metrics.

Come for the formulation and analytical expertise. Stay for the commercial manufacturing. Soon, clients of Metrics Contract Services will be able to do just that.

When we complete our $80-million facility expansion in early 2018 we will add commercial-scale solvent-capable fluid-bed and pan-coating systems plus modified-release manufacturing options. We'll be able to take your compound from development to commercial supply all in one site. These additional capabilities compliment the many other manufacturing process trains Metrics is able to offer at development and commercial scale.

Now you've got even more great reasons to talk to Metrics. To learn more, please visit MetricsContractServices.com/expansion.

Pharmaceutical Development • Analytical Testing • Commercial Manufacturing

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

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Noble®, the leader in onboarding and device training, is a full-service, patient-centered product development and manufacturing company. Noble works closely with the world's leading pharmaceutical and biotechnology companies to develop educational and training solutions designed to provide positive patient onboarding experiences, reduce errors, and improve patient outcomes. Cross-disciplinary designers and engineers provide fully customized solutions from the first concept sketch through production, in both regulated and non-regulated environments. Noble uses ISO 9001 and ISO 13485 supply chains and manufacturing facilities.

Connecting Patient Onboarding With the Patient Journey

The first 30, 60, and 90 days, commonly referred to as onboarding, are the most important regarding patient adherence. This is the time when a patient is expected to self-administer medication based upon prescribed regimen. While a patient's first exposure to a drug delivery device typically consists of training with a healthcare professional onsite at a medical facility, a patient will most often perform medication administration alone outside of a healthcare facility and without healthcare provider supervision.

There are many variables contributing to patient adherence and therapy acceptance during onboarding, including anxiety, confidence, memory, and understanding the correct administration technique. These patient factors can detrimentally influence attitudes and perception toward medications and drug delivery devices, resulting in training gaps and treatment barriers.

Injection & Respiratory Device Training

As the number of patients required to self-administer medication increases, so does the need for patient-centric training and education, including training devices such as autoinjectors, prefilled syringes, wearable injectors, and respiratory platforms.

Noble has developed a wide variety of patient-centric onboarding products to help patients administer correctly and improve adherence and patient outcomes. Noble's offerings range from mechanical training devices to smart error-correcting training platforms, assistive devices, and even patient support including travel packs and training instructions for use (IFU).

These devices have been designed to mimic actual commercial drug delivery devices while being a low-cost reusable solution to safely and effectively onboard users.

Injection Product Features – AI, PFS & Wearable Trainers:

- Off-the-shelf and customized solutions, including proprietary technologies
- Technologies range from resettable mechanical to smart features, such as sensors, audio, and error-correcting
- Trainers designed to mimic actual device characteristics
  - Shape and design
  - Needle insertion simulation
  - Forces: cap, unlock, actuation, breakout and glide
  - Sound replication
  - Plunger replication
  - Post injection safety

Respiratory Product Features – MDI & DPI Trainers:

- Off-the-shelf and customizable solutions, including proprietary technologies
- Technologies range from resettable mechanical to smart features, such as sensors, audio, and error-correcting
- Trainers designed to mimic actual device characteristics
  - Shape and design
  - Inhalation forces
  - Sequence

By providing patients a better understanding of a device, with the ability to practice administration technique as often as needed, trainers help promote positive onboarding experiences and empower patients to lead healthier lives. In the patient-centric era, companies providing reusable, device-comparable training products will be well positioned for competitive differentiation through improved patient satisfaction, adherence, and outcomes.

NOBLE
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Device training happens here.

There's life beyond chronic conditions. Distractions, anxiety and understanding correct administration technique can all affect compliance. Studies suggest 61% of patients don't completely read the IFU[1] and 12% of patients have proficient health literacy.[2]

Will your patients correctly administer their drug delivery device?

noble® Onboarding and Device Training

GONOBLE.COM 888.933.5646

Reference: 1. Noble. (2015, November). The link between device training and patient compliance. Poster session presented at PDA - Universe of Prefilled Syringes 2015, Vienna, Austria. 2. Kessels, R. P. (2003, May). Patients' Memory for Medical Information. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC539473/

Nemera

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 A HEALTHY SKIN

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 XL, Sof'Airless XS, SP943, delaminating systems, SP27/SP37, SP270+/SP370+, SP24/SP34.**

PARENTERAL

COMPLEX DEVICES, SIMPLE PATIENT CARE

Parenteral drug administration exposes patients and healthcare professionals to many hazards. To ensure adherence and user well-being, **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, Customized plastic syringes, 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.

we put patients first

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Pfanstiehl is a global leader in the manufacture of cGMP high purity, low endotoxin 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, and Maltose. Parenteral-grade, multi-compendial Mannitol is also offered as a key tool for formulation optimization. We are planning 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 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

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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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Needle Free Injections

Portal Instruments

PATIENT PREFERRED*

<1 SECOND DELIVERY TIME

ADAPTIVE TO DRUG VISCOSITY

1 ML DELIVERY VOLUME

***Portal Instruments** digitally controlled needle free injector.*
Game-changing technology for your game-changing drugs.

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DRUG DELIVERY PARTNERSHIP | **JAN 22-24** | WEST PALM BEACH, FL
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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

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.

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REVOX®
Sterilization Solutions
by Cantel Medical

ROOM TEMPERATURE STERILIZATION

The REVOX® Sterilization Solutions process uses a patented, room-temperature vaporized peracetic acid (VPA) sterilant that achieves exceptionally low-chemical residuals and unsurpassed materials compatibility. The REVOX™ technology eliminates inefficiencies associated with pre-conditioning and lengthy post-sterilization wait times. This allows REVOX Sterilization to offer manufacturers a quick-turn, off-site sterilization service or cost-efficient on-site, in-line processing. In May 2014, a Class II implantable device was granted FDA clearance with the REVOX sterilization process. The REVOX innovation is backed by Cantel Medical, a company with over 35 years of infection prevention and control advancements structured under strict regulatory compliance standards.

LEANER MANUFACTURING

The complete manufacturing stream should be exactly that: complete. Pulling components from the line for sterilization defeats the very purpose of having a production line. REVOX enables scalable in-line sterilization, which finally allows manufacturers to integrate sterilization into a lean manufacturing process. It speeds up production and gives manufacturers a substantial competitive edge. While some sterilization methods can take up to 44 cycles to sterilize two pallets of product, the REVOX 3000L machine takes just one. Think of it as JUST-IN-TIME™ sterilization. It's your time. Make the most of it.

SUPERIOR MATERIALS COMPATIBILITY

Until now, manufacturers have been limited by traditional sterilization methods that constrain their choices of materials and overall product design. Many materials that may otherwise be ideal for optimal product design simply are not suitable with common sterilization methods. REVOX changes that. With true room-temperature processing and demonstrated superior compatibility across a wider range of materials, manufacturers have more options to innovate more efficiently. Chemical and heat-sensitive materials that were once off-limits to innovative product development are now available. The REVOX sterilization process is compatible with over 100 materials, including biologics, implantables, electronics, pharmaceuticals such as combination devices, and more. You can now create the products that will demonstrate your true potential.

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PYRAMID Laboratories, Inc. is a contract Aseptic Manufacturing and Analytical Services provider for Sterile Injectable Drugs. PYRAMID builds lasting partnerships with its clients and provides expertise in formulation and process development, aseptic filling for vials and syringes, as well as lyophilization applications, and supports early development through to commercial manufacturing. PYRAMID has established a reputation of exceptional performance, integrity, and quality. PYRAMID is committed to continuous improvement in quality, knowledge, and expertise, and we take pride in working with our partners to translate this commitment into safe products that will ultimately benefit the people who need it most – the patients.

TECHNICAL SERVICES

PYRAMID offers a wide array of services for all phase of drug development, including:

- Formulation & Process Development
- Lyophilized Product Formulation Development
- Lyophilization Cycle Development
- Clinical & Commercial Vial & Syringe Fill/Finish
- Clinical & Commercial Lyophilization Batches
- Analytical Quality Control Support

Formulation/Product Development

PYRAMID's expertise in Formulation Development covers a wide range of products. The company assists clients through Product Development and Clinical phases to high-speed Commercial-scale production.

Lyophilization

PYRAMID's expertise in Lyophilization product and cycle development covers a wide range of matrices. The facilities are equipped with a research and development laboratory-scale 36-sq-ft Stokes Freeze Dryer for clinical supplies, and a state-of-the-art 213-sq-ft Telstar Freeze Dryer for commercial scale batches. The company's freeze-dryers process vials in sizes from 2 mL to 20 mL.

Aseptic Filling

PYRAMID offers vial fill ranges from 0.5 mL to 20 mL with 100% weight check, as well as syringe fill ranges from 0.2 mL to 3 mL.

Analytical Services

PYRAMID's extensive Analytical Laboratory has the technical capability, quality, and capacity to perform a variety of analytical applications and has served the biopharmaceutical industry since 1988. The company has extensive expertise in:

- Analytical Method Development & Validation
- Validation for Stability Indicating Methods
- Long-Term & Accelerated Stability Studies
- Protein, Peptide, Oligonucleotide Characterization Assays

Storage & Distribution

PYRAMID has a 27,000-sq-ft facility for Labeling, Storage, and Distribution Services to store and distribute parenteral drug products across the globe during the entire clinical and commercial life cycle. PYRAMID's latest addition includes 27,600 cubic feet of monitored, alarmed validated chambers with environmental conditions for clinical and commercial drug product and API storage at ambient, refrigerated, frozen or ultra-low storage.

FACILITIES

PYRAMID Laboratories, Inc. is located in Costa Mesa, CA. Our facilities are housed in three buildings covering more than 70,000 sq ft. The combination of our manufacturing facilities and state-of-the-art laboratory allows PYRAMID to offer the pharmaceutical and biotech industry both analytical and manufacturing support capabilities. An intensive in-house Quality Assurance and Quality Control program is maintained to ensure clients receive high-quality products.

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PYRAMID
Laboratories, Inc.

Contract Aseptic Manufacturing

- Aseptic Fill/Finish
- Lyophilization Services
- Clinical & Commercial
- Formulation Development
- Analytical Services
- Product Storage & Distribution

Quality • Performance • Integrity

www.pyramidlabs.com
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Year Founded: 1878
Number of Employees: 1,900 in Life Sciences worldwide; 90,000 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 20 Life Science laboratories with facilities in the US, UK, Canada, Belgium, France, Germany, Italy, Switzerland, China, India and Singapore. 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
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WORLD LEADER IN LIFE SCIENCE TESTING FOR OVER 40 YEARS

LOCAL SOLUTIONS GLOBAL NETWORKS

WHEN YOU NEED TO BE SURE

SGS

At **SGW Pharma Marketing**, 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. With 27 years of consumer and B2B pharma experience, you can count on us to deliver innovative solutions that make a difference. That's why the top pharmaceutical companies choose SGW Pharma.

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 re-organized 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

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Developing a formula for your brand's SUCCESS.

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SGW | Pharma MARKETING

Your brand's formula for success.

BRANDING • DIGITAL • WEB DESIGN • PRINT • OUTDOOR • TV • VIDEO • PUBLIC RELATIONS

SHL GROUP

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 enhance our broad pipeline of next-generation drug delivery devices. 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. Developing these drug delivery devices in-house allows us to customize existing platforms in our pipeline or develop completely new bespoke devices based on the unique requirements of our customers. With locations in Taiwan, Sweden, 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 3,700 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.

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SHL GROUP

Smallest Details Make the Biggest Difference

Innovative Cartridge-Based Devices
with Needle Isolation Technology

Solutions for Today on the Path to Tomorrow

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
- Liquid fill encapsulation

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

DEA Licensed / FDA Inspected

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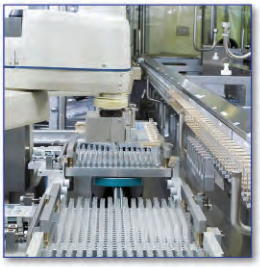


YOUR PARTNER IN ASEPTIC FILLING

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.

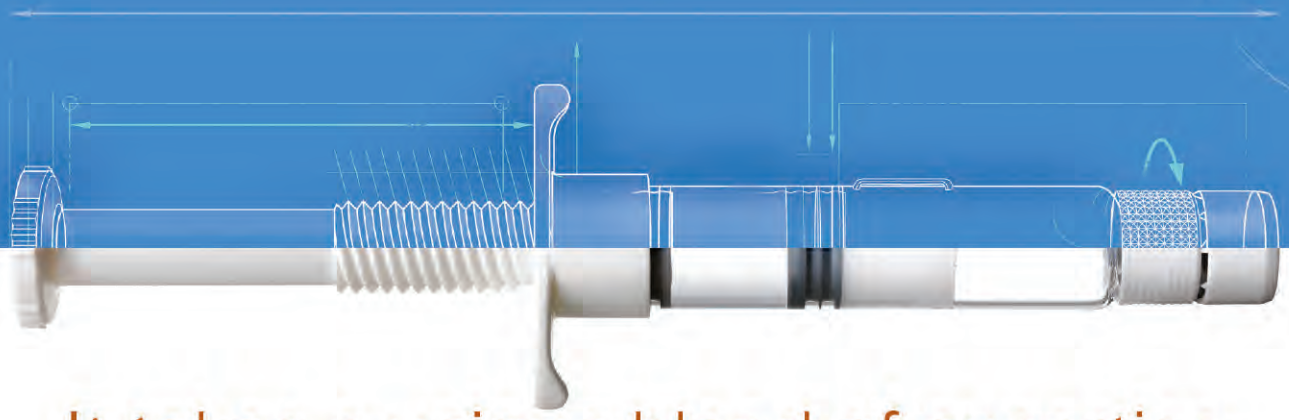
VETTER AT A GLANCE

- 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
- Approximately 4,300 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

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**
- **7,300 global employees**
- **Founded in 1923**
- **2016 sales: $1.5 billion**
- **West products used on a daily basis: approximately 112 million units***

*Based on 2016 annual sales.

Solutions for connecting your drug to the patient

West®

By your side for a healthier world™

Ensuring your drug product's efficacy and safety requires high-quality packaging components and administration systems. **With West, you have a partner by your side every step of the way**, from discovery to the patient.

- Injectable container components
- Prefillable syringe components
- Daikyo Crystal Zenith®
- Needle safety systems
- Self-injection platform technologies
- Technical support

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#9962 1017

Delivering the Future of Cancer Care

A Novel Site-Specific Drug Delivery System for Solid Tumors

Systemic administration of chemotherapy depends on the circulatory system to carry the drug into the tumor and achieve an adequate dose. However, high intratumoral pressure limits the flow of therapy into solid tumors. In fact, it is estimated that no more than 5% of the injected dose extravasates and accumulates in the tumor.

The Surefire® Infusion System (SIS) is a novel site-specific delivery device that is designed to overcome the pressure barriers posed by hostile tumor microenvironment, and increase the therapeutic index of drugs in solid tumors. To date, over 7,000 SIS procedures have been performed worldwide to deliver a variety of chemotherapy and radiotherapy agents in liver tumors. SIS has also been shown in a few studies to increase dose of therapy in the tumor while protecting healthy tissue.

How the Technology Works

The patent-protected Surefire technology consists of an intravascular catheter with a proprietary valve-like tip. Currently, interventional radiologists place the SIS in the tumor-feeding arteries before infusing therapy through the catheter. During infusion, the expanded tip creates a temporary increase in local pressure above the mean arterial pressure. This in turn generates a favorable pressure gradient that allows therapy to penetrate deep into the tumor. When backflow is present, the valve-like tip expands against the vessel wall, preventing therapy from reaching non-target areas.

The SIS & Immuno-oncology

With its ability to enhance tumor uptake and reduce non-target delivery, the SIS is poised to enable safe administration of immune-oncology (IO) drugs in solid tumors.

The ongoing HITM-SURE trial (NCT02850536) uses the SIS to administer anti-CEA CAR-T cells in liver metastases. The results will serve as proof of concept for using the SIS to effectively deliver and manage the safety profile of other IO therapies in solid tumors.

The SIS might also significantly reduce the cost of manufacturing these expensive new treatments. With its highly targeted approach, only a small, concentrated dose of the therapy may be needed to treat patients compared to the dose required for systemic administration.

Partnership, Licensing & Collaboration

Surefire Medical, Inc. designs, develops and manufactures the SIS in its ISO 13485 certified facility in Westminster, CO. We work in partnership with companies interested in using the Surefire technology to improve the effectiveness, safety, and differentiation of their products – whether in early phases of development or in the mature stages of the product lifecycle. Surefire owns a strong portfolio of patents that can be applied in a variety of solid tumors, including tumors of the liver, pancreas, kidney, head and neck, and brain. In addition, we also offer our expertise in device design, manufacturing, and regulatory affairs to help tailor Surefire technology to meet your commercial needs.

SUREFIRE MEDICAL
6272 W. 91st Ave
Westminster, CO 80031
www.surefiremedical.com
Please send inquiries to drugdev@surefiremedical.com

Bioavailability Enhancement

ABITEC
AN ABF INGREDIENTS COMPANY

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. For more information, visit Abitec at **www.abiteccorp.com.**

Protect Your Brand™

Protect Your Brand™ is a unique offering designed to support pharma-biotech companies pursuing a dual sourcing strategy. Under this program, Alcami will support tech transfer and validation of products in advance of potential manufacturing needs without any long-term commitment or minimum annual volume. It's that simple. Protect Your Brand offers three distinct dual supply solutions to prevent disruptions from occurring at the earliest during clinical supply through to post-approval commercial production. This service can be used for drug substance, drug product, and for clinical supplies, launch quantities, and commercial supply. Protect Your Brand allows you to determine the ideal State of Alcami Readiness™ needed for your product. Responding quickly allows Alcami to minimize the effects of a supply disruption, helping prevent shortages and delays. Alcami can be ready quickly to bridge unexpected gaps in your critical supply needs. For more information, visit Alcami at **www.alcaminow.com.**

CDMO Services

ALTHEA
THE POWER TO MAKE

Althea is a fully integrated, contract development and manufacturing organization providing clinical and commercial product development services. Althea offers cGMP drug product filling in both vials and syringes, and production of microbial-derived recombinant proteins and plasmid DNA. In conjunction with these manufacturing operations, Althea offers comprehensive development services, including upstream and downstream process development, analytical development, lyophilization cycle, complex formulation, product release and ICH-compliant stability testing. In addition, Althea offers a proprietary formulation technology platform, Crystalomics®, and an innovative recombinant protein expression technology called Corynex® technology. Althea is the manufacturing partner that delivers the relentless dedication and support our clients need. For more information, visit Althea at **www.altheacmo.com**.

Global CRO/CDMO

amri
Complex Science. Expert Solutions.

AMRI, a global contract research and manufacturing organization, partners with the pharmaceutical and biotechnology industries to improve patient outcomes and quality of life. With locations in North America, Europe and Asia, AMRI's team combines scientific expertise and market-leading technology to provide a complete suite of solutions in Discovery, Development, Analytical and Solid State Services, API Manufacturing and Drug Product. For more information about AMRI, visit **www.amriglobal.com**.

PremiumFill®

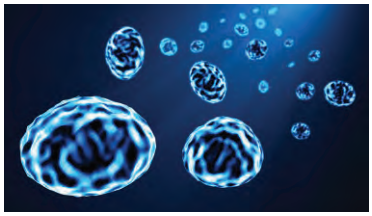
PremiumFill® reduces particulates, ensuring higher quality products and increased customer confidence. Aptar Pharma's commitment to delivering market-leading quality in injectable components is evident in the development of its Premium portfolio. The core of its Premium offering is PremiumFill, a guaranteed specification to our highest level of production, resulting in improved particulate reduction and an overall decrease in defects. PremiumFill products feature the highest possible quality specification. Its best-in-class guarantee is the result of over 50 years of experience and expertise in elastomer development, which is supported by dedicated manufacturing areas, technologies, and procedures to protect the integrity of the components at all production steps. Washing, siliconization, and packaging operations are in ISO 6 and ISO 5 environments. PremiumFill is a tangible execution of Aptar's commitment to deliver solutions to your injectable challenges. For more information, visit Aptar Pharma at **www.aptarpharma.com.**

Healthcare Communications

ArtcraftHealth
Education empowers℠

Artcraft Health is a specialized healthcare communications company and service provider that develops strategic solutions to engage, educate, and motivate behavior change among our clients' customer stakeholders. These stakeholders include the clinical and nonclinical decision-makers, physicians, nurses, pharmacists, patients, caregivers, and advocacy groups who play critical roles across the care continuum. We help enable these stakeholders attain the best possible outcomes for patients throughout their diagnostic, treatment, and disease-management experiences. DEMO/training devices and starter kits can be essential to ensuring success in this process. Our design and development work in this area reduces dosing/administration anxiety and assists in properly training and motivating patients to optimize treatment adherence. For more information, visit Artcraft Health at **www.artcrafthealth.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.**

Analytical Services

AVOMEEN ANALYTICAL SERVICES

From test method development to after-market support, Avomeen's experienced chemists support all segments of your drug development pipeline. As a full-service CMC/CRO laboratory, we provide customized services that aid pharmaceutical researches, developers, and manufactures. You'll be in good hands with our reliance on a Quality by Design (QBD) approach and rejection of the typical "list price testing." We recognize that every project is unique, which drives us to spend the time to find out the true nature of our clients' needs and develop a personalized plan just for you. For more information, visit Avomeen at **www.avomeen.com/pharma**.

Formulation Development

BASF We create chemistry

BASF creates chemistry for a sustainable future offering intelligent solutions to the pharmaceutical industry. With our expertise in polymer chemistry, R&D-capabilities, and commitment to developing excipients, BASF creates solutions for Instant & Modified Release, Solubilization, Softgels, Skin Delivery, and Biologic applications. We also are a leading supplier of selected APIs, such as ibuprofen and omega-3. Our team of experienced industry specialists are here to support you in developing effective, reliable solutions to the formulation challenges you face today and tomorrow. For more information, visit **www.pharma.basf.com.**

CRO/CDMO

BioDuro has expanded its spray drying capacity for development of poorly soluble drugs with the addition of an SPX Anhydro MicraSpray 150. We provide comprehensive solutions for increased solubility and enhanced bioavailability, from formulation to cGMP batches. Our suite of spray drying capabilities includes a Buchi Nano Spray Dryer B-90, Buchi Mini Spray Dryer B-290, SPX Anhydro MicraSpray 35, and SPX Anhydro MicraSpray 150. BioDuro is your partner for accelerating drug discovery and development and improving efficiency in establishing drug candidate success. For more information, visit Bioduro at **www.bioduro.com.**

Contract Laboratory Services

BioScreen® Pharmaceutical Services, Inc.

BioScreen Pharmaceutical Services, Inc. (est. 1985, FDA registered, ISO 9001:2008 certified, DEA Registered Class II-V), headquartered in Los Angeles, CA, offers a wide range of testing services in Analytical Chemistry, Microbiology, and ICH Stability services. BioScreen is prepared to assist companies in any stage of development from Preclinical through Phase IV. BioScreen specializes in development, validation, and testing for ICP-MS & OES, GC-MS, GC, HPLC, and UPLC. BioScreen can handle hazardous APIs and drug products, as well as perform a wide arrange of compendial testing. BioScreen's customer focused and flexible business model combined with its excellent technical and regulatory track record make it an idea partner. For more information, visit BioScreen Pharmaceutical Services at **www.bioscreen.com.**

HPMC Capsules

Vcaps® Plus capsules developed without gelling agents provide HPMC capsules with improved physical and operational features to match the needs of the pharmaceutical industry. A new in vivo study demonstrates that Vcaps Plus capsules are equivalent to gelatin in terms of human pharmacokinetics profile, making them an excellent alternative to gelatin or traditional hypromellose (HPMC) for optimizing delivery, performance, and stability of OTC, NCEs, and off-patent products. For more information, visit Capsugel at **www.capsugel.com.**

Platform Technology

CAPTISOL®

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 10 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

Catalent Pharma Solutions offers its partners end-to-end solutions, from drug formulation and drug delivery technologies, to manufacturing and clinical supply services. Each molecule has unique characteristics, and by using innovative and intelligent dose forms, it is possible to overcome challenges, and better meet the needs of prescribers, payers and, most importantly, patients. Catalent has multiple tools and technologies to assist in the development of innovative dose forms that can improve a drug's clinical efficacy and commercial success, including its multi-award-winning OptiForm® Solution Suite platform. 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 a molecule's 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, Oligonucleotides, Lipids & Carbohydrates - Injectables - Highly Potent & Oncology - Small Molecules - Antibiotics. With multiple cGMP manufacturing facilities across Europe and the US, CordenPharma experts translate your complex ideas, projects, and processes into high-value products at any stage of development. CordenPharma provides proprietary peptide, lipid, carbohydrate, and oligonucleotide technologies for cGMP-compliant products and services. We additionally specialize in the manufacturing and containment of highly potent peptide APIs (with exposure limits as low as 1 ng/m3), highly potent formulations (solid forms), cephalosporins & penicillins (oral & sterile), oncology drug products (oral & sterile), and packaging. For more information, visit CordenPharma at **www.cordenpharma.com.**

Differentiated Injectable Delivery

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

Super RefinedTM Excipients

CRODA

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

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.**

CMC Services

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**.

Unique Excipient Supplier

Fuji Health Science is the sales and marketing subsidiary of Fuji Chemical Industries Co., Ltd. Over the years, Fuji has developed a unique and proprietary powdering technology that led to the development of our unique excipients. Neusilin® (Amorphous mesoporous Magnesium Aluminometasilicate) is a multifunctional material that has made solid dispersion a viable technology and competent adsorbent carrier for liquid and SMEDDS. Fujicalin® (Unique mesoporous Dibasic Calcium Phosphate Anhydrous) is the perfect sphere for direct compression and granulation with improved blend uniformity even for micronized APIs with extreme low loading. F-MELT® (directly compressible ODT matrix) is a ready-to-use excipient for ODTs. Unlike other ODT platforms, there is no royalty and license fee required. For more information contact Fuji Health Science at contact@fujihealthscience.com or visit **www.fujihealthscience.com.**

Quality is Our Cornerstone

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.**

Excipient for Tablets

Compritol® 888 ATO is an inert, tasteless/odorless, hydrophobic white powder used in formulation of solid oral dosage forms. Listed in the IID database and USP-NF/EP/CP Pharmacopeias as Glyceryl Behenate, Compritol has been used for over 50 years in numerous marketed drugs – including pediatrics around the globe. Originally developed as a viable alternative to magnesium stearate as a tablet lubricant, Compritol is currently being used in sustained release by direct compression, taste masking by melt granulation or melt coating, and solid dispersions by melt extrusion. Additionally, Compritol is applied in the development of solid lipid nanoparticles. Key features of this excipient include: high purity, superior quality, safe, requires low compression force, easy to scale-up, and fully characterized by physico-chemical properties. For more information, contact Gattefossé at info@gattefossecorp.com or visit **www.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.**

BE Tech & Development Services

iCeutica has developed and commercialized SoluMatrix Fine Particle Technology™ for improving the oral bioavailability of poorly water-soluble drugs. The patented technology is based on drug particle size reduction and improves the dissolution properties of lipophilic compounds. Faster in-vivo dissolution can yield many clinical benefits, including greater extent of absorption, decreased time to onset of action, elimination of food effects, and reductions in pharmacokinetic variability. iCeutica also provides drug development services; with a team of seasoned pharmaceutical professionals, iCeutica can develop and characterize solid oral dosage forms, coordinate GMP manufacturing, prepare and submit regulatory filings, and manage clinical trials for partners who are seeking to advance new products into clinical development. For more information, visit iCeutica at **www.iceutica.com.**

Formulation Development

Latitude Pharmaceuticals, Inc. extends its reputation each day among drug developers as the go-to formulation group for problematic APIs. Whether the need is for a quick PK/Tox formulation or a complete IND-ready formulation development program that covers analytical, manufacturing process, and new IP protection, Latitude draws on its extensive experience and technical expertise to complete each project rapidly, efficiently, and cost effectively. We have the experienced personnel and an extensive range of analytical and manufacturing platforms to develop prototypes of nearly every kind of injectable, oral, topical, inhalation, and ophthalmic human and veterinary formulation – both simple and complex. If your API is insoluble, poorly bioavailable, irritating, physically and/or chemically unstable, tastes bad, requires a special PK or tissue distribution, or requires a proprietary, complex, or generic formulation, contact Latitude at (858) 546-0924, ext. 103, or visit **www.latitudepharma.com.**

Development & Manufacturing

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. For more information, visit Lonza Pharma & Biotech at **www.pharma.lonza.com.**

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.**

Drug Delivery Solutions

With over 1,500 people and 4 plants across two continents, Nemera is a world leader in the design, development and manufacturing of drug delivery solutions for the pharmaceutical, biotechnology, and generics industries.

Nemera leverages decades of experience in the devices sector, from full solution development to pure contract manufacturing, through customized solutions. Nemera's expertise covers several modes of delivery: Ophthalmic (multidose, preservative-free eyedroppers), Nasal, Buccal, Auricular (pumps, valves, and actuators for sprays), Dermal & Transdermal (airless and atmospheric dispensers), Parenteral (auto-injectors, pens, safety devices, and implanters), and Pulmonary (pMDIs, DPIs). Over 5 million diabetics and 10 million asthmatics use every day the devices manufactured by Nemera. For more information, contact Nemera at information@nemera.net or visit **www.nemera.net.**

Device Training Platforms

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.**

Specialized Products & Services

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

Global Data & Analytics

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

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

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. For more information, visit ProMed at **www.promedpharmallc.com.**

Aseptic Filling & Lyophilization

PYRAMID
Laboratories, Inc.

PYRAMID Laboratories, Inc. is a Contract, Parenteral Drug Product Manufacturer and Analytical Service provider for the pharmaceutical and biotechnology industries.

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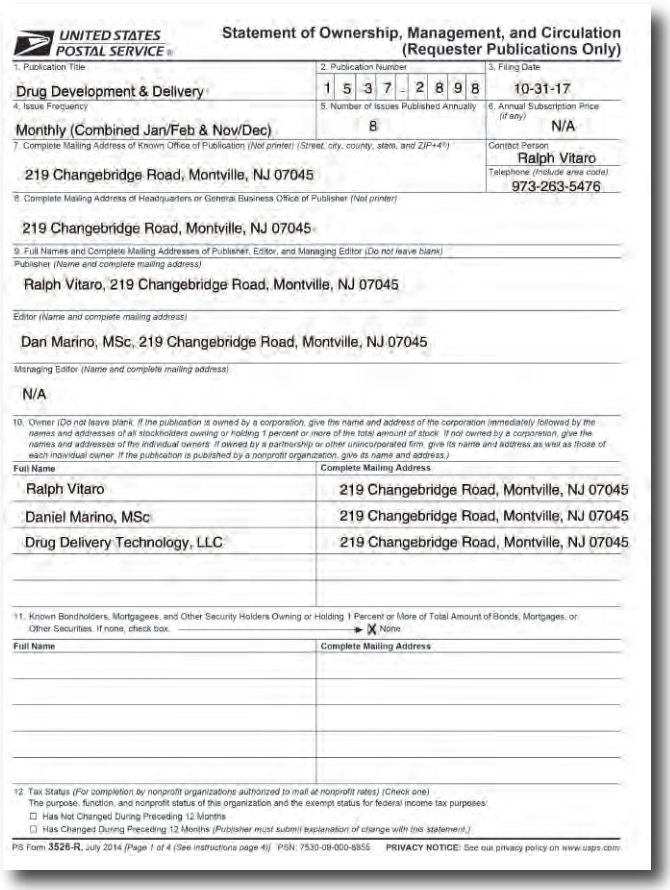

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1. Publication Title	2. Publication Number	3. Filing Date
Drug Development & Delivery	15-372-2898	10-31-17
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price (If any)
Monthly (Combined Jan/Feb & Nov/Dec)	8	N/A

7. Complete Mailing Address of Known Office of Publication (Not printer) (Street, city, county, state, and ZIP+4®): 219 Changebridge Road, Montville, NJ 07045 — Contact Person: Ralph Vitaro; Telephone (Include area code): 973-263-5476

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Publisher (Name and complete mailing address): Ralph Vitaro, 219 Changebridge Road, Montville, NJ 07045

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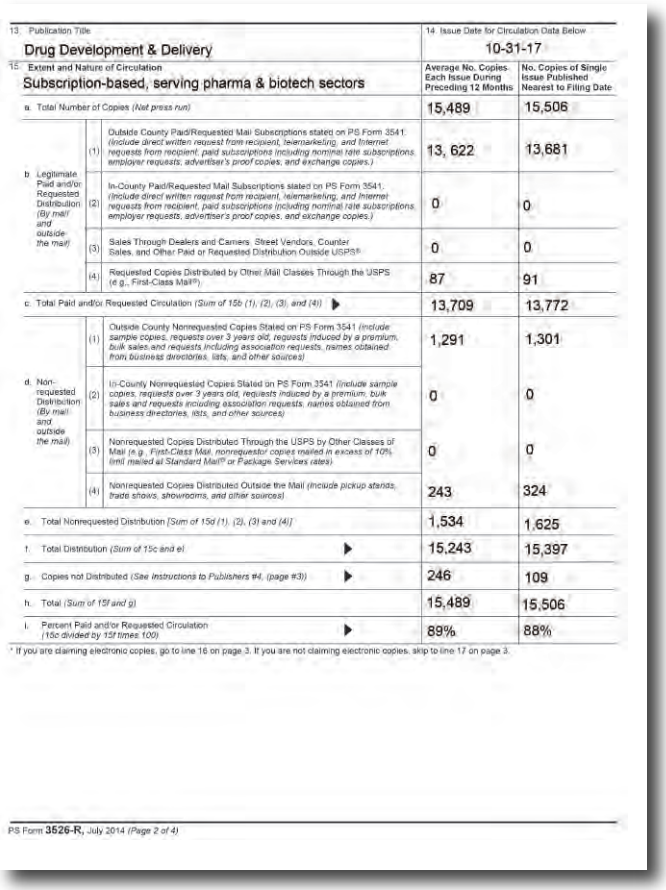

13. Publication Title: Drug Development & Delivery — 14. Issue Date for Circulation Data Below: 10-31-17

15. Extent and Nature of Circulation: Subscription-based, serving pharma & biotech sectors

			Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
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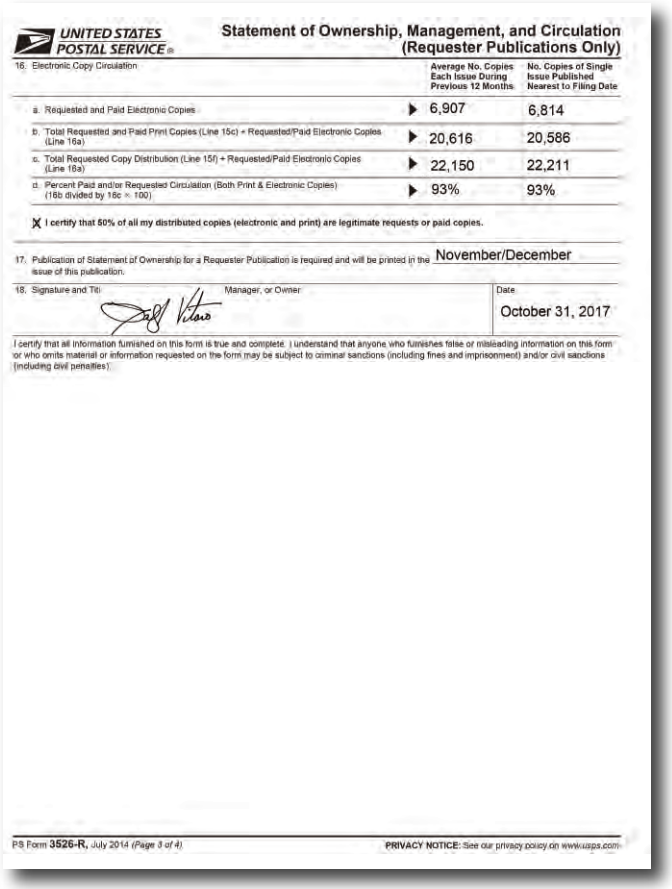

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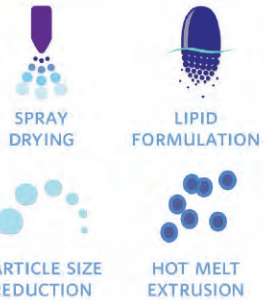

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