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Drug Development & Delivery

November/December 2014 Vol 14 No 9 www.drug-dev.com

Global Trends & Forecasts

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

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New Optimism in Pharma

"Pharmaceutical companies are under more scrutiny than ever regarding the quality of therapies and, concurrently, the return on investment they deliver to shareholders. To this end, many large cap pharma companies continue to reassemble their businesses in favor of greater transparency and operating efficiency. We have seen two firms, Gilead Sciences and Biogen Idec, both typically seen as being in the biotech mold, achieve astronomical success with their respective launches of Sovaldi (sofosbuvir) and Tecfidera (dimethyl fumarate) in 2013, with both new therapies recording uptake at a level never before seen in the industry."

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What's in the Pipeline?

"It's not hard to predict that we will see more and more abuse-resistant and deterrent formulations of opioids and stimulants hit the market in the near future, followed by their generic equivalents. The real money to be made will be found in those products that change the whole paradigm – novel molecules that retain desired analgesic or psychoactive properties but without any inherent addictive or abuse-reinforcing properties."

p.38

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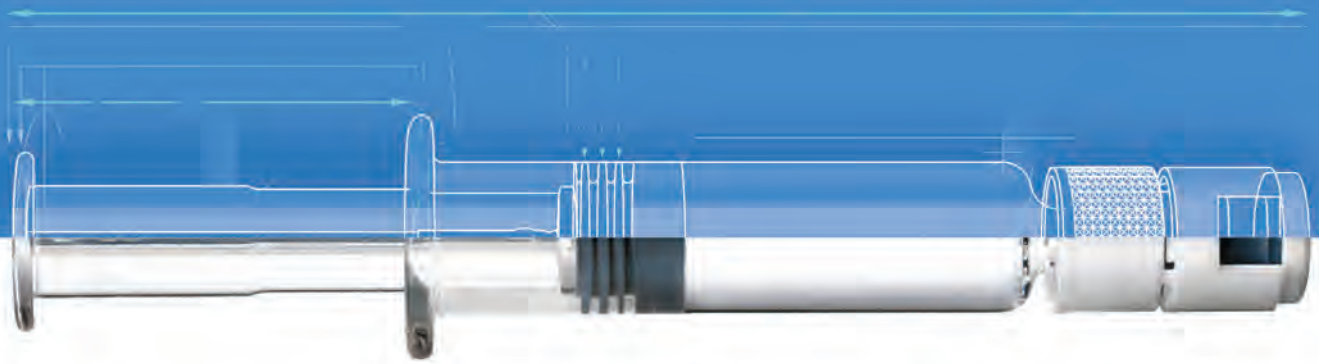

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Global Market for Radiopharmaceuticals to Reach $6.4 Billion in 2019

BCC Research reveals in its new report, Radiopharmaceuticals: Technologies and Global Markets, the global market for radiopharmaceuticals is forecast to expand through 2019 at a projected compound annual growth rate (CAGR) of 8%, approaching $6.4 billion.

The global radiopharmaceuticals market is driven mostly by an aging population and the growth of cardiovascular, oncological and neurological disorders. Most of the radiopharmaceuticals are used in nuclear imaging, as it offers a non-invasive, stationary and dynamic image of the body's organs. Radiopharmaceuticals are now a crucial part of the healthcare industry, due to their ability to identify various disease processes much earlier than other diagnostic tests.

US FDA approval of new radiopharmaceuticals coupled with the improved supply of technetium-99 has expanded the market between 2012 and 2014. North America is the market leader and is anticipated to grow from $2.1 billion in 2013 to $3.8 billion in 2019 at an estimated CAGR of 9.2%. This is followed by the European market segment. With a CAGR of 6.8%, this market is predicted to reach $1.6 billion by 2019. Emerging markets are increasing at a CAGR of 5.8%, and are foreseen to reach $762 million by the end of 2014 and $1 billion by 2019. Increasing awareness coupled with the rising diagnostic rates is the major growth factor for this market.

"R&D spending along with increasing competition, patent expiries and new technologies are directing this market," says BCC Research pharmaceuticals analyst Shalini S. Dewan. "Advancements and new product launches will influence market growth in the near future."

Morrison & Foerster's BioMeter Index Shows Re-emergence of Late-Stage Deals

Morrison & Foerster returns with its Q3 edition of BioMeter, which reveals a big jump in the number of deals and average payments for Phase 3 and approved products — the strongest numbers MoFo has seen since it created the BioMeter Index.

BioMeter reports seven Phase 3 transactions with an average up-front payment of $83.3 million, and five approved-product transactions with an average value of $86.7 million for the third quarter. The robust performance reflects "selective pipeline filling," as pharma companies switch from the focus on early-stage assets to pursuing products ready or almost ready for commercialization.

In Q3, the average BioMeter Index value for all transactions was $45.4 million, an increase over Q3 2013 as well as over Q2 2014 if the second quarter's two blockbuster deals ($1 billion Merck/Bayer and $710 million Celgene/Nogra) are excluded. Meanwhile, after an exceptionally high-value Q2, pre-clinical/discovery-stage transactions returned to more characteristic territory ($10.9 million average across four transactions). Phase 1 and 2 values in Q3 were weak—this despite the same number of Phase 2 deals as in Q2, a period in which their average value ($33.1 million) was more than 250% higher than in Q3.

The firm developed the BioMeter Index to measure the health of the biotech industry by averaging up-front payments in licensing, collaboration, and development agreements between biotech firms and companies that pay for commercialization rights. Up-front payments are not only the most concrete reflection of the value of a development-stage asset, but are also an increasingly necessary source of capital for companies to sustain development efforts.

Capsugel Advances First Intrinsically Enteric Capsule Technology

Capsugel recently announced the expansion of its lead-user customer-collaboration program for its intrinsically enteric capsule technology. This breakthrough drug delivery technology integrates industry-approved enteric polymers in the capsule design, enabling Capsugel to offer the first fully enteric dosage form without the need to apply functional coatings.

Capsugel's enteric capsule technology lead-user programs include feasibility studies with selected customers that target oral vaccine and peptide delivery, as well as early stage development programs for small chemical entities that could benefit from an intrinsically enteric dosage form. Under the feasibility program, lead users are granted access to the technology and associated intellectual property, as well as dedicated scientific, product development, and regulatory support services.

This new technology complements Capsugel Dosage Form Solutions' array of modified and targeted release technologies utilized to optimize drug delivery, including a range of multiparticulate formulation options, osmotic tablets, bi- and tri-layered matrices, dual capsule technology, and colonic delivery approaches.

Pharmaceutical Industry Feeling Force of Tax Inversion Legislation

The recent termination of AbbVie's deal to acquire Shire makes this pharmaceuticals' first major casualty of new US tax inversion legislation, and has jolted the industry out of its reverie, according to an analyst with research and consulting firm GlobalData.

Aparna Krishnan, MS, GlobalData's Analyst covering Healthcare Industry Dynamics, states that the decision by AbbVie's board of directors to terminate the Shire merger and acquisition (M&A) deal is due to the realization that its value would be too much of a financial risk without the tax incentive component.

Krishnan comments: "By acquiring UK-based Shire, AbbVie's effective tax rate would have dropped by 7%, enhancing its earnings by $350 million on a pro forma basis in 2013. In effect, the tax savings would have contributed anywhere between $15–18 billion in savings over the next 15 years, creating significant cash flow for the expanded AbbVie.

"As these tax savings were inherent in the value of the deal, it is no longer viable. Furthermore, new tax inversion laws are potentially corrosive to the industry earnings of others, meaning that the market may cool down on M&A deals in the near term."

The analyst notes that while Shire will receive a $1.6 billion termination fee from AbbVie, its share price has unsurprisingly been hit hard.

Krishnan continues: "Notwithstanding this near-term impact, Shire will push ahead with premerger plans to expand its orphan drugs portfolio through acquisitions.

"Meanwhile, AbbVie will have to take stock and reassess its M&A strategy with its next move to diversify its portfolio. This will counter the risks associated with the company's dependency on its highest revenue contributor, Humira, which could face biosimilar competition from as early as December 2016 in the US and April 2018 in other markets."

Ultra-Rapid-Acting Insulin Formulations Will Revolutionize Type 1 Diabetes Treatment Market

Ultra-rapid formulations of the currently marketed rapid-acting insulin analogs have the clear potential to radically change the insulin market over the next five years, according to a director with research and consulting firm GlobalData.

Valentina Gburcik, PhD, GlobalData's Director of Cardiovascular & Metabolic Disorders, says that the use of long-acting insulin analogs may decrease as rapid- and ultra-rapid-acting analogs gradually take over the type 1 diabetes market.

"A substantial and ongoing rise in insulin pump usage over recent years, alongside the rapid development of a closed-loop system, or artificial pancreas, strengthens the need for insulins that act even faster than the currently marketed rapid-acting analogs," said Dr. Gburcik. "An artificial pancreas, which combines continuous glucose monitoring, a control algorithm and an insulin pump device, will likely become reality over the next few years. Ultra-rapid-acting formulations will also help with developing artificial pancreas systems, as their fast reaction time could allow the pumps' algorithms to dose insulin in real time."

The director notes that a number of these formulations are currently in development and may profit from the increasing pump therapy use, as they better match the physiological profile of prandial insulin.

Gburcik addes, "Novo Nordisk's FIAsp (NN-1218) is an ultra-rapid-acting formulation of NovoLog/NovoRapid (insulin aspart), which aims to continue NovoLog's legacy and protect the franchise from generic erosion to biosimilars, as the drug's patent expires throughout 2014 and 2015. In addition, biotech companies Adocia, Biodel, and Halozyme Therapeutics are developing similar formulations that will likely reach the market over the next few years, due to the short duration of the pharmacokinetic/pharmacodynamic clinical studies that are necessary for these drugs."

The director also indicates that while Adocia's BioChaperon insulin lispro is the most developed of the three biotech offerings, the company will have to either raise more capital or enter into licensing or collaboration agreements with experienced and well-funded players to compete in the insulin market.

INVESTMENT TRENDS

A Rise in IPOs Revive Investments for the Global Pharma & Biotech Industry

By: Dr. E Saneesh, Financial Analyst, Frost & Sullivan

The heightened private equity and venture capital (PEVC) deal activity in the global healthcare industry during the recession years, 2008-2010, witnessed a decline post-2010. However, the fall in deals was not uniform among the constituent sectors, with the pharmaceutical, biotechnology, and healthcare equipment sectors experiencing a much sharper decline in investor interest than the healthcare technology and provider segments. Investors started to bet on providers based with the conviction they can provide quicker and safer returns than the pharmaceutical and biotechnology space, which is ridden with regulatory challenges and patent expiries.

New analysis from Frost & Sullivan's *Private Equity and Venture Capital Investment in the Global Pharmaceutical and Biotechnology Industry* reveals the total number of PEVC deals in the pharmaceutical and biotechnology industry decreased from 1063 in 2010 to 480 in 2013. Though the returns from the pharmaceutical and biotechnology industry have been dwindling, they are better compared to the performance of other industries.

PE deals in the pharmaceutical sector have been relatively stable over the post-recession period, whereas activity in the biotechnology segment began to decrease after reaching its peak in 2010, due to the uncertainty caused by healthcare reform in the US, long incubation periods, and delayed approvals. VC deals across both these sectors also started to plummet from 2011 due to risks associated with regulatory uncertainty, long gestation periods, and increased cost of production.

However, the strong comeback of initial public offerings (IPOs) in 2013 signals a positive outlook for investment in the pharmaceutical and biotechnology industry. The number of IPOs in the global biotechnology sector surged by 100% between 2012 and 2013, primarily on account of the 26 IPOs that took place in the US. IPOs in the pharmaceutical industry also rose with 11 deals in 2013, after the volume of IPOs declined to almost one-sixth of the sector's value between 2011 and 2012.

As a result of the rise in IPOs, exit opportunities are expected to increase for investors. The trend will be further fuelled by the anticipated growth of corporate investor-backed IPOs.

PEVC investors in the global pharmaceutical and biotechnology industry have demonstrated maximum interest in oncology drugs, followed by anti-infective drugs and pharmaceutical contract laboratories. They have also concluded the maximum pharmaceutical- and biotechnology-related PEVC deals in the US are expected to continue to do so in the forthcoming years. Industry players most aligned with these trends will be well positioned to obtain financial support from PEVC investors. ◆

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BIOGRAPHY

Dr. E. Saneesh is a healthcare research analyst with Frost & Sullivan's global Business and Financial Services practice. He has combined experience in clinical practices, research and consulting across specialties areas, such as pharmaceutical, healthcare delivery, and medical devices. His functional expertise is supported by his involvement with financial modeling, financial feasibility, business model development, and acquisition strategies. For more information about Frost & Sullivan's global Business and Financial Services, email Jennifer Carson, Corporate Communications at Jennifer.Carson@frost.com.

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IVD
TRENDS

In Vitro Diagnostics Players Go Global as US & Europe Markets Slow Down

By: Divyaa Ravishankar, MS, Senior Industry Analyst, Life Sciences, Frost & Sullivan

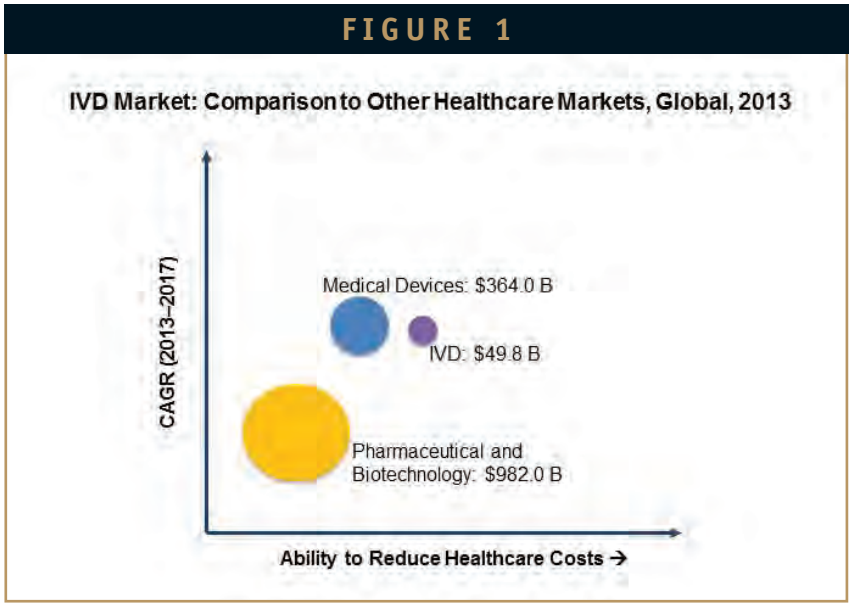
Despite economic and industry challenges, the global in vitro diagnostics (IVD) market is growing robustly – at double the rate of the global pharmaceutical industry (Figure 1). The market will remain buoyant as the recent success of cost-saving companion diagnostics tests and personalized medicine is driving the uptake of various IVD tests and opening up the opportunity to expand test menus. While the US and European markets remain important, their slowdown is demanding an alignment with the global market. As a result, the Asia-Pacific region is becoming a lucrative destination for IVD manufacturers.

New analysis from Frost & Sullivan's *Analysis of the Global In Vitro Diagnostics Market* finds the market earned $49.8 billion in revenue in 2013 and estimates this to reach $66.1 billion in 2017. The research covers immunochemistry, self-monitoring blood glucose (SMBG), point-of-care testing (POCT), molecular diagnostics, hematology, clinical microbiology, hemostasis, and tissue diagnostics.

The broad application potential, combined with downward pricing trends enabled by microfluidics integration, is fuelling the long-term growth of the point of care testing (POCT) segment. In spite of market uncertainties, the hematology segment too is gaining traction through the launch of new products, support of an existing installed base, and needs of emerging markets.

In addition to these segments, the molecular diagnostics space holds promise due to continued demand from the developed US and European markets. However, low public health reimbursement for SMBG products in the US and Europe is adversely affecting the development of this segment. IVD companies are pursuing emerging markets to compensate for the drop in market pace in developed nations. With pricing pressures and intensifying competition pervading emerging markets, IVD companies need to operate strategically in these

FIGURE 1



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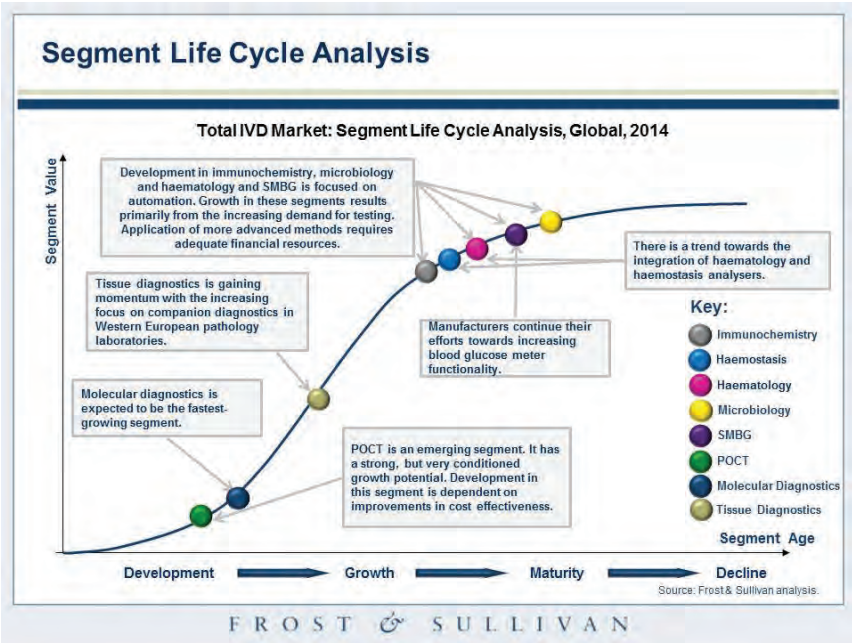

territories (Figure 2).

Further, strained laboratory budgets, workforce shortages, and fewer visits to the doctor by people who have lost their employer-sponsored health insurance are hindering the sale of IVD tests globally. Insufficient connectivity in healthcare facilities is limiting the ability to provide diagnostic testing, adding to market woes.

Nevertheless, as diagnostic testing moves toward process simplicity and decentralization, demand will rise. Not only will this encourage entry into the molecular diagnostic market through acquisitions but it will also increase penetration of biomarkers that can be tested at a point of care level.

Market participants need to employ a diverse set of strategies rather than rely on comprehensive product portfolios to expand their businesses. A mix of the following strategies are expected to be implemented: investing in next-generation sequencing, strengthening product portfolio in a specific area, venturing into emerging markets by establishing partnerships with local companies, acquiring a clinical laboratory improvement amendments (CLIA)-certified laboratory to rapidly commercialize new diagnostic tests, out-licensing of proprietary technology platforms or collaborations with major research institutes, integrating big data into product development and increasing connectivity of devices, and offering pared down personalized machines to improve access and clinical development. ◆

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BIOGRAPHY

Divyaa Ravishankar is a Senior Industry Analyst for Frost & Sullivan's Life Sciences practice. She has diverse expertise within healthcare IT and life sciences with a focus on in vitro diagnostics. Her expertise constitutes of laboratory research and management consulting. Ms. Ravishankar earned her MS (Hons.) in Biological Sciences from Birla Institute of Technology and Science, Pilani, India. For more information on Frost & Sullivan's global Life Sciences practice and offerings, please email jennifer.carson@frost.com or visit www.frost.com.

ORPHAN DRUG MARKET

Drug Developers Drawn to Orphan Drugs Market: Financial Incentives Create Rich, Competitive Pipelines

By: Frost & Sullivan

The global orphan drugs market presents plenty of opportunities for new drug development – while there are only 172 approved orphan therapies, over 6,800 orphan diseases exist according to the United States National Institute of Health (NIH). Advancements in drug discovery capabilities coupled with regulatory and financial incentives are helping generate rich, competitive pipelines of breakthrough treatments with true disease modifying properties.

Pharmaceutical and biotechnology companies are now rolling out therapies for serious, rare diseases – going beyond palliative care and targeting the underlying pathology to slow down or stop disease progression – as they value the financial and philanthropic rewards this brings.

New analysis from Frost & Sullivan's *Product and Pipeline Assessment of the Global Orphan Drugs Market* identifies rare cancers as the orphan therapeutic area with the highest level of drug development activity. Other disease areas witnessing considerable drug development activity include blood/lymphatic system diseases, infectious/parasitic diseases, neurological diseases, metabolic diseases, and immunological/inflammatory diseases.

In the past, pharmaceutical and biotechnology companies rarely developed new drugs to treat rare diseases due to the low return on investment realized because of the small patient population. Now, drug discovery for orphan diseases is becoming an important element of the business models of numerous small and large pharmaceutical and biotechnology companies looking to strengthen their presence in the global market.

As a result, pharmaceutical and biotechnology companies are introducing orphan drugs that use diverse approaches such as small molecules, antisense, gene therapy, monoclonal antibodies, bi-specific antibodies, peptide therapies, and stem cell therapies. Currently, such therapies command premium prices due to the huge clinical benefits they offer and the lack of alternative treatments for patients. Soon, however, they will have to be sold at competitive prices as the existing level of reimbursement will become untenable due to the anticipated approval and commercialization of several orphan drugs for neglected diseases.

As drug developers abandon the "blockbuster model" in favor of greater focus on drug development for rare conditions, the global orphan drugs market is becoming increasingly competitive. It is imperative that drug developers continually keep a tab of competitors' pipelines as approval and reimbursement of new orphan drugs are highly dependent on the availability of alternative therapies. ◆

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PERSONALIZED MEDICINE

Targeted, Personalized Therapy is the Future of Chronic Disease Therapeutics

By: Jennifer Lazar, Global Program Director, Life Sciences and Connected Health, Frost & Sullivan

The global life sciences sector is employing new research and development (R&D) and business models to cost effectively deliver innovation, value, and improved patient outcomes. With the incidence rate for chronic diseases on the rise, pharma companies have realized that the one-size-fits-all, blockbuster drug approach is not the way forward. Instead, they are prioritizing drug portfolios to core therapeutic areas and offering specialty products for specific patient groups.

Another driver for personalized medicine is the rapidly rising need for reimbursement. Payers are focusing on treatments that can provide patient outcomes and fulfill large unmet needs. As a result, pharmaceutical and biotechnology firms are looking to understand the patient genome better and develop therapeutics that target specific patient subsets for more effective and potentially cheaper treatment.

With the chronic disease treatment market ripe for innovation, personalized medicine will move beyond oncology and into areas such as virology and cardiology. For instance, the lipid modulator segment in the cardiology market is aiming at higher personalization. While drugs available today are used mainly to lower total low-density lipoprotein cholesterol (LDL-C) or triglyceride levels, several remedies to increase high-density lipoprotein (HDL) are under development.

Drug manufacturers are planning to take this further with next-generation drugs aimed at specific targets related to increased cardiovascular risk, such as lipoprotein(a), small dense LDL particles, oxidized LDL and HDL particle subpopulations, along with newly discovered targets. Companion diagnostics that employ gene-targeted therapies will also enable personalized treatment.

In the hepatitis C segment, meanwhile, a treatment revolution is underway as the market migrates from protease inhibitors and interferon regimens toward targeted, highly effective, easily tolerated, interferon-free oral therapies. Gilead's sofosbuvir/Sovaldi has gained first mover advantage and is expected to generate revenues of over $7 billion in 2014.

Moving away from the one-size-fits-all approach (interferons) to more targeted therapies will see the introduction of potent all-oral "terminator" therapies for targeted genotypes, shifting the treatment paradigm from disease management to eradication. Further innovation may even see an all-oral pan-genotypic therapy and a radically short 4- or 6-week treatment regimen for hepatitis C. ◆

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BIOGRAPHY

Jennifer Lazar is the Global Program Director of Frost & Sullivan's Life Sciences and Connected Health practices. Her expertise includes a deep understanding of various pharmaceutical sectors and impacts on the overall healthcare ecosystem. Her knowledge and thought leadership is supported by more than a decade of market landscape assessments and forecasting, product launch strategies, competitive intelligence, and management. For more information about Frost & Sullivan's global Life Sciences and Connected Health practices, email Jennifer Carson, Corporate Communications at Jennifer.Carson@frost.com.

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DNA VACCINES MARKET

DNA Vaccines: Strategic Markets & Emerging Technologies

By: Kevin James, Shalini Shahani Dewan, MS, and Jon Evans, MBA

INTRODUCTION

The vaccine industry is rapidly changing from a mostly empirical approach to one based on rational design. Rapid developments in molecular biology, DNA synthesis, and immunobiology enable rational design approaches. These technologies allow highly targeted vaccines aimed at specific epitopes. The result is new vaccines for a wider range of diseases than was previously feasible, including a new class of therapeutic vaccines. These new technologies allow pharmaceutical firms to discover and develop high-value vaccines for novel applications, creating a substantial new market opportunity.

DNA vaccines have many potential advantages, including specific targeting, use of multiple genes to enhance immunity, and reduced risk compared with conventional vaccines. Translating the advantages of DNA vaccines into the clinic has historically been difficult; however, new advances in the fields of vaccine design and DNA delivery are addressing previous issues. Achievements in these fields promise to overcome the translational hurdles and create strategic opportunity.

According to BCC Research (www.bccresearch.com), the global market for DNA vaccines is estimated at $305.3 million for 2014 and is forecast to grow at a stellar 54.8% compound annual growth rate (CAGR) to reach $2.7 billion by 2019. High growth during this period is a combination of a low starting base and forecasted introduction of several DNA vaccines late in the forecast period. While research tools and animal health clinical applications dominate the market today, by 2019 human clinical DNA vaccines will make up the vast majority of this market.

DNA VACCINES

The first DNA vaccine to be approved was the equine West Nile virus vaccine in 2005. This approval validated the DNA vaccine model in non-humans, and since then, the model has been validated in clinical trials in humans.

In 2006, Merck (together with its European partner, Sanofi Pasteur) launched its cervical cancer vaccine, Gardasil. The success of this vaccine, and its second-in-line competitor, Cervarix (GSK), marked a milestone in the vaccine industry. The products competed in an entirely new vaccine market for prevention of a specific cancer, precancerous genital lesions, and genital warts due to the human papillomavirus (HPV). These products provide blockbuster potential for their developers and change the way vaccines are marketed and distributed.

DNA vaccines arise from a simple concept - the coding sequence for a pathogenic antigen is incorporated into a pDNA, and the sequence is then expressed in the host cell. Because DNA vaccines do not use a pathogen itself or pathogenic protein, there is no need to prepare, purify, or deliver a pathogen or protein. This is a key advantage of DNA vaccines and one reason for their growing use in vaccine development programs.

DNA vaccines target a wide range of traditional pharmaceutical markets, such as cancers and allergies, as well as infectious diseases. The greater vaccine industry has proven that it can generate products with non-traditional applications and blockbuster potential, with the introduction of Gardasil by Merck. DNA vaccines are poised to follow this emerging model to generate significant future market potential.

New biotechnologies and nanotechnologies are driving DNA vaccine development. Particularly important to DNA vaccines reaching their potential are emerging delivery technologies, such as electroporation

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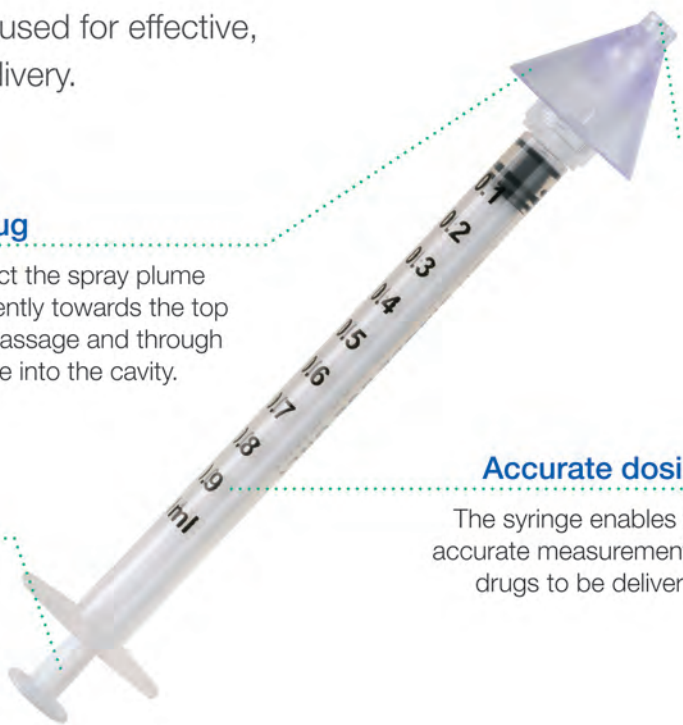

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(EP), innovative vaccine formats such as DNA prime-adenovector boost, and novel molecular adjuvant technologies. These technologies are providing the means for achieving higher efficacy in humans.

DNA vaccines have already made significant progress to date. Nearly 100 clinical trials are underway in humans for a wide range of diseases, and there is a deep pipeline of preclinical projects. A small but strategic market segment is commercial today, including research tools and animal health applications.

STRATEGIC MARKETS

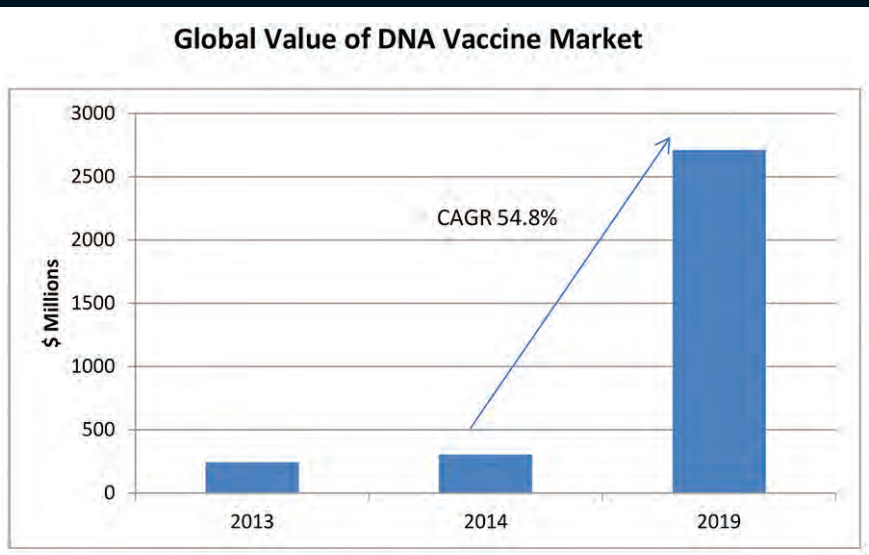
Research tools and animal health represent strategic markets for DNA vaccines. These market segments play a vital role in the development of the large, human vaccine applications in two ways: they provide current good manufacturing practice- (cGMP) grade pDNA to the industry to support the vast number of clinical trials now ongoing, and they demonstrate proof of principle for DNA vaccine safety and efficacy in animals.

Human clinical DNA vaccines represent the primary future market opportunity for this industry. The momentum for commercialization of a human DNA vaccine is growing due to the inherent advantages of DNA vaccines over other vaccine formats, amid an emerging consensus within the vaccine industry that DNA vaccines are safe and efficacious in humans.

Advanced formulation strategies, including combination vaccines (eg, DNA prime followed by viral vector/peptide/recombinant protein boosts), innovative delivery methods (eg, EP), and novel adjuvants (eg, DNA sequences encoding mutant cytokines) are proving their safety and efficacy in early and mid-stage clinical trials.

Cancer is a serious worldwide health threat, particularly in developed countries, where the populations are aging and disease is prevalent. For many cancers, there are significant unmet medical needs, resulting in high mortality rates. DNA vaccines targeted against these cancers are particularly attractive market segments. Clinical trials for DNA vaccines to treat several of these cancers, including metastatic melanoma, prostate, and pancreatic cancer, and other solid tumors, are showing promising results. These vaccines will follow the new vaccine market model of blockbuster cancer vaccines recently introduced - Gardasil and Cervarix - during their commercial introduction phase.

FIGURE 1



Biotechnology tools to produce, manipulate, and purify DNA are now standard in most laboratories. The means to discover and develop new pDNA vaccines are readily available to a large cross-section of scientists. Conventional vaccine approaches have not succeeded for a large proportion of infectious diseases, and have made only slow progress in treating cancers. As a result, there are still significant unmet medical needs in these disease areas. DNA vaccines may be able to meet these needs because they use immunological pathways that are not easily achieved by other technologies.

With the recent outbreak of the pandemic swine flu virus, it is apparent that there is an increasing need to protect against rapidly mutating pathogens. Viruses that change rapidly cause emerging infectious diseases as well as established diseases, such as influenza, SARS, acquired immunodeficiency syndrome (AIDS), and West Nile virus. There is an ongoing need for vaccine technologies that can protect against these threats. DNA vaccines can be developed and manufactured rapidly compared with conventional vaccines, and so are prime candidates for vaccinating against these diseases. The early testing of Ebola vaccine compounds points toward this unmet need.

COMMERCIAL STATUS OF DNA VACCINE TECHNOLOGIES

First-generation vaccines (live attenuated microorganisms) include traditional, registered products. These vaccines are mature, with a long history of use. Second-generation vaccines (protein or protein components) are registered, and there is a continuing active search for new vaccines using these platforms. Many of these vaccine candidates are currently in clinical trials.

Third-generation vaccines (including DNA, viral/bacterial vectored, and autologous protein) are earliest in the technology life cycle, with important new technologies being discovered and tested in preclinical and clinical studies.

Thus, DNA vaccines can be considered an emerging vaccine platform, with a substantial number of vaccine candidates in early to mid-stage human clinical trials. There remains much late-stage clinical work to be done; however, this vaccine platform has

shown sufficient promise in testing performed thus far to warrant serious attention by the vaccine industry.

The research tools segment is the most advanced commercially, with existing products in antibody generation (using genetic vaccination) and production of cGMP quality pDNA for preclinical and clinical studies. These markets are strategically significant for the DNA vaccine industry, as they provide tools for showing proof of concept of DNA vaccines in animal models and human clinical trials.

Several DNA vaccines for animal health have been introduced into the market, and there are additional vaccines under development for this market segment. DNA vaccines for animals have been easier to commercialize to date primarily because it is technically easier for a DNA vaccine to work in an animal than a human, and the regulatory route to approval is easier for an animal than a human. As a result, the animal health market is at the leading edge of the DNA vaccine commercial efforts.

Human health applications, like cancer and infectious diseases, have the highest market potential, but are at an earlier stage in their commercial status. In order to commercialize human health DNA vaccines, substantial technical and regulatory hurdles must be surmounted. This requires significant commitment of time and resources by biotechnology and vaccine companies. Despite this, the biotechnology and vaccine commercial community is committing to this effort, as evidenced by the 96 current clinical trials and deep preclinical development programs. These efforts are supported by a critical mass of supporting industries, including DNA delivery, pDNA manufacturing, molecular adjuvants, and nanotechnology. These commercial factors are positive signs for eventual success in this market segment.

The structure for the traditional vaccine industry involved high barriers to entry (difficulty of manufacture combined with low market attractiveness). This limited the number of traditional vaccine manufacturers. Threat of substitutes is low in traditional vaccines because the technology is not changing rapidly. As a result, traditional vaccine manufacturers were able to establish an attractive vaccine franchise.

These structural forces within the traditional vaccine industry have resulted in a highly concentrated competitor situation with, for example, three producers (Sanofi Pasteur, Merck, and GlaxoSmithKline) supplying more than 70% of the US vaccine market.

The emergence of new (including DNA) vaccines is changing this traditional industry structure. Because the technology is new and rapidly evolving for these vaccines, substitute technologies and new entrants become a significant factor. Barriers to entry are lower than for traditional vaccines. As a result, emerging vaccine industries like DNA vaccines are more fragmented, with multiple product offerings targeted at a wide range of market segments.

At the same time, the vaccine industry is evolving much of the character of the pharmaceuticals business, with a focus on both prevention and treatment, infectious diseases as well as cancer, and blockbuster market potential for any given product. The introduction of Gardasil (Merck), Cervarix (GSK), Rotarix (Merck), and Zostavax (Merck) followed the model of the first blockbuster vaccine, Prevnar (Merck). These vaccines, like the emerging DNA vaccines, target broad markets beyond the traditional limited pediatrician and specialist physician markets. DNA vaccines are expected to follow this new model, accessing substantial markets in infectious diseases, cancer, animal health, allergies, and biodefense. ◆

This article is based on the following market analysis reports published by BCC Research: **Global Markets for Vaccine Technologies (PHM014E)** by Shalini Shahani Dewan and **DNA Vaccines: Technologies & Global Markets (BIO067B)** by Jon Evans For more information, visit www.bccresearch.com.

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BIOGRAPHIES

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John Evans has been involved in business development and research for the medical industry since 1984. Mr. Evans' career includes 4 years as a diagnostic systems sales representative and over 15 years in market research and strategy analysis with Fortune 500 clients. He has developed expertise in assessing the unique business development challenges facing firms in the medical industry and designing strategies to optimize market performance. Mr. Evans earned his BS in Biology from Rutgers University in 1983, and his MBA in Business Analysis from San Francisco State University in 1989.

IMMUNOCHEMISTRY ANALYZER MARKET

Mutiplexing Technologies for Infectious Disease, Cancer, Cardiac & Autoimmune Testing Rise Above the Horizon

By: Divyaa Ravishankar, MS, Senior Industry Analyst, Life Sciences, Frost & Sullivan

CURRENT MARKET LANDSCAPE

Immunochemistry analyzers are just now beginning to take the place of clinical chemistry and immunoassay as new or improved assays are being added to the test menus incrementally. According to College of American Pathologists (CAP) product data, an estimated 184,136 immunochemistry analyzers were installed globally in 2013, and recurring consumable sales are a strong factor to segment growth. Only about 17% of these analyzers are installed in the United States, confirming rapid adoption patterns in emerging and rest of the world countries like China, India, and Japan, where there is an untapped opportunity in rural and hospital markets that lack basic diagnostic laboratory infrastructure.

Customer choices exceed combinations of needs in the immunochemistry market, which has more than 100 immunoassay analyzer models. Facing a high degree of competition, manufacturers modulate forecasts by shortening product cycles with new launches or adding value on existing installs.

The US immunochemistry market is also seeing an influx of many other newer companies from Canada, Japan, China, and Europe. The market has undergone a massive change from just a few vendors offering only enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), radioactive immunoassay (RIA), and flourescent immunoassay (FIA) to also multiplex assays, such as microarrays, flow cytometry-based platforms, recombinant immunoassays, and indirect immunofluorescence assays (IFA). Frost & Sullivan end-user analysis also revealed that in the US, some open system platforms are declining in their install base, leading to rapid transition to either FIA or CLIA systems.

MARKET METRICS

Globally, the immunochemistry market represents approximately 40.1% of the global in vitro diagnostics (IVD) market (Figure 1). Immunochemistry is by far the largest segment by volume, mostly due to routine testing. It is primarily driven by growing access to healthcare. Frost & Sullivan estimates that immunochemistry was a $19.9 billion market segment in 2013 and is expected to grow at a compound annual growth rate (CAGR) of 6.8% from 2013 to 2017. The US is a very important and established market for immunochemistry, primarily because it contributes to about $ 5.1 billion of the global immunochemistry market.

Demand for immunochemistry analyzers is slowing in the US and Western and Eastern Europe. Europe's challenges in this segment include laboratory consolidation in France and late payments from economically troubled Greece, Italy, Spain, and Portugal. China's growing rural hospital market lacks basic diagnostics laboratory infrastructure and represents an untapped opportunity for affordable immunochemistry analyzers.

INTENSIFYING COMPETITIVE LANDSCAPE

Leading brands, such as Siemens, Abbott Diagnostics, Beckman Coulter, Ortho Clinical Diagnostics, and Roche are focused on high-growth segments, such as infectious disease testing, cancer, cardiac, and autoimmune (Figure 2). Several specialty diagnostic companies are also making their way into the in vitro

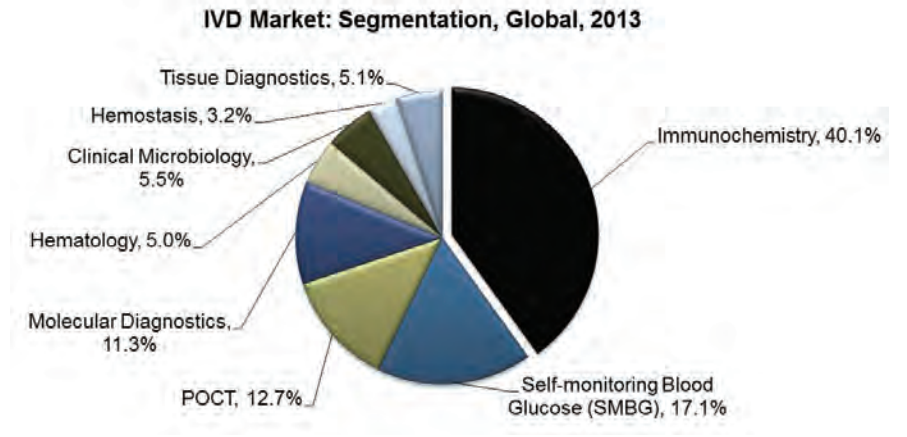
diagnostics (IVD) market, especially for autoimmune diagnostics. Key companies to pay attention to for innovative diagnostic technologies and products include Inova Diagnostics, SQI Diagnostics, Euroimmune, and Aesku Diagnostics.

WHAT IS DRIVING THE MARKET?

After the severe impact of the Patient Protection and Affordable Care Act (PPACA), there is heavy pressure to reduce healthcare costs. Under such challenging conditions, laboratories continue to look for ways to sustain in such a cost-crunched environment. With cuts in the clinical lab fee schedule (CLFS), cost per test is also falling; hence, it necessitates laboratories to focus more on volume of tests to maintain and sustain the inflow of lab funds. At the same time, there is also heavy pressure for quality, error-free results to ensure patient satisfaction. This forces labs to lean toward high throughput and more automated systems with effective workflow solutions.

Growing volumes due to an increase in the number of insured patients will encourage automation in laboratories. With a deficit in laboratory personnel, managing clinical laboratory flow is becoming difficult. Today's scenario demands laboratories to seek the help of systems that have a high throughput, owing to growing volumes and also offer remote data acquisition capabilities. Implementing informatics is critical, and the automated analyzers built today offer a full suite for barcode readers, rack detection systems, and sample/plate identification modules to avoid plate or sample switch.

FIGURE 1



Clinical chemistry revenues are included in the immunochemistry market. Source: Frost & Sullivan

COMPETITIVE FACTORS

Automation and integration, spurred by price and labor pressures inherent in U.S. clinical laboratories, are driving the analyzer market. Offering a broad assay menu, including infectious diseases, is a central competitive factor for increasing installed base of analyzers. Consequently, market participants of this highly competitive market are expected to continue infectious disease immunoassay product development and menu expansion.

Reagent sales typically comprise approximately 85% of fiscal revenues from any single system. Instrument placement is necessary for reagent sales. Therefore, many competitive factors in the immunoassay testing market lie with the instrumentation platform. The installed base of an instrument allows for an increase in test sales. When deciding on a particular testing platform, central laboratories value integrated and automated solutions. The number of tests offered for an instrument promotes the installed base and future reagent sales. A majority of testing platforms are closed systems in which the instrument does not facilitate tests of another provider.

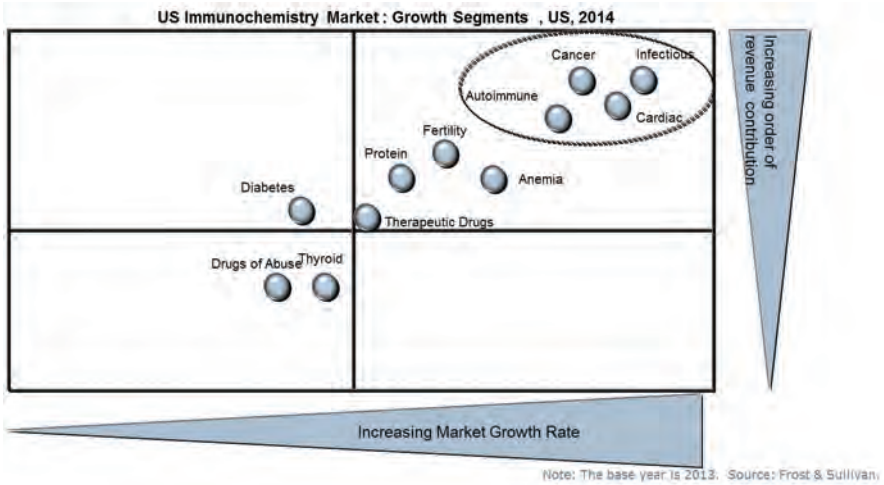
The competitive advantage in this market lies with companies that offer a broad testing menu on an integrated and automated system. Servicing the instruments installed in the laboratory is another significant part of the value proposition market participants should offer. Test performance is yet another competitive factor. However, it is becoming difficult for market participants to stand out on the basis of higher sensitivity or other testing characteristics.

COMPETITOR STRATEGIES

As the market becomes highly competitive, it is essential for manufacturers to retain their install base. This provides recurring reagent business, and hence, several market participants adapt to various strategies with their customers, such as:

Offering Large Discounts on the List price of the Analyzer – As the market for immunoassay and clinical assay systems is enormously shrinking and eroding, companies such as Roche are now adding immunoassay components or clinical chemistry systems to existing analyzers in order to make it an integrated analyzer. This allows the

FIGURE 2



manufacturer to retain their install base in customer groups. As a result, customers receive large discounts. This works in in their favor when laboratories have stringent budgets.

Bundle Reagent Rental Contracts – The tendency toward opting for reagent rentals varies from region to region. For example, laboratories in emerging markets will opt for multiple reagent vendors, while established markets, such as laboratories in the US and Europe, prefer to select the instrument and the reagent from the same vendor, ensuring compliance and accreditation standards.

Offering Upgrades & Add-On Analyzers & Components – In order to retain their install base, many vendors offer upgrades to existing analyzers at a very low cost to increase capabilities of existing outdated analyzers.

SUMMARY

The key challenge when building on install base is the high cost associated with transition. Even when dissatisfied, most lab managers endure outdated instruments to avoid resource-intensive issues, such as the purchase process, staff retraining, protocol standardization, and data management system reevaluation. As labs consolidate, the immunochemistry analyzer market relies on instrument replacements to generate the needed revenue. Nearly all manufacturers rely on key strategies, such as offering replacements for old clinical chemistry and immunochemistry systems or acquiring clients from other vendors. Competition is stiffening as most vendors face difficulties increasing their customer base.

The future will see CLIA as a growing analyzer segment with tremendous focus on areas, such as infectious disease testing, and autoimmune and oncology segments. The market is moving toward multiparametric assays, and many companies are exploring the use of multiplex technologies using protein and peptide arrays for autoimmune diagnostics. ◆

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BIOGRAPHY

Divyaa Ravishankar is a Senior Industry Analyst for Frost & Sullivan's Life Sciences practice. She has diverse expertise within healthcare IT and life sciences with a focus on in vitro diagnostics. Her expertise constitutes of laboratory research and management consulting. To supplement her expertise, she also has broad-ranging industry experience in varying sectors in which she has established long-standing working relationships with leading industry participants in areas like clinical diagnostics, pharmaceuticals, and biotechnology. Ms. Ravishankar earned her Master of Science (Hons.) in Biological Sciences from Birla Institute of Technology and Science, Pilani, India. For more information on Frost & Sullivan's global Life Sciences practice and offerings, please email jennifer.carson@frost.com or visit www.frost.com.

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MARKET ANALYSIS

Unprecedented Uptake of Sovaldi & Tecfidera Paves the Way for New Optimism in Pharma

By: Joshua Owide, GlobalData's Director of Healthcare Industry Dynamics

INTRODUCTION

Pharmaceutical companies are under more scrutiny than ever regarding the quality of therapies and, concurrently, the return on investment they deliver to shareholders. To this end, many large cap pharma companies continue to reassemble their businesses in favor of greater transparency and operating efficiency.

We have seen two firms, Gilead Sciences and Biogen Idec, both typically seen as being in the biotech mold, achieve astronomical success with their respective launches of Sovaldi (sofosbuvir) and Tecfidera (dimethyl fumarate) in 2013, with both new therapies recording uptake at a level never before seen in the industry.

A successful drug launch is pivotal in the corporate evolution of most innovative drug companies, allowing them to sustain growth momentum, or, as is more commonplace in the age of the blockbuster patent expiration, replenish existing revenues at risk from lower-cost equivalents. As witnessed with recent biotech success stories Alexion and Regeneron, a new drug launch also has the capacity to redefine a company, and, in the case of Gilead's and Biogen's latest offerings, successful innovation is rapidly propelling these firms to the realms of Big Pharma.

Indeed, while both Sovaldi and Tecfidera were hotly anticipated by investors, interim sales have exceeded expectation, driving their valuations up even further. In what will be the first full year on the market for Sovaldi and Tecfidera, analyst consensus had initially predicted sales of $4.5 billion and $2.4 billion in 2014, respectively, but both are on course to shatter these already optimistic expectations.

GILEAD & BIOGEN PROVE THAT EITHER EFFICACY OR SAFETY CAN WIN THE BATTLE

Against a backdrop of megamerger activity, Gilead and Biogen have been able to revel in their success in relative silence. The numbers they are posting are anything but quiet however, asking the question: what is driving this unprecedented growth?

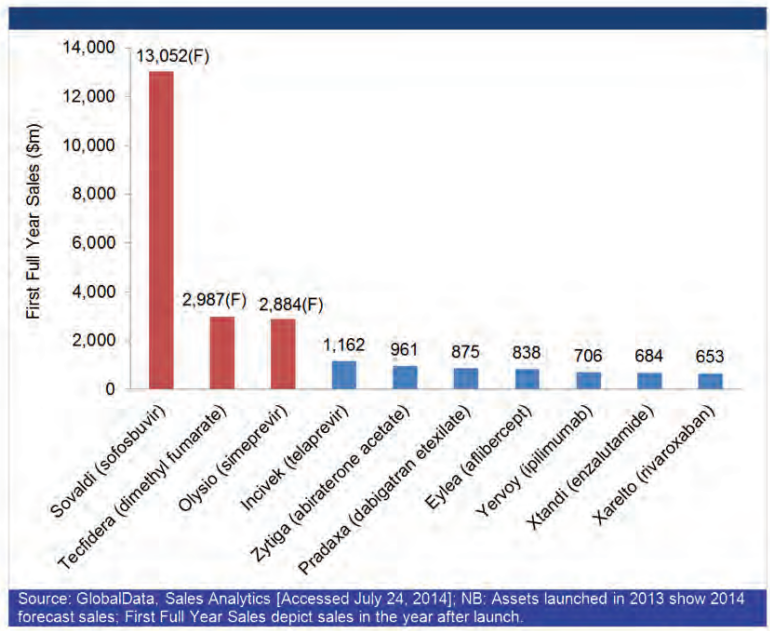
Gilead's total revenues for the first 6 months of 2014 were up over 110% year-on-year, from $5.3 billion in 1H 2013 to $11.5 billion in 1H 2014, due principally to the record uptake of Sovaldi since its approval toward the end of 2013. While Gilead's revenues have increased substantially, its major operating cost lines have risen disproportionately slowly, leading to significant operating margin gains. The returns from a high-value asset such as Sovaldi, which is relatively inexpensive to make, are clear from Gilead's Cost of Goods Sold (COGS) margin, which has been cut in half. Its Selling, General, and Administrative Expenses (SG&A) margin has also decreased significantly, despite increased commercial costs associated with the roll-out of Sovaldi. Having already been a clear leader on this metric across the sector in 2013, Gilead is on course to post a record operating margin of more than 60% in 2014, well above the 25.4% Big Pharma average.

Biogen also paints an impressive picture, albeit less prominently than Gilead, though its lead growth driver Tecfidera was launched at the end of Q1 2013, markedly earlier than Sovaldi. Nonetheless, in 1H 2014, Biogen reported total revenue growth of 45%, up from $3.1 billion in 1H 2013 to $4.6 billion in 1H 2014. Again, Biogen's growth can be attributed almost entirely to the success of Tecfidera. Like Gilead, Biogen boasts some of the best margins in the sector, and this looks set to continue further through 2014, with its Q2 2014 operating margin surpassing the 40% mark. Biogen's COGS, SG&A, and Research and Development (R&D) margins have all declined, despite rising in absolute dollar terms. This is again indicative of their success with Tecfidera, already a blockbuster small molecule, and, therefore, high-margin asset. This is despite the commercial costs Biogen has invested to compete with Sanofi and Novartis, both earlier arrivals in the Multiple Sclerosis (MS) market.

SOVALDI'S EFFECTIVENESS FAR OUTWEIGHS ITS COST

Not even the most optimistic analyst would have predicted Sovaldi's success, and, having already generated sales of $5.8 billion in the first half of 2014 alone, Gilead's Hepatitis C Virus (HCV) franchise could be on course to exceed $13 billion in first full- year sales, based on its current growth trajectory.

FIGURE 1



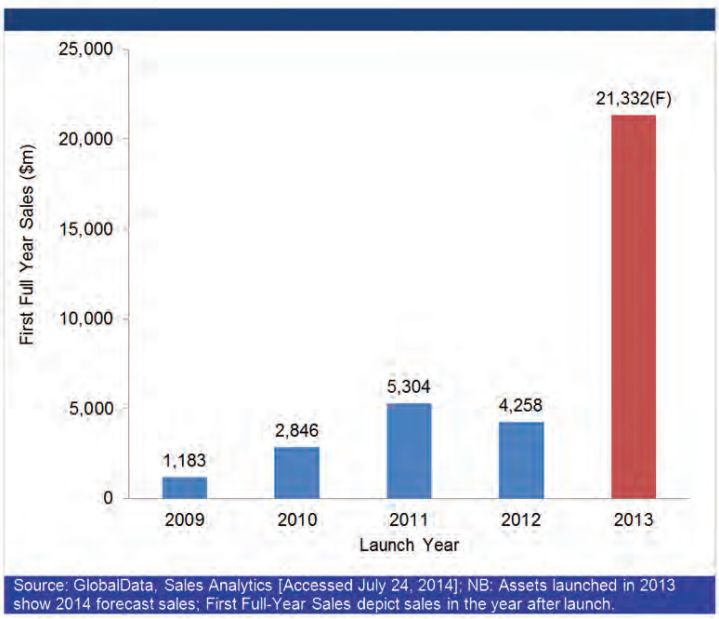
Top Ten Launches by First Full-Year Sales ($M)

GlobalData believes Sovaldi's approval in December 2013 has resulted in a surge in HCV treatment rates, driven by the unprecedented efficacy and tolerability of Sovaldi-based regimens. Sovaldi represents the greatest leap forward in HCV therapy since the arrival of the first NS3/4A protease inhibitors, Merck's Victrelis (boceprevir), and Vertex's Incivek (telaprevir), in 2011. While their improved efficacy compared with the prior standard of care initially drove their uptake, these drugs required multiple pills per day, a prolonged treatment duration, and co-administration with ribavirin and peginterferon, which are associated with debilitating side effects. The glaring weaknesses of Incivek and Victrelis created an opportunity for firms wishing to enter the HCV marketplace, as many patients decided to forego treatment in order to await better options.

Hoping to exploit this gaping void in the HCV treatment landscape, Gilead paid an 89% premium to purchase Pharmasset for $11 billion in 2011, a deal which included the rights to Sovaldi (then known as PSI-7977). At the time, the move was criticized by many industry experts for its high valuation, which was unprecedented for a company with no marketed assets, but the deal now appears to be one of the most shrewd and lucrative to be executed in the industry for some time. It has rapidly propelled Gilead to global leader in HCV treatment, complementing its dominance of the HIV market.

Despite its high cost, stakeholders have clearly accepted that the medical benefit bestowed on HCV patients by a course of treatment with Sovaldi far outweighs the financial burden, and this is validated by its uptake since approval. Indeed, Dr John C. Martin, Gilead's CEO, stated in the

FIGURE 2



First Full-Year Sales ($M) of Major Product Launches by Year Through 2009-2013

company's Q2 report that more than 80,000 patients across the US and Europe have been treated with Sovaldi, indicative not only of its clinical benefits, but also the efforts of Gilead to ensure rapid access to its cutting-edge treatment. GlobalData estimates global HCV prevalence to be more than 110 million, with the majority of cases being in China. In stark contrast, the treated population is currently estimated to be less than half a million, though the arrival of Sovaldi will have had a substantial impact on that number in the short time it has been approved.

Sovaldi's unparalleled success will be strengthened by the arrival of a fixed-dose combination of sofosbuvir with ledipasvir, an investigational NS5A inhibitor. This combination, which will be marketed under the brand name Harvoni in the US, was approved by the Food and Drug Administration (FDA) on 10 October 2014. Harvoni becomes the first interferon-free therapy for genotype 1 (GT1) patients, and its single pill, once-daily dosing offers increased convenience for patients. According to experts interviewed by GlobalData, Harvoni will be the most critical component of Gilead's HCV franchise over the next 2 to 3 years. Indeed, Gilead executives have indicated they are already beginning to see signs of patient warehousing in anticipation of Harvoni's arrival. Even as emerging competition from AbbVie, Bristol Myers-Squibb, and Merck & Co. threatens Gilead's dominance of the marketplace, GlobalData believes the paradigm shift toward simpler, more convenient therapy options will allow Gilead to remain the dominant player in the HCV market by leveraging regimens comprising its prized compound, sofosbuvir.

TECFIDERA'S ADVERSE EVENTS PROFILE ELEVATES BIOGEN TO MS MARKET LEADER

Tecfidera has also shown staggering early sales growth. Through the first two quarters of 2014, Biogen's flagship MS drug has generated sales of $1.2 billion and is on course to generate just over $3 billion in 2014, figures that would have made it the fastest drug launch in history, were it not for the concurrent launch of Sovaldi in HCV. Tecfidera, an agent which reduces inflammation and promotes neuroprotection through its activation of the Nrf2 transcriptional pathway, has beaten expectations not only in terms of sales growth, but also in proving that, in some cases, first-to-market status does not guarantee insulation from later competing therapies. While Tecfidera was only approved in the US in March 2013, becoming the third oral drug for relapse remitting MS, its entrance has been remarkable.

To this end, Tecfidera's surge in sales is notable particularly given that it is the third orally active MS drug to reach the market behind Novartis's Gilenya (fingolimod) and Sanofi's Aubagio (teriflunomide), and even more notable given that while Gilenya and Aubagio are administered once per day, Tecfidera boasts a less-desirable twice-daily regimen. The fundamental driver underlining Biogen's ability to overcome these barriers with such great effect is down to Tecfidera's safety profile, where the most commonly reported

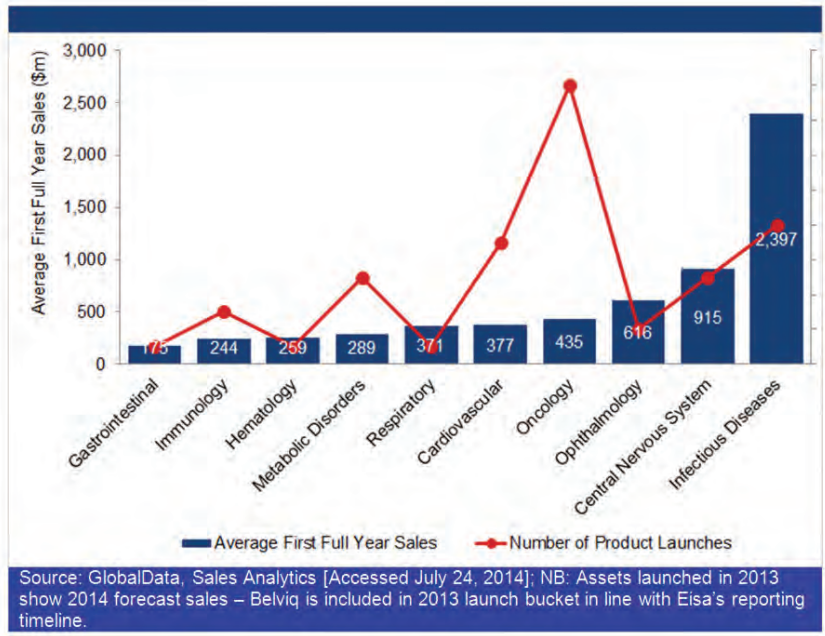
side effects are flushing and gastrointestinal symptoms.

In contrast, the first-to-market Gilenya, which is itself one of the fastest drug launches in recent years, is associated with a risk of serious adverse cardiac reactions, including bradyarrhythmia and atrioventricular blockage. Aubagio carries a black box warning from the FDA, highlighting the risk of severe liver complications associated with its use, and patients initiating treatment with Sanofi's MS treatment are required to have their liver function monitored. While Tecfidera may not be the gold-standard in terms of its efficacy, its safety profile confers huge advantages in a patient population extremely sensitive to adverse events.

DRUG LAUNCH RETROSPECTIVE: COMPARATIVE ANALYSIS

By all definitions, Sovaldi has shattered existing records and, including the arrival of Harvoni, is on course to generate first full-year sales well over the $11 billion Gilead initially paid to acquire sofosbuvir. To put this further into perspective, Tecfidera would have become the biggest launch in history with sales of $3 billion predicted in its first full year on the market. A third new launch from 2013, J&J's Olysio, would also have shattered previous records for sales uptake, held by another HCV therapy, Incivek. Interestingly, three of the first four most successful drug launches ever have been in the HCV market, highlighting the extent of the unmet need in this segment. The other biggest launches fell within oncology, cardiovascular, and ophthalmology.

FIGURE 3



Average First Full-Year Sales of Major New Drug Launches By Therapeutic Area

Figure 2 illustrates first full-year sales of 40 major product launches that took place between 2009 and 2013. Clearly, the magnitude of the value added from new launches in 2013, as determined by projected full-year sales in 2014, far exceeds that of any previous year, and this is due not only to the unrivalled success from new HCV therapies Sovaldi and Olysio, but from successful launches across other disease markets as well, including Central Nervous System (CNS) (Tecfidera/Abilify Maintena) and oncology (Imbruvica/Pomalyst/Kadcyla).

In short, there has clearly been a paradigm shift in 2013, and we may finally be seeing the kind of R&D progression the industry has been crying out for, which has in turn converted into significant financial gains for those companies leading the way.

An interesting picture is also painted when we look at the biggest launches in recent years by therapeutic area (TA). Even with the second highest number of high-value launches, 8 in total, average first full-year sales in the infectious diseases space still far outstrips that of any other TA, with major CNS launches coming in a distant second in terms of average first full-year sales. The unmet needs in infectious diseases, combined with the finite lifespan of a number of these new therapies, notably due to the leaps forward in terms of innovation in the HCV market, have forced companies into maximizing returns from new launches.

Interestingly, despite the impact of generics on several key franchises, a number of valuable assets have continued to emerge in the CNS segment, demonstrating

impressive uptake levels. Another mature segment, cardiovascular, has also seen multiple strong launches. Oncology represents by far the most prolific TA in terms of the number of high-value launches, 16 in total, with average first full-year sales of oncology assets exceeding $400 million, again highlighting the unmet needs that exist. Oncology has been the focal point of R&D activities for many major pharma companies over the past decade, and this effort and investment has clearly been justified. In contrast, major launches in increasingly crowded immunology and metabolic disorder markets have been relatively slow, despite the strategic importance of these disease segments.

DISTINCT FACTORS INFLUENCING LAUNCH STRATEGIES

Recent launch trends suggest that pharma firms are fulfilling their promises by making significant progress in disease areas in which unmet needs remain high, and therefore, physicians and patients are more receptive to new, and most importantly, better, treatment options. While not mutually exclusive from this migration toward untapped markets, current launch strategies are vastly different from those previously used by Big Pharma in order to penetrate primary care markets with typically high prescribing rates. The success stories of the past 12 months or so denote a dynamic shift in commercialization strategy that has contributed to key successes, including those of Sovaldi and Tecfidera.

Undoubtedly, while we have seen massive strides in terms of efficacy and safety across a number of disease areas, pricing has been a key driver for this recent growth. Indeed, in the US market - the world's largest for drug manufacturers - Sovaldi was launched at a retail price of $84,000 per year and Tecfidera at $54,900. Despite pricing being an impediment toward attaining reimbursement, the commercial success of these therapies challenges the notion that higher priced drugs may not achieve sustained commercialization success. This is apparent in this instance, as the clinical benefits bestowed by these new therapies far exceed those that have gone before. However, while Sovaldi and Tecfidera have both enjoyed great commercial success in the short time since their respective launches, it is imperative to note that both Gilead and Biogen are facing increased pressures from payers, as more and more patients demand access to these best-in-class therapies. ◆

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BIOGRAPHY

Joshua Owide is GlobalData's Director of Healthcare Industry Dynamics, overseeing the production and development of numerous industry reports and analytics tools. His expert comments on the pharmaceutical industry have been cited by top publications worldwide, including the Financial Times and the Boston Globe. Prior to joining GlobalData, Mr. Owide was a senior pharmaceutical company analyst at Datamonitor, covering large-cap companies from the US, EU, and Japan. Before this, he undertook a bioinformatics studentship at the Ludwig Institute for Cancer Research, where he analyzed a genome-wide RNAi screen, identifying the importance of specific proteins in cell morphology. Mr. Owide earned his BS in Physiology from the University of Leeds.
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ABUSE-DETERRENT MARKET

What's in the Pipeline? Abuse-Deterrent Products

By: Tugrul Kararli, PhD, MBA, Kurt Sedo, and Josef Bossart, PhD

INTRODUCTION

Reducing misuse and abuse is one of the more interesting applications of formulation and drug delivery technology to real-world challenges. Problems related to the abuse of central nervous system-acting products are well known and yet remain a significant challenge for the medical community, families, as well as law enforcement and the courts.

Serious attempts to reduce the abuse of prescription drugs, most notably opioids, have been ongoing for more than a decade with some significant advances realized. Yet there remains much to be done.

From the perspective of the pharmaceutical industry, there are at least two approaches that promise at least some relief for this problem. The ideal solution from the perspective of many is the development of increasingly well-tolerated novel agents capable of treating indications such as pain, anxiety, depression, and hyperactivity, without any abuse liability. This "holy grail" solution is yet to be realized. The fallback approach has been to look to the pharmaceutical sciences for ways to reduce the abuse and misuse of agents that have a long history of efficacy and safety when used as prescribed. We will use the term "abuse-deterrent" to describe these desired features and benefits. This expression encompasses a wide variety of actions all related to reducing the non-prescribed use of a product, in terms of intent or procedure.

We decided it would be interesting to interrogate the PharmaCircle database and see what successes have been achieved with respect to abuse-deterrent formulations in terms of approved and pipeline products. We also took a more general look at the formulation approaches being applied to abuse deterrence.

Some background; this short review includes only products and technologies that have reached the stage of clinical development. Research and preclinical products, and their associated technologies, have not been included. For the purpose of this article, some products that have not reported results or activity for 4 or more years have been labeled as inactive, even though the sponsoring companies may still list them in their product pipelines.

THE ABUSE-DETERRENT PRODUCT PIPELINE – APPROVED & CLINICAL-STAGE PRODUCTS

Querying the PharmaCircle Products & Pipeline database with the terms "abuse- deterrent" and "abuse-resistant" returned a total of 129 products as being at some stage of announced development, marketed through clinical to preclinical and research. Limiting this list to products that are active and either approved, filed with regulatory bodies, or in clinical development reduces the number to a much more manageable list of 53 products. This excludes an additional 10 clinical products that have been formally discontinued or have provided such limited updates to suggest they are in effect discontinued. This list is current as of mid-September 2014.

The distribution of these products

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by type and stage are summarized in Table 1. What is a little bit surprising is the number of generic abuse-deterrent products (19) that have received tentative approval or have their applications under review. The four approved products being targeted by these generics are Shire's Vyvanse, Endo's Opana ER Crush-Resistant, Acura's Oxecta, and Purdue Pharma's reformulated OxyContin.

If we take out the generics, there remain a total of nine products that are Marketed, Approved, or in Registration. A total of seven products have been approved with a direct or implied abuse-deterrent or abuse-resistant claim. These products are listed in Table 2.

TABLE 1

Type	Total	Stage				
		Approved / Marketed	Registration / Tentative Approval	Phase III	Phase II	Phase I or Bioequivalence
New Combination	3	2				1
New Formulation	25	3	2	4	1	15
New Molecular Entity	5	1		1	1	2
OTC	1	1				
Generic	19		19			
All	53	7	21	5	2	18

Active Pipeline & Approved Products by Type & Stage (All)

FORMULATION STRATEGIES

Four general formulation strategies are currently employed to reduce or eliminate the potential for the abuse and misuse of psychoactive pharmaceuticals. These are:

Type 1- Formulations that physically limit the ability of products to be mechanically or chemically modified for the purpose of injection, insufflation, or rapid oral absorption.

Type 2 - Formulations that include an antagonist or aversive agent that blocks the desired properties of the product when abused, or makes it unpalatable or toxic when repurposed for administration by injection or insufflation.

Type 3 - Modified formulation-release products that limit the possibility of rapid absorption of the active. This can be achieved through some sort of molecular modification (prodrug) or sustained-release engineering not easily overcome using mechanical, physical, or kitchen chemistry procedures.

Type 4 - The fourth approach combines two or more of the aforementioned approaches, most commonly some sort of modified-release combined with physical/chemical- resistance features. The subcategories are:

Type 4a: Type 1 & Type 2

Type 4b: Type 1 & Type 3

Type 4c: Type 2 & Type 3

Type 4d: Type 1 & Type 2 & Type 3

An analysis of the approved and clinical development pipeline as a function of technology approach is presented in Table 3. (Note: generic products are not included in this analysis.) Some assumptions were made regarding the exact abuse strategies of certain pipeline products of which there was limited public information. A little bit of explanation is in order to address what appear to be inconsistencies with the figures in Table 3.

There are no "pure" Type 2 products in development as best as can be determined. The Type 2 strategy, incorporating an antagonist or aversive agent, is only seen in combination with some sort of modified/extended-release technology. Of course, extended-release, Type 3 was the original abuse-deterrent strategy until it was realized that these products could be crushed, overcoming the modified-release characteristics of the products and negating any abuse-prevention benefits. One immediate-release development program using an aversive agent, niacin, as opposed to an antagonist, was terminated after an

TABLE 2

Product	Active(s)	Company	Indication	Abuse Reduction Strategy	Approved	Dosage Form	First Approval	Current Status
Vyvanse	Lisdexamfetamine	Shire	ADHD	Prodrug, ER	Global	Oral, Capsule	2007 (US)	Marketed
Embeda	Morphine, Naltrexone	Pfizer	Pain	Antagonist, ER	US	Oral	2009 (US)	Off Market
Targin	Oxycodone, Naloxone	Purdue Pharma	Pain	Antagonist, ER	US, EU, Other	Oral, Tablet	2009 (EU)	Marketed
OxyContin (Abuse Resistant)	Oxycodone	Purdue Pharma	Pain	Physical, ER	US, Canada	Oral, Tablet	2010 (US)	Marketed
Opana ER (Crush Resistant)	Oxymorphone	Endo	Pain	Physical, ER	US	Oral Tablet	2011 (US)	Marketed
Oxecta	Oxycodone	Acura	Pain	Physical	US	Oral, Tablet	2011 (US)	Marketed
Nexafed	Pseudoephedrine	Acura	Allergies	Physical	US	Oral, Tablet	2012 (US)	OTC

Global - includes, US, EU, Japan, and various other markets

Approved Abuse-Deterrent/Resistant Formulations

FDA Advisory Panel suggested this approach introduced safety issues.

At this point, there are no approved or clinical stage products identified as being Type 4d, incorporating all three abuse-deterrent strategies, although there appear to be a couple in the preclinical stage.

The sharp-eyed reader will note that there is a one-product discrepancy between Tables 1 and 3. This is an outlier product, a transdermal formulation of fentanyl that makes claim to reducing the potential for abuse by exhausting the fentanyl through efficient delivery and leaving a negligible amount of active in the patch after the prescribed 3-day dosing. This makes the "used" patches less attractive for "smoking" or extraction using kitchen chemistry techniques.

REGULATORY CONSIDERATIONS & GENERIC FORMULATIONS

It's remarkable to see how many 505(j) products are lined up at the US FDA waiting to capture the generic opportunity represented by currently approved abuse-deterrent products. The leading product from a units and revenue perspective, Purdue Pharma's OxyContin, is likely to be subject to generics as soon as October 2014 on the basis of a settlement with Actavis. This agreement limits the number of units that Actavis will be permitted to distribute after the FDA approves their generic.

The whole question of the regulatory requirements necessary to secure a label claim of abuse-resistant or deterrent is still not clear. Purdue managed to secure language in its US product labeling for OxyContin that reviewed the abuse-deterrence studies conducted for the product. This contrasts with the new formulation of Opana ER from Endo that is identified as crush-resistant, but carries no abuse-resistant or deterrent information in its package insert. Clearly, there is a minimal amount of data that needs to be provided to secure abuse-resistant and/or deterrent language in the product labeling. Exactly what this might be is not obvious to the casual observer.

This issue of exactly what performance targets and studies are required to capture an abuse-deterrent claim will have an impact on the approval and claims of future products, including generics. Regardless, products that include any sort of abuse-resistant or deterrent features are a net benefit to the public whether or not they receive the corresponding claims from the regulatory bodies.

ABUSE-DETERRENT FORMULATIONS – THE FUTURE

Although still in relative infancy, the whole area of abuse-deterring formulations is likely to grow up very quickly, and likely without any privilege. It's not unlike the mid-1990s, where sustained-release formulations quickly became a standard part of every company's formulation toolbox. It was at this point no longer

TABLE 3

	Total	Approved / Marketed	Phase I-III
Type 1	9	2	7
Type 2			
Type 3	5	1	4
Type 4 (All)	19	2	17
Type 4a	*1*		*1*
Type 4b	*14*	*1*	*13*
Type 4c	*4*	*1*	*3*
Type 4d	*0*	*0*	*0*
Totals	33	5	28

Clinical Stage & Approved Products by Abuse-Deterrent Strategy

necessary to secure external expertise to create a long-acting formulation of a proprietary molecule. This point was emphasized by the parallel emergence of sustained-release generic products in the mid to late 1990s.

It may be that the golden age of abuse-deterrent formulation technologies has already passed before it has had a chance to flourish. That's not to suggest abuse-resistant and deterrent formulations in the pipeline won't be approved and provide important therapeutic benefits. Rather, the opportunity to profit through market share and pricing flexibility as a result of any significant technology or regulatory exclusivity will be limited. The actives, for the most part multi-source opioids and stimulants, provide no real patent exclusivity. And with the development of multiple abuse-deterrent formulation strategies, there appears to be little potential for any true exclusivity from a technology perspective. It is difficult to imagine that any company will be able to capture the type of profit with abuse-deterrent products or technologies as has been enjoyed by Purdue Pharma and their reformulated OxyContin.

It's not hard to predict that we will see more and more abuse-resistant and deterrent formulations of opioids and stimulants hit the market in the near future, followed by their generic equivalents. The real money to be made will be found in those products that change the whole paradigm – novel molecules that retain desired analgesic or psychoactive properties but without any inherent addictive or abuse-reinforcing properties. It's possible these molecules will be discovered, but it does not seem it will be anytime soon. In the meantime, patients, physicians, and society as a whole will need to look to the ingenuity of pharmaceutical science professionals to provide meaningful near-term solutions. ◆

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BIOGRAPHIES

Dr. Josef Bossart is Managing Director of The Pharmanumbers Group, a boutique research and consulting group providing the biopharmaceutical industry with analysis and insights that improve business outcomes. He has more than 3 decades of experience in the biopharmaceutical sector, including senior sales, marketing, business development, and management positions within Big Pharma, Specialty Pharma, and Emerging Pharma companies. He earned his PhD in Medicinal Chemistry from The Ohio State University, College of Pharmacy.

Dr. Tugrul T. Kararli earned his PhD in Pharmacology from the University of Florida and his MBA from DePaul University. Dr. Kararli worked at Searle/Pharmacia for 18 years and held various positions and responsibilities within the Pharmaceutical Sciences department, participating in pharmaceutics, product development, and drug delivery activities. As the Chairman of the Global Drug Delivery Technology Team at Pharmacia, he was responsible for identifying, planning, and executing the drug delivery technology strategies for marketed and development products. Dr. Kararli has authored numerous articles on various aspects of pharmaceutics and drug delivery and holds more than a dozen US and international patents. Currently, he is the Founder and President of PharmaCircle LLC, a knowledge management service company in the drug delivery and pharmaceutical/biotechnology fields.

Mr. Kurt Sedo is Vice President of Operations at PharmaCircle LLC. He earned his BS in Chemistry and Mathematics from the University of Wisconsin Stevens Point. Prior to joining PharmaCircle in 2003, he held various R&D Scientist positions within Searle/Pharmacia's Pharmaceutical Sciences Department in Analytical Development and Drug Delivery.

NANOTECHNOLOGY MARKET

Nanotechnology Markets in Healthcare & Medicine

By: Kevin James, Jackson Highsmith, and Paul Evers

INTRODUCTION

In the field of nanomedicine research, the US accounts for one-third of all publications and half of patent filings. A comparison between Europe as a whole and the US shows that while Europe is at the forefront of research, the US leads in the number of patent filings. The strong patenting activity of US scientists and companies indicates a more advanced commercialization status.

According to BCC Research (www.bccresearch.com), the global market for nanoparticles in the life sciences is estimated at over $29.6 billion for 2014. This market is forecast to grow to more than $79.8 billion by 2019, to register a healthy compound annual growth rate (CAGR) of 22%. The biggest increase will come in the area of drug delivery systems.

As products complete clinical trials and gain US FDA market approval, the revenues from these products will grow at 23%. Basic biotechnology research revenues will increase due to the quest to find more nanoparticle applications, as more drugs become successfully delivered by these carrier systems. Drug development and formulation will show steady sustained growth at 20.7%. Nanoparticles for use in diagnostic imaging will continue to show healthy growth at 20.1%. This will result from the need to develop more definitive nanoparticle markets for disease diagnosis.

APPLICATIONS IN MEDICINE

Nanomedicine includes several distinct application areas, including drug delivery, drugs and therapies, in vivo imaging, in vitro diagnostics, biomaterials, and active implants. In these fields, nanomedicine has seen increased research activity during the past decade. Currently, nanomedicine accounts for about 5% of nanotechnology research publications worldwide.

The dominant research field in nanomedicine is drug delivery, contributing 76% of the scientific publications, followed by in vitro diagnostics with a contribution of 11%. The countries of the European Union account for 36% of all nanomedicine publications worldwide, compared to the US with a contribution of 32% and Asia with 18%. Research efforts in nanomedicine are driven by significant governmental nanotechnology funding programs. Three countries - the US, Germany, and Japan - have given clear commitments to nanomedicine by establishing focused nanomedicine research programs.

However, when one looks at the commercialization of this field, the US emerges as having about half of the world market for nanomedicine products. US companies manufacture 45% to 50% of marketed nanomedicine products, while European companies have a 35% share. Product pipelines suggest that this gap will widen, reflecting mainly the weak position of European nanomedicine companies in the drug delivery sector, where they represent less than one-quarter of all the companies in this field, compared to 60% for US companies.

Of the approximately 200 companies identified as active in nanomedicine worldwide, some three-quarters are start-ups and SMEs focusing on the development of nanotechnology-enhanced pharmaceuticals and medical devices. Another 40-plus major pharmaceutical and medical device corporations have nanomedicine products. Individual

nanomedicine application areas are defined below.

Drug Delivery: Nanoscale particles/molecules are developed to improve the bioavailability and pharmacokinetics of therapeutics. Examples are liposomes (and virosomes), polymer nanoparticles, nanosuspensions, and polymer therapeutics. Drugs in which a protein is combined with a polymer nanoparticle or chemical nanostructure to improve its pharmacokinetic properties would qualify as nano-enhanced drug delivery.

Drugs and Therapy: Nanoscale particles/molecules used in the treatment of diseases that according to their structure have unique medical effects and as such differ from traditional small-molecule drugs; examples include drugs based on fullerenes or dendrimers.

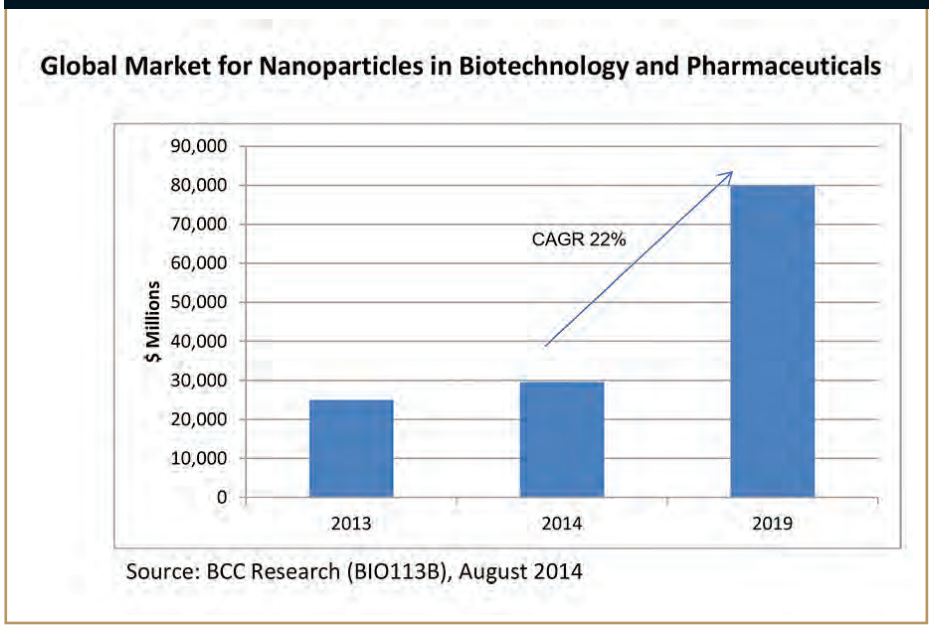
In Vivo Imaging: Nanoparticle contrast agents, particularly for MRI and ultrasound, provide improved contrast and favorable biodistribution; for example, superparamagnetic iron oxide nanoparticles for use as MRI contrast agents.

In Vitro Diagnostics: Novel sensor concepts are based on nanotubes, nanowires, cantilevers, or atomic force microscopy applied to diagnostic devices/sensors. The aim of these sensors is to improve sensitivity, reduce production costs, or measure novel analytes (eg, Alzheimer plaques) that could not otherwise be detected reliably.

Biomaterials: These include self-assembling particles or other types of nanomaterial that improve the mechanical properties and biocompatibility of biomaterials for medical implants; examples include nanocomposite materials used as dental fillers and nanohydroxyapatite used for implant coatings and bone substitutes.

Active Implants: Particles/materials improve electrode surfaces and biocompatibility of device housings. Examples include magnetic nanoparticle-based coatings that make medical implants safe for use with MRI imaging.

FIGURE 1



NANOMEDICINE MARKET

Nano-enabled medical products began appearing on the market over a decade ago and some have become best-sellers in their therapeutic categories. The main areas in which nanomedical products have made an impact are cancer, CNS diseases, cardiovascular disease, and infection control.

At present, cancer is one of the largest therapeutic areas in which nano-enabled products have made major contributions; these include Abraxane, Depocyt, Oncospar, Doxil, and Neulasta. Cancer is a prime focus for nanopharmaceutical R&D, and companies with clinical-stage developments in this field include Celgene, Access, Camurus, and Cytimmune.

Treatments for CNS disorders including Alzheimer's disease and stroke also feature prominently in nanotherapeutic research, seeking to build on achievements already posted by products such as Tysabri, Copazone, and Diprivan. According to BCC Research, this is a field hungry for successful therapeutic advances and annual growth from existing and advanced pipeline products is expected to reach 16% over the next 5 years.

Autoimmune-related inflammatory disease has an increasingly high profile, and nanotechnology has contributed to the success of products such as Remicade and Humira. Enzon is among companies vigorously pursuing new product development in this field, and new products are expected to add to the continuing market penetration of existing therapies, contributing to annual growth rates around 15%.

In addition, nanotechnology has contributed to a wide variety of anti-infective products, from PEGylated interferons used in viral disease to nanocrystalline silver used topically in wound infections. Biosanté and NanoBio are among companies actively involved in this field.

The US market is by far the largest in the global nanomedicine market, and is set to continue to dominate the world marketplace, but other national markets are expected to increase their shares over the next 5 years.

COMMERCIALIZED & FUTURE MARKETS

Apart from targeted cancer chemotherapy, nanotechnology is being used more widely in creating a new generation of drug delivery systems. A key factor in its adoption is that nanoscale particles have a greater surface-to-volume ratio than macroparticles. Thus, a drug-bearing nanoparticle can release a drug more quickly and more abundantly than larger particles. This is helpful when the drug poses problems with solubility and absorption, as is the case with a considerable proportion of new drugs.

Already on the market in the US and elsewhere are wound dressings that exploit the antimicrobial properties of nanocrystalline silver. Ionic silver is a powerful antibacterial, effective even against problem organisms like MRSA, and nanotechnology offers a way to optimize its effect when incorporated in a wound dressing.

While current medical nanotech applications focus on single nanoparticles and simple structures, future possibilities will involve combing such single elements into structures that can carry out more complex tasks than, for example, releasing drug payloads. Thus, nanostructures may be developed that can insert probes into elected cells and inject DNA or protein to correct genetic abnormalities.

Another possibility is to design nanostructures that can foster and direct the regeneration of nerve cells; these would be used in the treatment of stroke and trauma victims, and possibly for the restoration of lost function in Alzheimer's disease. However, a sober estimate of timing would warn us not to expect these developments to become reality until 10 to 20 years from now.

The nanomedicine market is in early growth. While nano-enhanced drug delivery products are already a commercial reality, more advanced nanotech-based medical devices are still in development, although some are at the clinical testing stage.

Most of the money being spent on the wider field of nanotechnology R&D comes from government and established corporations. In the nanomedicine field, pharmaceutical and specialist companies are at the forefront of research into the medical applications of nanotechnology.

To date, drug delivery has been the main near-term opportunity for medical nanotechnology. This market has an estimated value of $15.8 billion for 2014 and is forecast to grow to $44.5 billion by 2019, to register a significant CAGR of 23%. The drug development category, the second fastest-growing opportunity, was projected at nearly $12.6 billion for 2014 and is expected to increase to $32.2 billion by 2019 at a 20.7% CAGR. ◆

This article is based on the following market analysis reports published by BCC Research: **Nanoparticles in Biotechnology, Drug Development & Drug Delivery (BIO113B)** by Jackson Highsmith, and **Nanotechnology in Medical Applications: The Global Market (HLC069B)** by Paul Evers. For more information, visit www.bccresearch.com.

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BIOGRAPHIES

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Paul Evers has been involved in analyzing pharmaceutical and medical markets for 20 years. His expertise includes nanotechnology in medical applications, generic drugs, pharmaceutical regulatory issues, and trends in major therapeutic categories.

GLOBAL DELIVERY MARKET

Advanced Drug Delivery Systems: mAb, RNAi, & Breaking the Blood-Brain Barrier

By: Kevin James, Shalini Shahani Dewan, MS, Kim Lawson, and Usha Nagavarapu

INTRODUCTION

A significant challenge for both drug and drug delivery companies is to produce existing and emerging drug technologies in a manner that improves drug administration for the patients. Advantages of advanced drug delivery systems over traditional systems are more convenient routes of administration, greater efficacy and duration of drug activity, decreased dosing frequency, improved targeting, as well as reductions in toxic metabolites. New and emerging delivery systems - including rectal, vaginal, lymphatic implanted, or transdermal applications - for traditional pharmaceuticals are more effective and cause fewer side effects if delivered in forms that allow a continuous or extended release of the drug. These factors, along with new developments in targeted drug delivery, are aiding localized treatment of diseases with minimized harm to healthy surrounding cells. Consequently, these developments are driving significant growth in the global drug delivery markets.

Indeed, research-based pharmaceutical companies are continuously working toward the discovery and development of new drug delivery systems. This has led to mergers and profitable partnerships between pharmaceutical companies. Transdermal technologies alone have opened new doors for pharmaceutical partners seeking to create delivery mechanisms for existing molecules with no viable delivery system and existing drugs that could benefit from additional delivery systems, such as compounds that were previously unable to be delivered through the skin.

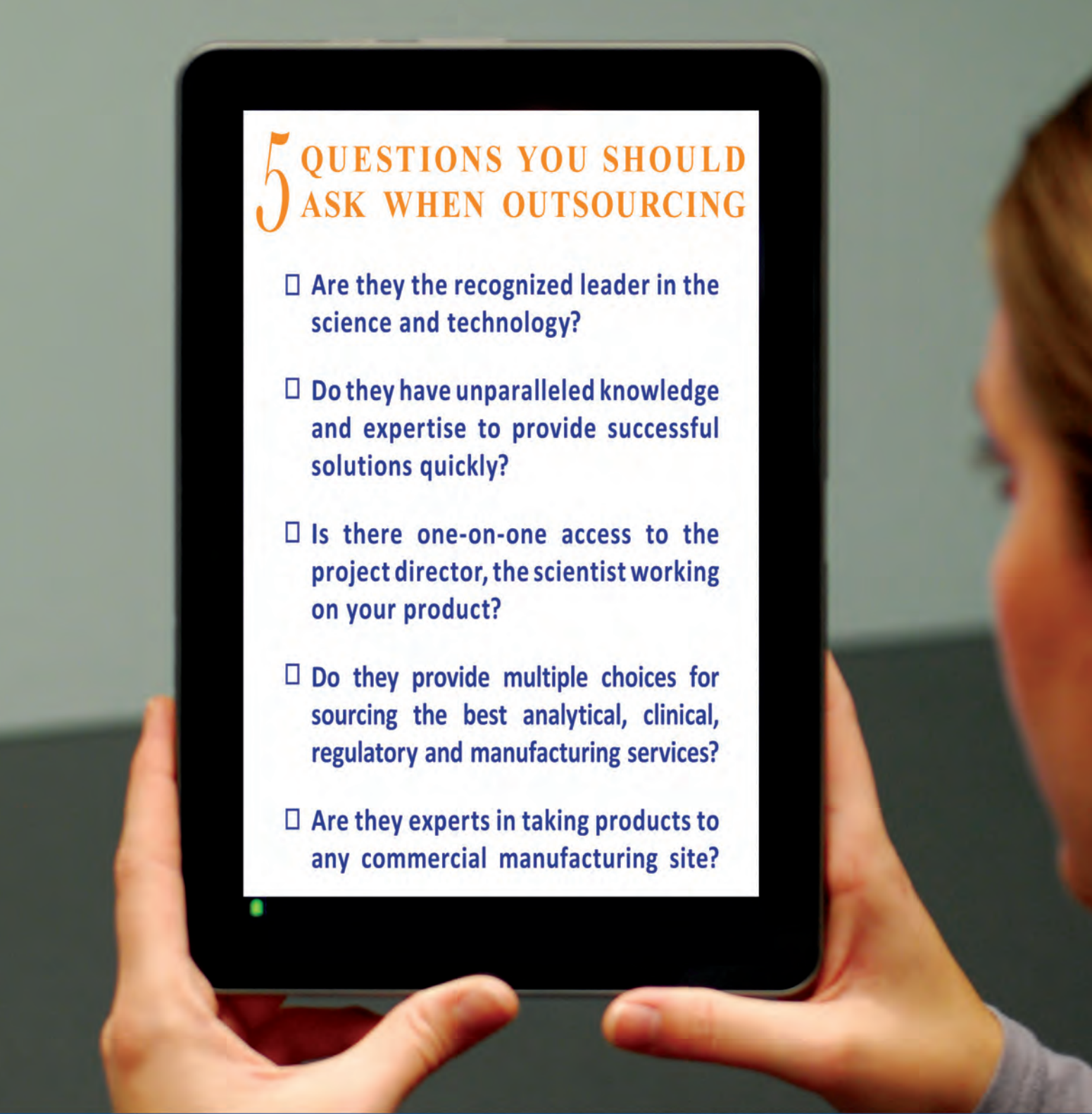
Advances in understanding human biology and diseases are opening new and exciting possibilities in the biotechnology industry. R&D spending, along with increasing competition, patent expiries, and new and emerging technologies will continue to shape growth in this market for the foreseeable future.

According to BCC Research (www.bccresearch.com), the global market for advanced drug delivery systems was valued at $151.3 billion in 2013. This market is forecasted to reach nearly $173.8 billion in 2018, registering a 5-year compound annual growth rate (CAGR) of 2.8%.

ANTIBODY DRUGS

Monoclonal antibody (mAb) drugs are a new generation of pharmaceuticals created by using modern technologies, such as genetic engineering and recombinant DNA (Deoxyribonucleic acid) technology. These protein drugs, which are produced by living cells and organisms like Escherichia coli (E.coli), yeast, and mammalian cells, have gained significant importance with the dramatic global rise of chronic conditions, such as asthma, multiple sclerosis, arthritis, and fatal diseases like cancer and cardiovascular diseases.

The mAb market has grown rapidly in the past decade. With the development of the hybridoma method of murine antibody production in 1975, the production of the first mAb was made possible by Johnson & Johnson through its product, Orthoclone OKT3 (muromonab). Orthoclone OKT3 was introduced in 1986. This highly innovative market has moved from murine to chimeric, humanized and fully human antibodies. Oncology, autoimmune, and inflammatory disorders are the traditional markets for these drug technologies.



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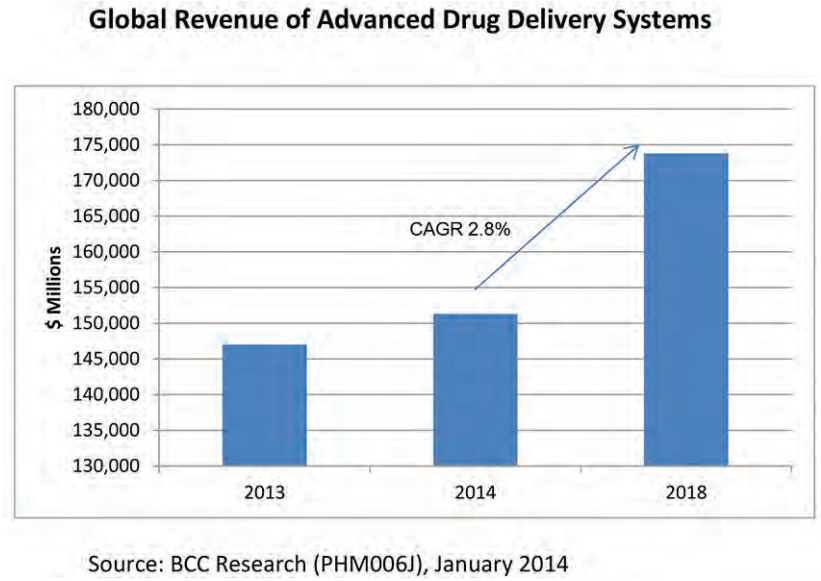
Also, the market has seen vast clinical growth globally as a result of its pivotal role in the development of effective targeted treatments to prevent these chronic and life-threatening diseases. Technological advancements are aiding in further investigation and development of novel antibody drugs, including antibody drug conjugates and bi-specific antibodies that attack the proteins present inside a cancerous cell. In addition, therapies that more effectively suppress the progression of diseases like arthritis, multiple sclerosis, hepatitis, Crohn's disease, and AIDS are moving forward.

Horizontal broadening indication strategies (approval for two or more indications) are also supporting the growth of this market. The broad spectrum mode of action is another remarkable advantage of monoclonal antibodies that makes for use of therapy in various diseases. For instance, bevacizumab (Avastin) is used to treat various cancers, including colorectal cancer, lung cancer, breast cancer, kidney, and ovarian cancer.

Recombinant DNA technology also has brought enormous change in the market with increase in different expression systems like transgenic mice, E. coli expression systems, and yeast expression systems. Research is going on using transgenic plants as a source for expression systems, thus changing the way antibodies are produced and bringing growth in the market.

The mAb market has benefited considerably from the participation of a wide range of pharmaceutical companies, including Roche, Biogen, GlaxoSmithKline, Abbvie, Johnson & Johnson, Novartis, and Merck Serono. Companies are keen on developing new technologies to produce antibodies that are more efficient with fewer side effects.

FIGURE 1



Source: BCC Research (PHM006J), January 2014

The commercial achievements earned by mAbs within the past few years are incomparable with any other drug class. As a result, the global antibody drug market is expected to reach $122.6 billion by 2019 and expected to grow at a CAGR of 12.2% through 2019. Humanized mAbs are the largest segment in terms of revenues followed by other mAb categories like human, chimeric, and murine. The use of mAbs in therapeutics such as oncology, auto immune and inflammatory diseases are expected to increase as well.

However, the mAb market scenario is expected to change with the onset of biosimilars by 2015. Rituxan/MabThera (rituximab) will be the first biosimilar mAb to emerge in the market, possibly in 2015. AcellBia from Biocad Biopharmaceutical is the first rituximab biosimilar to be approved by the Ministry of Health of the Russian Federation in May 2014. Sandoz declared the entry of GP2013, a rituximab biosimilar for the treatment of follicular lymphoma, into Phase III clinical trials.

These will be followed by the launch of eight other biosimilar molecules, one by one, by 2020, which are being investigated. The series of launches, however, may not immediately shake the branded antibody market because the complex structure of mAbs, long complex manufacturing process, and high regulatory requirements will restrict the entry of biosimilar manufacturers within the market.

RNA INTERFERENCE (RNAI)

Since the Nobel-prize-winning discovery of RNA interference (RNAi) in 1998, considerable resources have been invested to study the therapeutic potential of RNAi - an evolutionarily conserved, endogenous process for post-transcriptional regulation of gene expression - and its application in understanding human diseases. Recently, RNAi therapeutics have shown tremendous growth and have moved forward in clinical trials.

RNAi's popularity stems from its utility as a molecular biology tool, which enables the in vivo functional analysis of thousands of genes. Recent advances in the field include the design of new libraries of RNAi effectors, effective delivery systems, and read-out methods. In 2005, delivering RNAi triggers

was the biggest obstacle in creating effective RNAi-based therapies. Research into new and effective delivery methods has taken place, although there are still major issues to be addressed. The first human trials of a systemic RNAi-based therapeutic were initiated in 2007 by Quark Biotech. Understanding of the mechanism of action and intracellular pathways of micro RNA (miRNA) has developed over the years. miRNA is also now an alternative gene knockdown technology that is being applied in research, and for therapeutic and diagnostic applications.

RNAi as a mechanism to selectively degrade messenger RNA (mRNA) expression has emerged as a potential novel approach for drug target validation and the study of functional genomics. Small interfering RNA (siRNA) therapeutic have developed rapidly and already there are clinical trials ongoing or planned. Although other challenges remain, delivery strategies for siRNA become the main hurdle that must be resolved, prior to the full-scale clinical development of siRNA therapeutics.

There has been immense progress in the field of nanotechnology for drug delivery, and efforts have been dedicated to the development of nanoparticle-based RNAi delivery systems. A carefully engineered, multifunctional nanocarrier with targeting capabilities is needed to address the delivery challenges.

New developments show positive growth and confidence in RNAi therapeutics. The future of RNAi drugs depends on IPOs like the newly public RNAi therapeutics company, Dicerna. The company initiated its first Phase I study of a Dicer-substrate-based RNAi therapeutic this year. DCR-MYC targets the well-known Myc oncogene utilizing a liposomal delivery formulation (EnCore) for targeting a variety of cancers - solid and hematological malignancies.

Global RNAi therapeutics are forecast to generate sales of around $3 billion by 2018, and this market has significant potential. Therapeutic companies in this space have many challenges, the most critical being delivery. Recently, Novartis decided to leave the RNAi therapeutics development field, due to lack of suitable delivery technologies.

The RNAi market has been very dynamic and to some extent unpredictable. Some of the key companies operating in this space are Alnylam Pharmaceuticals, Isis Pharmaceuticals, Tekmira Pharmaceuticals, Calondo Pharmaceuticals, Dicerna Pharmaceuticals, Marina Biotech, Quark Pharmaceuticals, RXi Pharmaceuticals, and Silence Therapeutics. Earlier this year, Alnylam decided to acquire Merck's wholly owned subsidiary Sirna Therapeutics, with intellectual property and RNAi assets including preclinical therapeutic candidates, chemistry, siRNA-conjugates, and other delivery technologies.

The markets for RNAi are difficult to define as no RNAi-based product is in clinical development yet. The global RNAi drug delivery market was worth nearly $11.7 billion in 2013 and is expected to grow to more than $38.8 billion by 2018 at a 5-year compound annual growth rate (CAGR) of 27.2%. However, RNAi delivery is not easy and challenges are expected.

BLOOD-BRAIN BARRIER (BBB) TECHNOLOGY

Blood-brain barrier technology enables therapeutics to pass through the previously impenetrable blood-brain barrier (BBB), which protects neural tissue from chemicals and infections and helps to regulate the brain's environment (ie, levels of ions and peptides and the movement of water and salts). The barrier provides such a protective shield to the brain that approximately 98% of small molecule drugs and 100% of large molecule drugs cannot cross it. Advanced BBB drug delivery technologies essentially produce central nervous system (CNS) drugs that can pass the BBB using a platform technology or drug delivery technologies.

Through this type of technology, therapeutics are delivered orally or through injection and have reached the brain in therapeutic amounts to treat whole new areas of CNS disease. Currently, treating the brain largely involves treating only a fraction of CNS diseases through the BBB using small molecules, or bypassing the BBB, such as nasally with a spray or opening the head to insert a catheter or some other device, the latter of which is not desirable unless it is the only option. The CNS disorders treatable with small molecules to date include schizophrenia and bipolar disorder, depression, pain, epilepsy, insomnia, and attention deficit hyperactivity disorder (ADHD), or similar disorders. Largely cut off from most treatments, large and small, have been: cerebrovascular disease, the neurodegenerative diseases (Alzheimer's, Huntington's, and Parkinson's disease, and cognitive effects from AIDS), and amytrophic lateral sclerosis (ALS), multiple sclerosis, brain cancer, stroke, brain or spinal cord trauma, autism, lysosomal storage disorder, Fragile X syndrome, inherited ataxias, and blindness. This means the potential upside for successful BBB technologies is enormous.

The most common means of BBB passage or type of technology is receptor-mediated transport, or RMT, which involves crossing the BBB via certain receptors that include the insulin or transferrin receptors.

This refers to transcytosis, whereby a cell encloses extracellular material in an invagination of the cell membrane to form a vesicle, and that vesicle carries the enclosed material through the cell and disposes of it outside of its membrane on the other side.

The other technology to emerge as a vehicle for taking a drug across the BBB is carrier-mediated transport. In this type of technology, a protein typically exists at the BBB that is a "transporter" with an active site so that it effectively brings the "nutrient" that it is expected to bring, such as glucose, into the brain area. XenoPort has been working on a BBB technology using the LAT1 transporter to carry a form of L-Dopa across the BBB for Parkinsonism.

According to BCC Research, all of the top pharmaceutical companies are involved in BBB technology or have explored it, with six of the top 10 companies having active licensing deals with BBB technology companies that have chosen to specialize in the competency of delivery compounds, including MedImmune (AstraZeneca) with Bioasis (that is looking at lysosomal storage disease), GlaxoSmithKline with Angiochem (also looking at lysosomal storage), Lundbeck with Ossianix and Nanomerics (looking at several targets). Rather than develop this expertise in-house, which pharmaceutical companies have tried to do, the emerging industry model is for larger companies to license or acquire this expertise - with the exception of Genzyme that developed its own BBB-branded technology called LipoBridge - now called Cerense, after being bought by UK-based Pharmidex.

Today, three compounds using BBB technology are currently in the clinical development pipeline, but by 2019 they will number approximately eight. The global market for BBB technologies was valued at $21.8 million in 2013 and $38.7 million in 2014. The market is expected to grow to $471.5 million by 2019, and register a tremendous 64.9% CAGR from 2014 through 2019.

In addition to the sheer potential of the untapped CNS market, near-term growth in the BBB segment will be driven by patent expiries, increasing commercialization of biologics-based drugs (and moving away from small molecules) that require some sort of BBB technology adaptation to move across the barrier, as well as greater numbers of commercialized biologics, such as antibodies. Additional growth will be spurred by the overall expansion of the CNS therapeutic area further into brain cancer, neurodegeneration, and psychiatric medications for disorders such as schizophrenia, bipolar disorder, and depression.

Some of the challenges involved in BBB technologies or even in developing CNS therapeutics include the lack of cooperation among companies specializing in BBB technology; lack of sufficient investment due to risk avoidance; CNS side effects (given the significant role of the brain and nervous system in the human body), and the lack of suitable biomarkers or preclinical models for BBB simulation. ◆

This article is based on the following market analysis reports published by BCC Research: **Global Markets & Technologies for Advanced Drug Delivery Systems (PHM006J)** by Shalini Shahani Dewan, **Blood-Brain Barrier Technologies & Global Markets (PHM075B)** by Kim Lawson, and **RNAi Drug Delivery: Technologies & Global Markets (BIO076B)** by Usha Nagavarapu. For more information, visit www.bccresearch.com.

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BIOGRAPHIES

Kevin James is a New York City-based healthcare and medical communications professional with more than 15 years of experience in the private and public health sectors.

Shalini Shahani Dewan earned her Master's degree in Pharmaceutical Chemistry and has more than 14 years of industry experience. Ms. Dewan was awarded a Gold Medal by the Prime Minister of India for her work and has worked with top companies in India and in the US.

Kim Lawson is a graduate of Mount Holyoke College with a degree in English Literature. She acquired experience as a healthcare journalist, including working for John Wiley & Sons as a print reporter, before serving as a research analyst in a small market research firm that focused on pharmaceuticals and biotechnology in the Research Triangle Park area of NC. Before joining that firm, Ms. Lawson published reports on emerging and established diagnostics and therapeutics for benign and cancerous breast disease.

Usha Nagavarapu is an experienced pharmaceutical professional with business development experience. She has more than 10 years of preclinical, alliance management, discovery, and technology development marketing experience. Her strong focus areas include oncology and cardiovascular diseases, with expertise in molecular and cell biology and complex cell-based biological assays ranging from drug discovery, in vitro and in vivo screening, in vivo model development, and pharmacokinetics.

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Tom Johnson
Senior Director, Pharma & Life Science Solutions
Exostar

"Security is at the heart of what we do. Our Life Sciences Identity Hub is a cloud-based, connect-once solution that is the centerpiece of our community. Rather than establishing point-to-point connections with each and every partner, organizations simply create a single connection to the Life Sciences Identity Hub. The result is a hub-and-spoke rather than full-mesh architecture, which saves time while reducing cost and risk."

The business model for the development and delivery of new drugs and therapies is in the midst of a radical transformation. Collaboration with external partners has become an essential part of the process. Exostar, headquartered in Herndon, VA, is focused on implementing the cloud-based, scalable, high-performance operating environment and applications that enable communities in the life sciences, healthcare, aerospace, defense, and financial services industries to collaborate securely and productively. Drug Development & Delivery recently interviewed Tom Johnson, Exostar's Senior Director of Pharma and Life Science Solutions, to discuss how Exostar's Life Sciences Identity Hub efficiently and cost effectively brings organizations, individuals, applications, and information together to promote the external collaboration initiatives imperative to today's drug research and development processes.

Q: How are you addressing changes in the drug development model?

A: The drug development model continues to become more partner-centric. Companies are looking to leverage external expertise to speed the research and development lifecycle and get products to market as rapidly as possible to maximize revenues during the period of patent exclusivity.

As companies strive to expand the depth and breadth of their external partner relationships, the concept of community makes more and more sense. A community allows companies to discover and socially engage with potential partners, and subsequently connect to and share information with those with whom relationships have been consummated.

Exostar is helping build a community of life sciences and healthcare organizations, from manufacturers, contract research organizations, and universities to laboratories and providers. Our community empowers participants by giving them three essential capabilities. First, we facilitate

collaboration by ensuring the security of applications and information through enforcement of secure industry identities. Second, we promote faster time-to-market by providing a ready infrastructure within which the community operates. And finally, we offer access not only to the applications of external partners, but also to third-party industry toolsets.

Q: How do you enable secure partner engagement?

A: I believe we all understand the benefits that external partner collaboration brings. However, more participating organizations in the drug development process bring more risk and vulnerability. The process is rife with sensitive data, be it intellectual property or personally identifiable information. That data must be protected at all times from unauthorized access in order to preserve a competitive edge and comply with appropriate standards and regulations.

Security is at the heart of what we do. Our Life Sciences Identity Hub is a cloud-based, connect-once solution that is the centerpiece of our community. Rather than establishing point-to-point connections with each and every partner, organizations simply create a single connection to the Life Sciences Identity Hub. The result is a hub-and-spoke rather than full-mesh architecture, which saves time while reducing cost and risk. Organizations can make their applications and information available to the community through the Life Sciences Identity Hub. Exostar also provides applications through an as-a-Service delivery model, and we make sure these tools are configured for data control and compliance.

Individuals access applications connected to the Life Sciences Identity Hub by presenting credentials that help authenticate their identities. The credentials must be trusted, or federated, meaning they are issued by a participating organization, by Exostar, or by a trusted third-party. In fact, we have partnered with the SAFE-BioPharma Association to issue identity credentials via SAFE-BioPharma's government-approved Trust Framework Provider service.

Our Secure Access Manager controls access to connected applications by validating the presented credentials and enforcing the rules and privileges assigned by application owners. Individuals can present a single credential to access all partner applications to which they have been granted permission, which improves the user experience while simultaneously mitigating the risk that comes with the need to maintain multiple credentials.

Q: How does this infrastructure help drug developers get products to market faster though?

A: The connect-once architecture and single sign-on access I just mentioned bring operational efficiencies in addition to security. Our as-a-Service delivery model plays a key role in productivity as well. We've developed the processes and tools to execute the on-boarding and provisioning of organizations and their personnel. Don't underestimate the challenge and complexity of on-boarding and provisioning into the community. The concepts sound simple, but the execution has proven to be another story.

Our customers have consistently told us that prior to joining our community, it would take them weeks or months to bring a new partner into the fold. Now, the process takes just a couple of days. Think about the time savings and productivity gains, especially as the partner network expands into the hundreds or thousands of organizations and tens of thousands of individuals. Our delivery model also means we provide the training, maintenance, and customer care functions that support organizations and individuals throughout the product research and development lifecycle.

Another way we jump-start collaborative activities is through the credentials we issue. As you can imagine, application and information owners have

differing thresholds for allowing external parties to access their assets. The higher the threshold, the longer the process for obtaining the credential can take, as more stringent background checks and proofing must be conducted. We support flexible level of assurance credentials. In other words, individuals can very quickly receive low-level of assurance credentials that let them engage with applications with low thresholds virtually immediately. Over time, these credentials can be upgraded to permit access to applications with higher thresholds. In short, individuals can be as productive as possible as rapidly as possible.

Q: How are you facilitating improved collaboration beyond the Life Sciences Identity Hub?

A: Organizations and individuals need to share ideas, commercial agreements, research proposals and plans, and the research itself. The Life Sciences Identity Hub gives them the conduit to do so securely. However, participating organizations may not have the applications in place to take full advantage of their connections to other community members.

In addition to connecting organizations and their personnel to the Life Sciences Identity Hub, we are identifying and federating third-party industry tools that we can connect to the Life Sciences Identity Hub for trusted access by the community. For example, we recently announced a relationship with BT that provides secure, seamless access to the BT for Life Sciences Cloud Compute Platform. The Platform lets scientists tap into rich sources of information and develop virtual "scientist workbenches" tailored to disciplines such as bioinformatics and cheminformatics.

We also have developed and connected our own applications that promote collaboration across corporate boundaries. Secure Share is an enterprise-class Microsoft SharePoint-based solution that combines the best features of SharePoint with strong security and functionality and workflows specifically designed for the life sciences industry. Secure Share users benefit from capabilities including data encryption at-rest and in-transit, digital rights management, and restricted access to WebEx meetings. Our Secure File Transfer offering facilitates the secure exchange of information residing in very large files through a simple web interface. The solution authenticates the identities of sender and recipient to mitigate risk and then moves files of virtually any size through a secure infrastructure at speeds 100 to 1000 times faster than a standard file transfer protocol. Both of these solutions enhance productivity without sacrificing security.

Q: How do you see your solution suite evolving?

A: We believe we're off to a great start with the important fundamentals. We've done the heavy lifting putting an infrastructure in place to create an industry community that's easy to join and facilitates secure, productive collaboration amongst its participants. Our framework provides strong authentication access control and single sign-on to external partner applications, applications we have developed, and third-party tools and platforms. In just over a year, we have nearly 1000 organizations and over 10,000 individuals working together on drug research and development initiatives.

Our next step is to expand along multiple vectors. We want to add more manufacturers, contract research organizations, investigators, academic institutions, providers, and others to the community. We want to make more applications available to community members. And we want to expand the number of identity providers and the types and levels of credentials we'll accept to make it even easier for individuals to collaborate with one another while strengthening the overall security of the community.

We're confident we can grow without negatively impacting solution performance or availability, given our track record of success in the aerospace and defense markets. Our A&D Identity Hub is the centerpiece of a community that boasts over 100,000 organizations and 300,000 individuals in more than 150 countries on all 7 continents. Growth aside, our ultimate goal is quite simple: provide a solution that lets drug developers focus on the science. If that happens, we all win.◆

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COMPANY BACKGROUND

Ashland Inc. is a manufacturer and marketer of pharmaceutical-grade excipients supported by global research and development and highly trained technical service teams with expertise in oral solid dosage formulation techniques and current drug delivery trends, including drug solubilization and bioavailability enhancement.

COMPANY DESCRIPTION

Ashland is a solutions destination for:

- Increasing the bioavailability of poorly water-soluble active pharmaceutical ingredients (APIs);
- Designing controlled-release profiles specific to product needs;
- Increasing patient compliance by enabling reduced tablet sizes while maintaining API load;
- Improving disintegration speed of orally disintegrating tablets; and
- Understanding implications of continuous oral-dosage form manufacturing processes.

Ashland manufactures cellulose-derived and vinyl pyrrolidone-based polymers that enable us to provide formulators with innovative technologies. Our global manufacturing sites operate in accordance with cGMP standards ensuring consistent production of high-quality products.

Research taking place at Ashland is the foundation of technical solutions that will address formulation and manufacturing challenges in the future. Ashland offers formulators industry-changing technologies and unique opportunities for research and development collaboration.

MARKETS SERVED

Ashland meets formulators' needs by providing the widest available range of excipients and technologies, as well as longstanding polymer expertise and technical support from benchtop to commercialization for binders, disintegrants, controlled-release coatings and matrix formers, film coatings, solubilizers and low-endotoxin polymers.

PRODUCTS, SERVICES & CAPABILITIES

Ashland's leading position in drug solubilization is underscored by its broad network of technical support and laboratories down to the regional level. The company operates pharmaceutical centers of excellence in Wilmington, DE, and Hyderabad, India, and regional supporting laboratories in Düsseldorf, Germany; Istanbul, Turkey; São Paulo, Brazil; Buenos Aires, Argentina; and Shanghai, China. Products include:

- Aqualon™ and Blanose™ sodium carboxymethylcellulose (CMC)
- Aqualon™ ethylcellulose (EC)
- AquaSolve™ hypromellose acetate succinate (HPMCAS)
- Aquarius™ film coating systems
- Benecel™ DC HPMC
- Benecel™ methylcellulose and hypromellose (HPMC)
- Benecel™ HPMC custom grades
- Cavamax*, Cavitron™ and Cavasol* cyclodextrins
- Klucel™ hydroxypropylcellulose (HPC)
- Natrosol™ 250 hydroxyethylcellulose (HEC)
- Plasdone™ povidone and copovidone
- Polyplasdone™ crospovidone
- Pharmasolve™ N-methyl-2-pyrrolidone

*Registered trademark owned by Wacker Chemie AG. Ashland acts as a worldwide distributor for Wacker.

On September 30, 2014, Ashland Specialty Ingredients, a commercial unit of Ashland Inc., celebrated the opening of a state-of-the-art pharmaceutical center of excellence in Wilmington, Del. The new facility, which will primarily focus on drug development and bioavailability enhancement, expands Ashland's global network of pharmaceutical research and development centers. The facility also includes formulation development and supports early-stage clinical trials, spray-drying and extrusion processes.

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BioPharma Solutions, a business unit of Baxter, works with pharmaceutical companies to support their commercialization objectives by providing scientific expertise, sterile manufacturing solutions, parenteral delivery systems, and customized support services needed to meet the unique challenges that parenteral products face. As a dedicated CMO with over 25 years of successful collaborations supporting commercialization objectives, we understand what it takes to deliver value to our clients throughout their products' lifecycle.

Industry Leader with Global Presence/Expansive Network/Manufacturing Resources

With more than 50 manufacturing facilities across six continents, Baxter's global presence provides opportunities for unique manufacturing collaborations to provide the most value for our clients. The power of an extensive network lies in the coordination of, and efficiencies resulting from, a systemic approach to cGMP manufacturing. Baxter's versatile, worldwide manufacturing resources gives you the assurance needed to meet global market demand, from form/fill/finish of small molecule parenterals to production of cytotoxics and biologics, such as monoclonal antibodies and recombinant proteins.

Meeting Parenteral Manufacturing Challenges

Parenteral manufacturing can be a complex process. Cytotoxics, antibody-drug conjugates (ADCs), highly potent compounds, biologics, and lyophilized products require specialized understanding and our dedicated facility in Halle/Westfalen, Germany, has almost 60 years of experience handling cytotoxics and highly potent drug manufacturing. Our Round Lake, IL, facility is the world's leading provider of manufacturer prepared IV solutions and offers best-in-class aseptic solution manufacturing, and our Bloomington, IN, facility is one of the largest contract manufacturers of sterile products in North America.

Areas of Expertise

As a parenterals specialist, BioPharma Solutions offers unique delivery systems and a variety of manufacturing solutions to meet complex and traditional manufacturing challenges.

- **Sterile Manufacturing Solutions**
  - Prefilled Syringes
  - Liquid Vials
  - Lyophilized Vials
  - Cartridges
  - Diluents for Reconstitution
  - Ampoules
  - Powder Filled Vials
  - Sterile Crystallization
- **Parenteral Delivery Systems**
  - Frozen Premix System
  - Liquid Premix System
  - BIO-SET Luer System
- **Drug Categories**
  - Small Molecules
  - Biologics
  - Vaccines
  - Cytotoxics
  - Antibody-Drug Conjugates (ADCs)
  - Highly Potent Compounds
  - Cephalosporins / Penicillins

We Take Partnering Seriously

We have alliances with over 60 pharmaceutical clients and realize that having successful collaborations are critical in this extremely competitive environment. BioPharma Solutions has developed strong organizational capabilities to help ensure that we provide the value you deserve and expect.

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BioSpectra is an FDA-registered, cGMP-compliant, contract manufacturer and commercial producer of biological buffers, pharmaceutical excipients, and active pharmaceutical ingredients.

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The Excipients offered by BioSpectra are produced in accordance with cGMP guidelines to provide the highest quality materials available to the biopharmaceutical industry. These excipients include Tromethamine, Tris Hydrochloride, Urea, Ammonium Sulfate, Guanidine Hydrochloride, MOPS, HEPES, MES, and other related intermediates.

BioSpectra's Laboratory Reagents undergo stringent product testing to ensure that customers receive only the highest quality material for use in their laboratory applications.

BioSpectra delivers the highest quality Custom Manufactured Products using mutually established supply agreements and quality agreements, including:

- Specifications - customer provided or BioSpectra developed
- Requested batch sizes from 1 kg to 50,000 kg and 100 mL to 20,000 L
- Versatile packaging options to meet customer needs
- Fast delivery of finished products

Our custom products are manufactured, packaged, tested, and approved in our secure, FDA-registered facilities to ensure contamination-free, traceable, reliable materials.

SYNTHESIS

High Purity Crystalline Compounds

Our extensive line of manufacturing suites, qualified equipment, and advanced quality systems produce BioPharm/Pharmaceutical-targeted versions of chemicals using ultra-purification methods, Acid/Base reactions, substitution chemistry, particle manipulation, and other synthesis.

Custom Solutions

Formulated based on customer requests and industry demand, BioSpectra's custom solutions are produced in closed, clean environments and can be sterile filtered into final packaging.

Purifications

Our Process Development Team has over 15 years of experience designing purification systems based on process parameters that achieve the correct, critical quality characteristics of the end product. Our extensive range of manufacturing equipment offers a safe home for your product from evaluation samples through bulk commercialization.

Particle Manipulation

Managing flow characteristics and dissolution rates requires consistent and defined starting crystals. BioSpectra uses the best available technology to manipulate crystals to meet your processing parameters. Current equipment includes our 316 S/S Fitz-Mill™, 316 S/S hammer mill, 316 S/S 30ft3 rotary blender, 316 S/S air sieve, 316 S/S Jet Mill, and 316 S/S Ribbon Blender.

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

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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 initially filed with the FDA and is updated annually.

This regulatory safety data package, which continues to grow and now includes more than 70 volumes, supports the use of CAPTISOL® in parenteral formulations as well as substantial registration support for other routes of delivery. In addition, in 2007, a Type IV DMF was filed and contains extensive Chemistry Manufacturing and Controls (CMC) information regarding our GMP-manufactured CAPTISOL®. 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. 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 20 gram sample, please visit www.captisol.com and click on "TRY CAPTISOL" button located on the Home Page within the beaker photo.

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ABOUT CAPSUGEL DOSAGE FORM SOLUTIONS

Capsugel's Dosage Form Solutions business unit, with the addition of Bend Research and Encap Drug Delivery, solves customers' most pressing product development challenges, including bioavailability enhancement, modified release, abuse deterrence, biotherapeutic processing, and inhalation formulation. We utilize an integrated product development approach ensuring that our clients can rely on one partner from design to commercial scale production of innovative drug product intermediates and finished dosage forms.

Capsugel Dosage Form Solutions accelerates and improves product development through an array of technologies, including lipids and liquids, spray-dried dispersions, hot-melt extrusion, and through specialized manufacturing, including FDA/MHRA-accredited finished dosage sites that can handle highly potent, controlled substance, hormonal, and oncology compounds. High-quality science and engineering is core to our offering at each stage of the product development cycle and has enabled the successful advancement of hundreds of compounds.

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Catalyst + Talent. Our name combines these ideas. Catalent is the global leader in development solutions and advanced drug delivery technologies, providing world-wide clinical and commercial supply capabilities for drugs, biologics and consumer health products. With more than 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 thousands of innovators, both established and emerging, in over 80 countries, including 83 of the top 100 pharmaceutical and 38 of the top 50 biotech marketers. Our team of over 1,000 talented scientists has supported nearly half of innovative drug and biologic approvals since 2005, and we have more than 450 active development programs for new customer products. We have 18 development teams in 10 markets.
From nearly 30 global sites, Catalent serves over 1,000 customers and supplies around 70 billion doses annually. Our significant intellectual property includes over 1,400 patents and patent applications.

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Development

With our broad range of expert services – including analytical, biologics, pre-formulation and formulation – we drive faster, more efficient development timelines and produce better products. With innovative SMARTag™ technology to advance ADC development and our robust GPEx® mammalian cell line engineering technology, large molecule drugs can be accelerated from discovery to clinic, and our unique Optiform™ technology ensures maximum API optimization. With our deep expertise and our extensive formulation capabilities across a wide range of dose forms, we can solve even the most complex bioavailability, solubility, and permeability challenges.

Delivery

We are a world leader in drug delivery solutions with a proven track record of helping our customers create better treatments by boosting bioavailability, solubility, and permeability; improving ease and route of administration; and increasing patient compliance. Our unique delivery technologies – including RP Scherer softgel and OptiShell™ capsules, Zydis® fast-dissolve, controlled release, including OSDrC® OptiDose™ flexible dose delivery and OptiMelt™ hot melt extrusion, as well as inhaled and injectable dose forms – improve how products work in and for patients.

Supply

We reliably supply our customers through operational and quality excellence, and we have regulatory inspection results exceeding the industry average. As a seamless extension of your supply chain, we offer global, integrated manufacturing and packaging solutions to take your product from design to clinical trial to plant and to pharmacy. We manufacture oral, sterile and inhaled dose forms and produce biologics for pre-clinical and clinical studies.

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broadest expertise.
faster development.

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CONTROLLED RELEASE TECHNOLOGIES
OPTIMELT™ HME TECHNOLOGY
OSDrC® OPTIDOSE™ TECHNOLOGY

Our 18 R&D teams in 10 countries are now working on 500+ projects, applying multiple proven and innovative drug delivery technologies to help you deliver optimal release profiles, enhanced bioavailability and better dose forms—preferred by patients and payers.

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Pharmaceutical formulators need to achieve API solubility and stability to create market-leading products with maximum efficacy, quality, and performance. Superior quality and ultra-high purity make Croda a supplier of choice in the global pharmaceutical market. Our proprietary manufacturing and purification technology yields high-quality products that meet the exacting requirements of international Pharmacopoeia. Offering one of the widest ranges of chemical specialties, surfactants, and high-purity lipids available to the pharmaceutical industry, with products manufactured at multiple sites throughout the world, Croda provides a complete range of products for topical dosage forms as well as multi-compendial solvents and surfactants suitable for parenteral, oral, ophthalmic, nasal, vaginal, and suppository formulations.

Technical Services

Croda's ongoing investment in GMP API technologies and R&D ensures the continual delivery of exceptional ingredients and the development of new specialty products to answer current and future health and wellness needs.

To achieve products with such superior quality and purity, Croda developed a proprietary flash chromatographic process called Super Refining™. This process physically removes impurities from pharmaceutical excipients and nutritional oils without altering their fundamental structure in any way.

Major 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™ - Harness the Power of Purity
  - 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
  - Etocas™ 35: high-purity polyoxyl 35 castor oil
  - Polysorbates
  - Castor oil
  - Propylene glycol
- 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™: medical-grade lanolin designed to surpass USP requirements for lanolin, modified

DPT Laboratories
318 McCullough Ave.
San Antonio, TX 78215
T: 1-866-Call DPT
Website: www.dptlabs.com
Number of Employees: 1,000
Date Founded: 1938

Confab Laboratories
4355 Sir Wilfrid Lauier Blvb.
Saint-Hubert (Quebec) J3Y 3X3 Canada
T: 1-888-826-6322
Website: www.confab.com
Number of Employees: 350
Date Founded: 1979

Company Description: For pharmaceutical companies seeking solutions to achieve clinical and commercial success, DPT and Confab offer an unmatched breadth of service and vast experience in resolving development and manufacturing challenges in sterile and non-sterile semi-solid & liquid and complex solid dosage forms. Through our purpose-built Centers of Excellence, we're tenacious about discovering solutions and maximizing efficiencies. By asking the right questions and thoroughly investigating your options, our experts give you the answers you need from development through commercialization.

Services & Capabilities

	DPT LABS	CONFAB
DEVELOPMENT	●	●
STERILE		
INJECTABLES	●	○
OPHTHALMICS	●	○
NASAL SPRAYS	●	○
OINTMENTS	●	○
NON-STERILE		
AEROSOL FOAMS & SPRAYS	●	○
METERED DOSE PUMPS	●	○
SYRINGES	●	○
RECTAL/VAGINAL APPLICATORS	●	○
EXTRUSIONS	●	○
TABLETS	○	●
CAPSULES	○	●
LIQUID FFS	○	●
SUPPOSITORIES	○	●
PLASTIC AMPOULES	○	●
CREAMS	●	●
EMULSIONS	●	●
GELS	●	●
LOTIONS	●	●
OINTMENTS	●	●
SOLUTIONS	●	●
SUSPENSIONS	●	●

Facilities

Center of Excellence for Research & Development

Location: San Antonio, Texas Size: 258,000 sq ft

Focus: Pre-formulation and formulation development and analytical development services
Our scientists and technicians provide research and development services and handle technical transfers to the appropriate manufacturing center of excellence. Our Center of Excellence for Research and Development also stores raw materials and finished goods and facilitates worldwide product distribution.

Center of Excellence for Sterile & Specialty Products

Location: Lakewood, NJ Size: 175,000 sq ft

Focus: Aseptic production of sterile dosage forms
This area features state-of-the-art aseptic processing suites and filling equipment for small-volume parenterals, ophthalmic preparations, preservative-free nasal sprays and sterile ointments.

Center of Excellence for Semi-Solids & Liquids

Location: San Antonio, Texas Size: 450,000 sq ft

Focus: cGMP pilot, clinical and commercial-scale manufacturing for prescription and over-the-counter (OTC) products. This campus features a dedicated 60,000-square-foot cGMP aerosol manufacturing facility, a 225,000-sq-ft raw material dispensing and distribution center, and a 150,000-sq-ft compounding, fill and finish area.

The Confab Facility

Location: Saint-Hubert, Quebec, Canada Size: 140,000 sq ft

Focus: Confab is one of the most well-respected cGMP-compliant pharmaceutical outsourcing CDMOs in the world. We are licensed by Health Canada's Therapeutic Products Directorate, and our purpose-built facility has been inspected and licensed by the US FDA and the National Health Surveillance Agency of Brazil (ANVISA) and follows the International Conference on Harmonization's (ICH) good clinical practice (GCP) guidelines.

Features: -36 manufacturing suites
-18 packaging suites
-8 independent ventilation, air conditioning and heating systems

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VISIONARY KEYNOTES

Bridging Science and Technology to the Healthcare of Tomorrow—Lessons Learned And New Paths to Explore

John Ludwig
SVP, BioTherapeutics Pharmaceutical Sciences,
Pfizer

Overcoming Challenges in Delivery of Biologics: Combining Patient Centric Devices with Improved Formulations

Anand Subramony
Vice President, Drug Delivery & Device Development,
MedImmune

Pharmacogenomics and Personalized Medicine: Providing Patient Specific Therapies to Monitor Adherence and Therapeutic Outcome

Sven Stegemann
Professor for Patient Centric Product Design and Manufacturing,
Graz University of Technology, Austria

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- **Product Analysis:** Our pipeline platform provides an interactive, comprehensive and analytical view of marketed and pipeline pharmaceutical products, with in-depth records of assets across developed and emerging markets on a user-friendly platform with flexible data output options.
- **Clinical Trials and Investigators Analysis:** Our clinical trials database provides accurate and detailed intelligence on a wide range of therapy areas. Trial activity is monitored in real-time by experts, with data crossed-checked with key registries, conferences, associations and journals.
- **Epidemiology and Market Size Analysis:** Our team of epidemiologists provide country-specific forecasts of epidemiological metrics and demographics, including prevalent and/or incident cases, number of cases treated, market size, and other data relevant to the indication, covering an unrivalled range of disease areas.
- **Industry Dynamics Analysis:** We offer a range of analytics tools for forecasting, segmentation, benchmarking and valuation analysis of assets and companies across a wide range of financial metrics.
- **Deals Analysis:** Our comprehensive deals platform tracks a range of deal types across the healthcare sector, from M&A to Strategic Alliances and Venture Capital, while providing a proprietary analytics tool to perform unlimited segmentation analysis on the deals landscape.

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Specialty Disease Experts

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EMD Millipore is the Life Science division of Merck KGaA of Darmstadt, Germany and offers a broad range of innovative, performance products, services and business relationships that enable our customers' success in development and production of biotech and pharmaceutical drug therapies. EMD Millipore serves as a strategic partner to customers and helps advance the promise of life science.

Consistent, reliable performance is the key to drug development and manufacturing success – and that means choosing a partner who understands your goals, and can supply everything you need from a single, proven source. With trusted EMD Millipore products, in-depth expertise and unrivalled regulatory support, we can help you improve your product's consistency and bring it to market faster.

EMD Millipore offers an extensive range of over 400 EMPROVE®-grade excipients, including our Parteck® products, and APIs for the production of solid, liquid and semi-solid dosage forms. EMPROVE® dossiers comprise detailed, usage-specific documentation that includes information on manufacturing, test methods, purity and stability data.

With our application know-how and regulatory expertise, we support you throughout the entire formulation process, enhance the bioavailability of your final drug product. In addition, we support biopharmaceutical applications with chemicals needed in the process and products to modify proteins, such as activated PEGs.

We are able to meet standards easily with state-of-the-art production facilities providing you with global and comprehensive support, at every step of your formulation process. All this simplifies the complexity of your supplier qualification and speeds up processes, thus reducing total cost of ownership.

At EMD Millipore, we work to minimize complexity, improve productivity, reduce risk, lower cost and give you confidence — thereby, together assuring the quality, bioavailability and safety of life-enhancing drugs brought to market.

Visit www.emdmillipore.com or contact us at pcs.salessupport@emdmillipore and 800.647.5476 for more information.

EMD Millipore is a division of Merck KGaA of Darmstadt, Germany. The division is headquartered in Billerica, Massachusetts and has approximately 10,000 employees, operations in 67 countries and 2011 revenues of EUR 2.4 billion. EMD Millipore is known as Merck Millipore outside of the U.S. and Canada.

Note: Merck KGaA or Merck shall mean Merck KGaA, Darmstadt, Germany.

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To help organize your time, exhibitors will be separated into two featured zones: **cGMP** and **Specialty**.

Tailored Show Schedule

The show floor schedule and surrounding events have been adapted to meet the needs of the InformEx community. Kicking off the event will be the **Exhibitor & Technology Showcases** followed by a Grand Opening of the Exhibit Floor.

Cutting Edge Content

The 2015 Conference will cover a diverse range of emerging issues and trends relevant to the chemical industry including an economic overview and state of the custom manufacturing industry.

For more information, go to InformEx.com
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UBM

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30 Indian Drive
Ivyland, PA 18974-1431
T: (215) 396-8373 F: (215) 396-8375
E: inquiry@lyo-t.com
Website: www.lyotechnology.com
Year Founded: 1992

CORPORATE DESCRIPTION

A dedicated staff supports clients bringing new products to patients and improving existing products and operations. Clients gain with successful development and clinical manufacturing, bridging discovery through product approval and commercial manufacturing. A talented, dedicated staff skilled with experience is coupled with well-equipped laboratories and flexible manufacturing capabilities. Support services span product development, process engineering, clinical manufacturing and technical service. Internationally recognized as an industry leader, clients have fostered our reputation for providing innovative solutions, achieving desired results, and exceeding expectations. This reputation is demonstrated by collaborative relationships with clients for over 22 years.

Capabilities

- Pre-clinical through Phase III Clinical Materials, lyophilized/liquid products
- Containment for cytotoxic/high potent products
- Dedicated/disposable equipment
- Vials: 2 to 160 mL: novel delivery systems
- Cartridges/syringes: 1 to 50 mL
- Lyophilizers: 0.2 m2 to 4.5 m2
- Praxair ControLyo™
- Bulk Lyophilization
- Batch sizes: up to 75L
- Drug and Device Registration/DEA license
- US/EU compliant

Services

LTI successfully developed formulations, processes or prepared clinical material for over 493 diverse products:

- Anti-infectives
- Human/Recombinant Biologics
- Vaccines
- Nanoparticles/emulsions
- Oncolytics/HPCs
- Small Molecules/Therapeutics
- Diagnostics
- Bioengineered materials

Development Sciences

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

- Thermal Analysis
- Product Design
- Formulation Development
- Product/Process Feasibility
- Cycle Design/Refinement
- Product Characterization
- Toxicology Material
- Stability Batches

Clinical Manufacturing

US/EU compliant Clinical Manufacturing Area (CMA) for preparation of clinical material is for processing a wide range of products, including unique requirements. The CMA includes an aseptic suite featuring unique disposable negative pressure isolators for containment/isolation technology, inspected and approved for handling BSL-2, cytotoxic and highly potent material.

- Aseptic compounding
- Pre-clinical through Phase III
- Small to medium batch sizes
- Liquid/diluents

Technical Services

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

- Customized Training
- Qualification/Validation Support
- Investigations
- Quality/Compliance

MAJOR MARKETS

LTI provides Development and Clinical Trial Material Manufacturing to more than 354 biopharmaceutical companies spanning virtual, small, large and multi-national companies. Gaining an international reputation, projects are with clients in US, Canada, Mexico, Eastern and Western Europe, Australia and Japan.

PLEASE MARK YOUR CALENDARS AND PLAN TO ATTEND!

RDD EUROPE 2015

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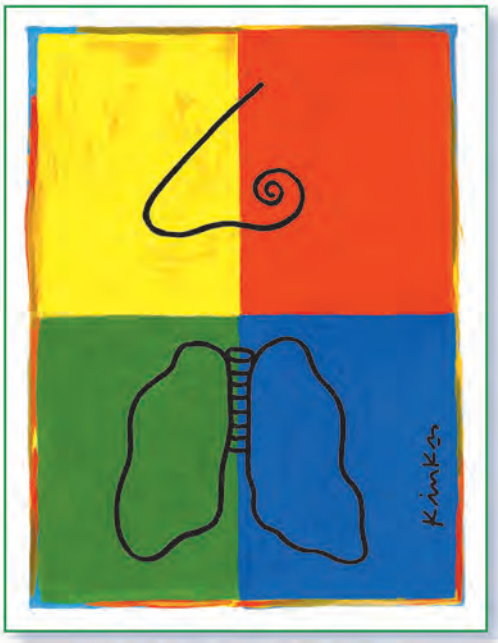

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Website: www.metricsinc.com

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 solid oral dosage forms. Today, as a subsidiary of Mayne Pharma Group, we offer clients more resources and capabilities than ever before.

PHARMACEUTICAL DEVELOPMENT

We offer full formulation development services from pre-clinical through Phase III CTM including: tableting, immediate release, modified release (including controlled/matrix and sustained release), capsule filling, over-encapsulation, milling, micronizing, enteric coating, spray drying, extrustion, and spheronization. Our facilities and processes are designed to handle potent products, cytotoxic compounds and controlled substances.

POTENT PRODUCTS

Our segregated potent facility provides total engineered containment through customized, hard-wall 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 wash-room, 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 130 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.

CTM PHASE I, II, III

Our CTM capabilities offer capacity for all clinical trial phases. Our state-of-the-art, flexible manufacturing facility and equipment can handle up to 450-kilo batch sizes. We also offer expertise in over-encapsulation for comparator studies, as well as potent drug handling capabilities. CTM packaging is also available.

COMMERCIAL MANUFACTURING

Seven manufacturing and packaging rooms for large scale Phase III clinical trial or commercial manufacturing offer high-quality manufacturing of solid oral dose formulations, including DEA II-V controlled products. Full analytical support is available – release testing, stability, microbiology testing and custom analytical development and validation.

Global Data and Analytics for Pharmaceutical Professionals

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PharmaCircle is the leading information and analytics provider serving pharmaceutical sciences professionals. PharmaCircle's best-in-class data system and analytics tools provide expert assessments on innovative drug delivery technologies, and detailed insight on formulations and excipients. PharmaCircle also provides a comprehensive view on all aspects of the pharmaceutical business with in-depth, global coverage and intelligence on life sciences companies, products and pipelines, clinical trials, regulatory filings, and strategic business transactions.

Most multinational pharmaceutical companies as well as numerous commercial and emerging stage biopharmaceutical companies and suppliers rely on PharmaCircle for a full service solution for seamless content integration, layered analytics and data-driven tactical support, enabling them to uncover new opportunities and make informed business decisions.

PharmaCircle's Pharmaceutical Science and R&D Searchable Databases and Analyses Include:

DD Technology (>5,100 Technologies)	Products & Pipeline (>97,000 Products)	Drug Delivery Analyses (49 Topics)
FDA Excipient (>11,700 Excipients)	Molecule (>31,000 Molecules)	How Supplied Injectable (>4,400 Products)
Drug Delivery Reviews (46 Topics)	FDA Package (>173,000 Packages)	How Supplied Non-Injectable (>11,900 Products)
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Norwich Pharma Services is a recognized leader in full-service contract development and manufacturing. From development, clinical research, and formulation to commercialization and manufacturing, Norwich offers a complete range of pharmaceutical development services for solid dose products.

For more than 127 years, Norwich has built a reputation for dependable product supply and established an unparalleled history of regulatory compliance. Norwich has a proven record of successfully meeting compliance requirements for regulatory agencies worldwide including FDA, EMA and ANVISA.

Our development and manufacturing facility, located in Norwich, New York, is equipped to handle challenging programs including: solvent formulations; DEA Schedule II-IV products; and intermediate potency products. The Norwich team works with both immediate and modified release products and has expertise in a number of unique dosage forms including:

- Holt melt liquid filled capsules
- Extruded and spheronized beads
- Fluid bed coated beads and granules
- ODT tablets
- Bi-layer and tablet-in-tablet compression
- Mini-tablets filled into capsules

Norwich has developed a program execution platform built on providing our customers with quality data, program oversight and open lines of communication. This platform ensures accessibility to project management with a primary and a secondary project manager assigned to each project.

Norwich also streamlines product lifecycle management by housing analytical services, formulation development, CTM and commercial/manufacturing/packaging capabilities all at one site. This helps us to achieve our goal of keeping the same core team on projects through commercial validation.

By combining our full range of synchronized solutions in contract development and manufacturing, our unsurpassed quality and our program management platform, Norwich has become an industry leader. We are forward looking, anticipating each customer's needs and discovering new opportunities to meet them. Mutual respect and understanding enables us to work together and create solutions for the benefit of customers and patients.

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Website: www.pfanstiehl.com

Pfanstiehl is the premier manufacturer 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.

SiO2 Medical Products
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Auburn, AL 36832
T: 334.321.5000
Website: www.SiO2Med.com

BACKGROUND

SiO2 Medical Products manufactures a product line of plastic primary containers (eg, vials, cartridges, and prefilled syringes), which incorporates a SiO2-based coating system that is applied to the interior surface of the containers. These coated containers effectively address the current issues being experienced by the parenteral drug industry and regulatory concerns with primary containers. Our coated containers are ideally suited for sensitive biological drugs. The company has a 160,000 sq ft facility with 30,000 sq ft of Class 7 clean rooms, located in Auburn, AL.

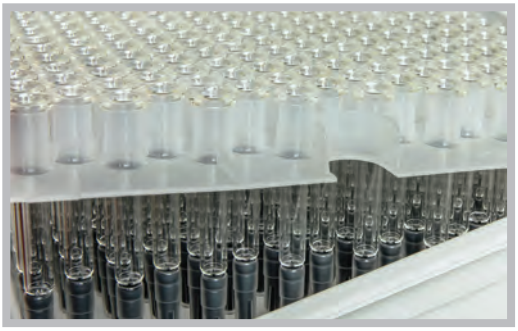
TECHNICAL SERVICES & CAPABILITIES

The coating system is transparent and thin, measuring less than 300 nanometers thick, and is applied to plastic containers using plasma-enhanced chemical vapor deposition (PECVD). Our primary containers have the following characteristics:

- gas barrier properties approaching traditional Type I borosilicate glass
- no delamination, SiO2 coating does not contain any of the metals associated with Type 1 borosilicate glass that have been associated with glass delamination
- solute barrier that blocks potential extractables or migration
- dimensional tolerances many times more precise than Type 1 borosilicate glass containers
- resistant to cracking and breakage
- extremely low level of sub-visible particles
- may be sterilized by ethylene oxide, e-beam and steam
- supports lyophilization
- excellent Container Closure Integrity (CCI) due to the precision of the manufacturing process

SiO2's manufacturing process incorporates the following features:

- **Product Traceability** - from inception to final shipping, each product is marked with a unique identifier permitting the most comprehensive traceability system of its kind.
- **Particle Control** - all aspects of the product production (molding, coating, and packaging) are done in particle controlled conditions in an inline process.
- **State-of-the-Art 100% Inspection System** - in both the molding and coating processes, providing a six sigma or better quality level on every part shipped.



SiO2's coated containers address the critical challenges that pharmaceutical companies face in primary packaging of parenteral drugs.

Teleflex VaxINator™

Intranasal Drug Delivery Device

TELEFLEX MEDICAL INCORPORATED
79 West 4500 South, Suite 18
Salt Lake City, UT 84107
T: (801) 281-3000 F: (801) 281-0708
E: vaxinator@teleflex.com
Website: www.vaxinator.com

Teleflex VaxINator™

With a reputation for excellence, together with decades of experience, Teleflex offers a compelling proposition to pharmaceutical partners looking for the latest innovations in intranasal drug delivery. The Teleflex VaxINator™ from Teleflex is a brand at the forefront of intranasal drug delivery. Although part of the clinically proven MAD Nasal™ range of nasal delivery devices, the Teleflex VaxINator is available for supply exclusively to OEMs for incorporation into intranasal drug-device combination products.

The Teleflex VaxINator™ is an easy-to-use and cost-effective solution for intranasal drug delivery. Applications include vaccines, pain medications, anaesthetics, antimicrobial, and many other possibilities.

The design of the Teleflex VaxINator™ enables a standardized position in the nasal passageway that directs the spray plume through the nasal valve, where the broad angle of the plume allows for broad deposition across the nasal mucosa. The atomizer output is a fine mist of particles 30-100 microns in size. The range of droplet size delivered by the device allows for particulate deposition across both anterior and posterior areas of the nasal cavity to facilitate rapid absorption.

The Teleflex VaxINator™ is made from radiation-stable medical-grade polycarbonate material and is compliant with USP Class VI and ISO 10993 requirements. In addition to the provision of the nasal atomizer, Teleflex also provides a range of accessories, for example, dose dividers, auto-disable syringes etc., to meet our customers' needs.

At Teleflex, we fully understand our role within your supply chain. We realise that in choosing Teleflex VaxINator™ for intranasal drug delivery, it becomesan integral part of your product offering, and any delays or issuesin device production can have major implications on finished product supply.

Teleflex's core business is high-volume manufacturing and supply of consumable medical devices worldwide. Through its global manufacturing capability and extensive expertise in demand planning, inventory, and warehousing management, and logistics, Teleflex is ideally positioned to mitigate supply chain risks. With Teleflex as your intranasal drug delivery partner, you gain access to this network and expertise. We are committed to investing significant time and effort into demand planning and risk mitigation to ensure high quality product supply when you need it and where you need it.

VETTER
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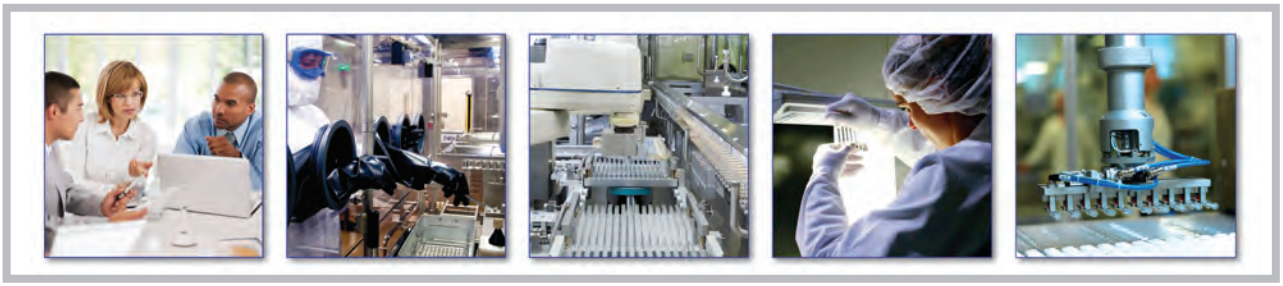
Website: www.vetter-pharma.com



Vetter is a leading contract development and manufacturing organization (CDMO) that specializes in the aseptic filling of syringes, cartridges, and vials. The company has extensive experience with biologics and other complex compounds, including monoclonal antibodies, peptides, interferons, and vaccines. Collaborating with pharma/biotech clients worldwide, Vetter supports products from preclinical development through global market supply. Through its US and European facilities, Vetter Development Service provides state-of-the-art support for early stage products, with seamless transfer at Phase III to Vetter Commercial Manufacturing for large-scale production. The company offers state-of-the-art technology and innovative processes to promote product quality and maximize API yield.

Vetter Development Service

At Vetter Development Service, we partner with our clients from preclinical development through Phase III. Because we plan for commercial production from a product's earliest stages, we develop processes that mirror those at our commercial production facilities. That enables seamless product transfer at Phase III to Vetter Commercial Manufacturing for scale-up and large-scale production. With a growing need for early stage support in North America, in 2011 we expanded Vetter Development Service to Chicago, Vetter's first US facility.

Vetter Commercial Manufacturing

Vetter Commercial Manufacturing provides Phase III manufacturing through global market supply. To strengthen security of supply, we take active steps both downstream and upstream to maintain the integrity of the supply chain, including regular quality reviews of all suppliers and cross-linked IT systems to monitor manufacturing processes. Vetter manufactures products for the top 10 pharma/biotech firms worldwide.

Vetter Packaging Solutions

Vetter Packaging Solutions helps clients match their product with the appropriate drug delivery system (primary packaging); secondary packaging, such as cartoning or blister packing; and packaging services, such as pen-system assembly.

West Pharmaceutical Services, Inc.
530 Herman O. West Drive
Exton, PA 19341-0645
T: US: (610) 594-2900 or (800) 345-9800, EU: +45 7561 6000
Website: www.westpharma.com

By Your Side

Every day, injectable drugs improve the lives of millions of patients around the world. And every day, West is working by your side to design and manufacture drug packaging and delivery systems that will bring your drugs from concept to the patient more efficiently, reliably, and safely. West understands your challenges and helps with solutions every step of the way. We provide cutting-edge production technologies, an unmatched expertise in global regulatory compliance, and an ever-growing knowledge base of pharmaceutical drug product testing, development, packaging, and delivery. Whether your focus is on one piece of the process or you want an end-to-end solution, West is by your side for a healthier world.

NovaPure® Components

Patient safety influenced the design process for NovaPure stoppers and syringe plungers from start to finish. West developed NovaPure components by incorporating Quality-by-Design principles to help ensure enhanced component reliability and an unrivaled level of quality. With NovaPure components, pharmaceutical manufacturers can help ensure a safe injectable drug product for patients.

West Spectra® Seals

Tamper-evident West Spectra seals help ensure patient safety and product security by incorporating multiple layers of protection to combat drug counterfeiting and help keep supply chains safe.

Injection System Platform Technologies

West's platform technologies provide solutions for self-injected drugs covering a range of dose volumes and drug viscosities. West's platform technologies include the ConfiDose®, SmartDose®, and SelfDose™ injector technology platforms.[1]

Needle Safety Systems

West's needle safety systems have been designed to provide protection for healthcare workers and patients against accidental needlestick injuries. In extreme cases, needlestick injuries can lead to serious problems, such as hepatitis B and C and HIV. West's platform technologies include NovaGuard® SA2 and NovaGuard LP.

Daikyo Crystal Zenith® Ready-to-Use Solutions

The Crystal Zenith polymer is break-resistant and highly transparent. Available in a variety of vials, containers, and syringes, a solution using Crystal Zenith polymer is the answer to drug product life-cycle management.

Administration Systems

West develops and manufactures safety and administration systems for the reconstitution, mixing, transfer, and administration of injectable drugs. Mixing and transfer systems include MixJect®, Mix2Vial®, Vial2Bag®, and vial adapters.

For investigational use only by our pharmaceutical and biotechnology development partners. These platforms are intended to be used as an integrated system with drug filling and final assembly completed by the pharmaceutical/biotechnology company.

West markets the NovaGuard® SA platform technology as an integrated system. Final assembly is performed by the pharmaceutical manufacturer.

XCELIENCE
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E: info@xcelience.com
Website: www.xcelience.com
Contact: Sharon Burgess, Senior Vice President

Suite Science

Xcelience offers a suite of services enabling clients to partner with a single CDMO for all of their clinical outsourcing needs. Services include preformulation, analytical services, formulation development, GMP manufacturing, small-scale commercial manufacturing, and clinical supplies packaging and logistics. Xcelience takes pride in delivering the highest standards in science and service with an emphasis on quality, cost, and speed. Our goal is to provide superior drug product development and global clinical supplies solutions to our pharmaceutical and biotech customers in support of their global clinical needs. As the premier, trusted CDMO and Clinical Supplies Solutions (CSS) global partner, we are steadfast in our commitment to providing sound solutions. We take a personal approach to each customer relationship, and pride ourselves in our ability to deliver superior clinical trial supplies, when and where our clients need them.

SERVICES & CAPABILITIES

Preformulation

- Polymorph Identification
- Salt Screen/Selection
- Thermal Evaluation
  - DSC, TGA and/or Hot Stage
- pKa Determination
  - Calculated & Experimental
- Log P/Log D Determination
- pH Solubility Profiles
- XRPD
- Particle Size
- Moisture Content
- Hygroscopicity
- Water Activity
- Solid State Characterization

Analytical Services

- Method Development, Qualification & Validation
- Raw Material Testing
- Release Testing
- Stability Sample Analysis
- Cleaning Evaluations
- Technical Packages for Drug Substances

Formulation Development

- Tablets
- Capsules
- API into Capsule
- Liquid into Capsule
- Semi-Solids
- Non-Sterile Liquids

GMP Manufacturing

Clinical supplies manufacturing capabilities include:

- Tablets
- Capsule
- API into capsule
- Liquid into Capsule
- Semi-Solids
- Non-Sterile Liquids
- Reference Product Blinding
- Small-Scale Commercial Manufacturing

Global Clinical Supplies Packaging

- Bottling
- Blister Packaging
- Labeling for a Multiple Variety of Primary Containers
- Kit Assembly Including Ancillary Supplies
- Blister Card/Wallet Sealing
- Comparator Sourcing
- Cold Room Labeling
- Clinical Labeling

Global Clinical Supplies Distribution & Logistics

- Global Distribution
- Cold Chain Capabilities include:
  - 2°C -8°C
  - Dry Ice
- Point of Distribution (POD) Labeling and Distribution
- Clinical Supply Storage
- Retains
- Returns
- Reconciliation
- Destruction

FACILITES

Xcelience currently has 4 locations. The West Laurel Street headquarters houses preformulation, analytical services, formulation development, and GMP manufacturing. The West Grace Street facility is dedicated to primary and secondary packaging and clinical supplies distribution and logistical services. In 2013, Xcelience opened a new facility in Burton-on-Trent, near Birmingham, UK. This facility provides a central hub for labeling and distribution throughout Europe. Xcelience has an additional facility used for return processing, retain storage, and destruction of clinical trial supplies.

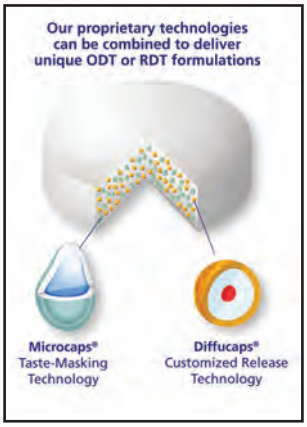

Xcelience®
SUITE SCIENCE
Xcelience® offers a suite of services from preformulation and development through manufacturing and clinical distribution. Entrust all your clinical outsourcing needs by partnering with a single CDMO.
Preformulation Development
Analytical Services
Formulation Development
GMP Manufacturing
Clinical Supplies Packaging & Distribution
Xcelience's responsibility is delivering the best science and service with commitment to quality, cost and speed.
Contact us: www.xcelience.com 813.286.0404

Technology & Services Showcase

Analytical Support Services

ABC provides IND-enabling, registration, and post-commercialization support for the development, quality control, and lifecycle management of innovative therapies and generic medicines. Our personalized, results-based approach to development strategy is backed by decades of experience delivering GLP- and CGMP-compliant analytical testing services across all types of APIs and formulations. Through development know-how, cross-disciplinary technical expertise, and applied experience with evolving global regulatory frameworks, we help efficiently advance and manage programs for large and small molecule drugs, medical devices, and combination products. Our mission is to become a trusted extension of our client's product development teams, helping them meet the global demand for safer, more effective products. Our approach to doing business promotes relationships beyond a simple transaction. This, in turn, improves decision-making, expedites development, and reduces risk. In other words, "better insight, better outcomes." For more information, visit ABC Laboratories at **www.abclabs.com**.

Oral Delivery Technologies



Aptalis Pharmaceutical Technologies is focused on developing high-value products with robust, defensible proprietary positions that grow the commercial value of our partners' portfolios. We develop new formulations or license existing product formulations that leverage our broad range of proprietary technologies, which include microencapsulation, taste-masking, and orally disintegrating tablets (ODTs), customized drug release, and bioavailability enhancement. AdvaTab® Orally Disintegrating Tablets enable rapid disintegration in the mouth without water, and are formulated to achieve an acceptable taste and desired release profile. AdvaTab® Tablets can be combined with Microcaps® Taste-Masking Technology and Diffucaps® Customized Release Technology to create IR or controlled-release ODTs, with high drug-loading capability. Transform the value of your portfolio by visiting Aptalis at **www.AptalisPharmaceuticalTechnologies.com**.

Specialty Ingredients

Ashland Specialty Ingredients offers industry-leading products, technologies, and resources for solving formulation and product performance challenges in key markets, including personal care, pharmaceutical, food and beverage, coatings, and energy. Using natural, synthetic, and semi-synthetic polymers derived from plant and seed extract, cellulose ethers and vinyl pyrrolidones, Ashland offers comprehensive and innovative solutions for today's demanding consumer and industrial applications. Ashland is a highly respected supplier of excipients and tablet film-coating systems to enable the formulation and delivery of active ingredients. Using our wide range of products, developers create reliable formulations for tablet binding, controlled-release formulations, tablet film coating, drug solubilization, and tablet disintegration applications. For more information, contact Ashland Specialty Ingredients at (877) 546-2782 or visit **www.ashland.com/ddd/pharmaceutical.**

Biopharma Solutions

BioPharma Solutions, a business unit of Baxter, partners with pharmaceutical companies to support their commercialization objectives by providing scientific expertise, sterile manufacturing solutions, parenteral delivery systems, and customized support services needed to meet the unique challenges that parenteral products face. Experience makes the difference: with nearly 80 years of parenteral expertise, we can help to navigate the pathway of success for your molecule. BioPharma Solutions provides our clients with confidence of delivery, service, and integrity - we know the work we do is ultimately vital to the patients you serve. BioPharma Solutions offers resources to help solve the high-stakes challenges you face in today's complex parenteral marketplace. For more information, contact Baxter BioPharma Solutions at (800) 4-BAXTER or visit **www.baxterbiopharmasolutions.com**

Technology & Services Showcase

Dosage Form Solutions

CAPSUGEL®
BEND RESEARCH encap drug delivery

Capsugel's Dosage Form Solutions business unit solves customers' most pressing product development challenges, including bioavailability enhancement, modified release, abuse deterrence, biotherapeutic processing, and inhalation formulation. We utilize an integrated product development approach ensuring our clients can rely on one partner from design to commercial-scale production of innovative drug product intermediates and finished dosage forms. Capsugel Dosage Form Solutions accelerates and improves product development through an array of technologies, including lipids and liquids, spray-dried dispersions, hot-melt extrusion, and through specialized manufacturing, including FDA/MHRA-accredited finished dosage sites that can handle highly potent, controlled substance, hormonal, and oncology compounds. High-quality science and engineering is core to our offering at each stage of the product development cycle and has enabled the successful advancement of hundreds of compounds. For more information, contact Capsugel Dosage Form Solutions at DFSInquiry@capsugel.com or visit **www.BendResearch.com.**

US-Manufactured Tromethamine

BioSpectra's cGMP, US-manufactured ICH Q7-based Tromethamine, for use as an API, will be produced in its new FDA-registered facility in Bangor, PA, in Q4 2014. Regulatory Packets, Validation Reports, and Type II Drug Master File Authorization are scheduled for contract customers of Bio Active Tromethamine during Q2 2015. Bio Active Grade Tromethamine, Product Code TR22, will be manufactured in a qualified, validated ICH Q7-compliant API manufacturing suite as a highly purified crystal with optimum solubility, purity, and traceability. Future versions of will include liquid and spray-dried forms, both of which are currently scheduled for release in Q3 2015. This product will be added to the current portfolio, which already includes BioSpectra's Bio Excipient Grade Tromethamine, Product Code TR32, which is an ICH Q7-compliant Excipient supported by a Type IV Drug Master File. For more information, contact BioSpectra at (877) 982-8333 or visit **www.biospectra.us.**

Platform Technology

CAPTISOL®

Ligand is a biopharmaceutical company that develops and acquires technology and royalty revenue generating assets that are coupled to a lean cost structure. Ligand's Captisol® platform technology is a patent protected, chemically modified cyclodextrin with a structure designed to optimize the solubility and stability of drugs. Captisol® has enabled five FDA-approved products, including Pfizer's VFEND® IV and Baxter's Nexterone®. For licensing opportunities, call Captisol Services at (877) 575-5593 or visit **www.captisol.com.**

Biologics Development

Catalent's proprietary Gene Product Expression Technology (GPEx®) sets the standards in mammalian cell line engineering. GPEx allows rapid selection of the best clinical candidate from a group of potential molecules, providing a stable Master Cell Bank to rapidly generate proteins for clinical trials. GPEx technology can ensure genetically stable cell lines are produced 100% of the time. The advanced mammalian cell line technology in GPEx accelerates timelines, increases reliability and yield, and provides superior cell stability compared to any other method, with flexibility and unmatched versatility. Catalent provides a faster path from gene to clinic and offers high-performance cell line biologics development and biomanufacturing. Catalent boasts a new, state-of-the-art, biologics manufacturing facility in Madison, WI, allowing for batch sizes from 10-1,000 L. To learn more about Catalent's global Biologics capabilities, call (877) 587-1835 or visit **http://www.catalent.com/index.php/development/biologics/overview.**

Technology & Services Showcase

Super Refined™ Excipients

CRODA

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

Development & Manufacturing

DPT

Confab

A DPT COMPANY

DPT and Confab are leading contract development and manufacturing organizations (CDMOs) offering extensive sterile and non-sterile services for solid, semi-solid, and liquid dosage forms. We have aligned our businesses to leverage the expertise and strengths from both DPT and Confab. Our scientific teams provide a solutions-oriented approach that drives research excellence. With an exemplary regulatory compliance record, cGMP-compliant facilities, and specialists in technical transfers and scale-up, we are your premier pharmaceutical development and manufacturing partner. For more information: Contact DPT at (866) 225-5378 or visit dptlabs.com; or Contact Confab at (888) 826-6322 or visit **confab.com.**

Regulatory Documentation

With the ever-increasing regulatory challenges drug manufacturers are facing, creating documentation for your pharmaceutical products on your own can be costly and time-consuming. That's why we developed the EMPROVE® concept. With a portfolio of 400 raw materials, EMD Millipore helps you obtain the documentation and approvals you need to bring your products to market faster than ever. Backed by our proven expertise and reputation for uncompromising reliability, you can avoid potential error sources of manual documentation. Benefits include speed approval preparation for faster time to market, time and money savings, and creating formulations with full regulatory compliance. Our EMPROVE dossiers comprise detailed, usage-specific documentation that includes information on manufacturing, test methods, purity, and stability data, helping you to successfully navigate regulatory challenges. For more information, visit EMD Millipore at **www.emdmillipore.com/emprove**.

Marketing & Communications

Get Noticed. Get Funded. Grow Faster. When you need to connect with investors, business partners, and regulatory agencies, LifeSciencePR can make that happen. Our integrated communication strategies and well-established industry contacts will help your life science company achieve its short- and long-term corporate objectives. We work seamlessly with your senior management team to develop the most effective communication initiatives to reach your prospective investors and partners. Our experienced staff knows what it takes to break through with your breakthroughs, powering your engine in your continued drive toward your success. LifeSciencePR will get you there smarter, faster, and easier than any other marketing and communications firm in the industry. For more information, contact LifeSciencePR at (800) 724-2372 or visit **www.LifeSciencePR.net.**

Technology & Services Showcase

Development/Clinical Trial Manufacturing

LYOPHILIZATION TECHNOLOGY, INC.
Integrating Science and Technology

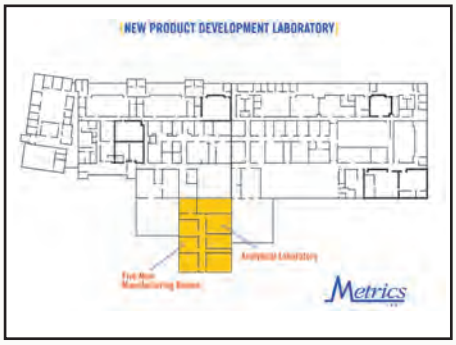
Lyophilization Technology, Inc. (LTI) provides Development and Clinical Trial Material Manufacturing services to biotechnology and pharmaceutical clients spanning virtual, small, and large multi-national companies. Experience with a diverse range of products, including small molecules, cytotoxics, biologics, highly potent compounds, vaccines, medical devices, and diagnostic agents, LTI has developed formulations, manufacturing processes and prepared material for clinical trials. The operation is able to process a broad range of container closures, including 2-mL to 160-mL vials, 1-mL to 50-mL cartridges/syringes, bulk trays, and unique devices for batch sizes up to 75 L. Services consist of thermal analysis, product design, formulation development, process design/refinement, product characterization, preparation of preclinical through Phase II clinical supplies, along with technical consultation, technology transfer, validation, product/process evaluation, troubleshooting, streamlining operations, auditing, and training. For more information, contact LTI at (215) 396-8373, inquiry@lyo-t.com or visit **www.lyotechnology.com**.

Development & Manufacturing

Norwich
PHARMA SERVICES

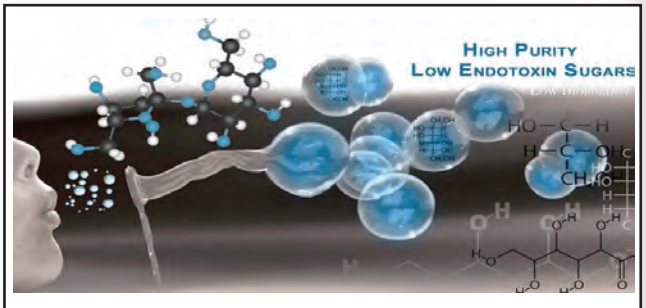
Norwich Pharma Services is a recognized leader in full-service contract pharmaceutical development and manufacturing. Through its Synchronized Outsourced Solutions, Norwich offers customers a single source with the highest level of quality and reliability from product development to scale-up and commercial manufacturing through clinical services. By offering complete services for a product's entire lifespan, Norwich provides your project with an efficiency and consistency of service that helps bring it to market faster and more cost-effectively. For over 126 years, Norwich has built a reputation for dependable product supply and established an unparalleled history of regulatory compliance. For more information, visit **www.norwichpharma.com**.

Product Development Lab



Metrics is making significant investments in facilities and equipment for the benefit of contract services clients with a new laboratory to better support fast-track development of pharmaceutical products. The $1.6-million, 4,524-sq-ft facility provides maximum flexibility for early formulation and analytical method development. The facility is designed for preclinical development of early formulation prototypes and related analytical methods. In this laboratory setting, formulators and chemists will have significant autonomy to conduct development activities more quickly. Segregated from the main Metrics operations and containing fully dedicated equipment, these new processing suites have independent HVAC systems and state-of-the-art engineering controls, such as interlocking airlock doors, room air pressure differentials, high-volume room air turnover, and 100% HEPA air filtration. For more information, visit Metrics Inc. at **www.metricsinc.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**.

Technology & Services Showcase

Knowledge Management

PharmaCircle is an innovative knowledge management company specializing in the drug delivery, pharmaceutical, and biotechnology fields, with a current client base ranging from start-up life science companies to world leaders in Big Pharma. Clients choose PharmaCircle's services and content for its comprehensive technical (pipeline, products, molecule, and technology) and business (deals, acquisitions, royalty, licensing, drug revenues, market information, etc) related information and analysis, which are ideal for all segments of small and large companies. PharmaCircle helps facilitate product life cycle management (LCM), partnering, licensing, and competitive intelligence efforts as well as supplements internal efforts and costs at a fraction of the cost if performed internally. For more information, contact PharmaCircle at (920) 850-3056 or visit **www.pharmacircle.com**.

Molded Dosage Forms & Combination Products

For over 20 years, ProMed Molded Products has specialized in the molding of small, intricately designed silicone and thermoplastic components. In 2006, ProMed Pharma leveraged this expertise to begin production of polymer-based drug-releasing implants and combination devices. Working with both established and early stage medical device and pharmaceutical companies, we develop robust manufacturing processes and platforms for controlled release of drugs utilizing a variety of materials. Representative drug-device applications include steroid-eluting pacing and defibrillation leads, drug-eluting stents and balloons, antimicrobial catheters, and orthopedic implants. From preclinical materials to fully packaged products, ProMed supports pharmaceutical companies in the contract manufacturing of extended-release formulations utilizing subcutaneous implants, intrauterine devices, intravaginal rings, and ophthalmic implants. For more information, contact Jim Arps at jim.arps@promedpharmallc.com or visit **www.promedpharmallc.com**.

Glass-Lined Plastic Containers

With an increasing focus on the safety and quality of injectibles, SiO2 Medical Products (SiO2) has taken a new approach in parenteral packaging. SiO2 manufacturers primary containers precision-molded from medical-grade plastics, with a thin interior coating of glass deposited using a unique plasma coating technology. Our containers combine the favorable properties of both glass and plastic. SiO2 is privately held and supported by CV Holdings, LLC, an organization with 90 years of experience developing and manufacturing packaging for medical and diagnostic applications worldwide. SiO2's newly constructed 160,000-sq-ft manufacturing facility in Auburn, AL, has three 10,500-sq-ft ISO Class 7 clean rooms, dedicated to development and manufacturing of coated containers. SiO2's commercial facility is fully equipped with analytical and mechanical laboratories. For more information, please visit SiO2 at **www.sio2med.com**.

Intranasal Vaccine Delivery

Teleflex Medical is a global provider of medical devices with over 20 years' experience servicing OEM partners with bespoke device requirements. The Teleflex VaxINator™ is an easy-to-use and cost-effective solution for intranasal drug delivery. The droplet size output of the VaxINator allows for drug coverage across the anterior and posterior areas of the nasal cavity, thereby facilitating rapid adsorption. The VaxINator is a syringe-and-atomizer-based system, and a range of accessory items are available to meet your intranasal drug delivery needs. At Teleflex, we are committed to investing significant time and effort into demand planning and risk mitigation to ensure high-quality product supply when you need it and where you need it. For more information, including contact details, visit Teleflex Medical at **www.vaxinator.com**.

Technology & Services Showcase

Wearable, Disposable Injectors

Unilife has developed a flexible, scalable portfolio of wearable, disposable injectors for the subcutaneous delivery of large-dose volume therapies with optimal patient comfort and convenience. Multiple customization options are available to address specific therapeutic, operational, branding, and patient needs, including dose volume and controlled bolus, constant or variable delivery duration rate. Each device leverages human factors data with target patient populations to provide a highly intuitive, effective, and confident user experience. Designed for seamless integration with approved manufacturing methods and primary container materials, Unilife is ready to support customer needs for the commercialization and lifecycle management of their injectable therapies. For more information, call (717) 384-3400, email info@unilife.com ,or visit **www.unilife.com**.

Clinical Development Services

Vetter Development Service (VDS) provides expert support for your drug development projects, from inception to market launch. Our services include state-of-the-art clinical manufacturing at our facilities in Chicago and Europe, with scale-up and transfer to our large-scale manufacturing facilities. Thanks to the latest technology and innovative processes, we help increase your API yield. Vetter Development Service provides Formulation Support, Process Development, Clinical Trial Manufacturing, Analytical Service, and Regulatory Support. For US inquiries please contact +1-847-581-6888 or infoUS@vetter-pharma.com.
For EU inquiries please contact +49-751-3700-0 or info@vetter-pharma.com.
Visit **www.vetter-pharma.com** for more information.

West PFS Solutions

You need prefillable syringe systems and components designed to compete in an evolving industry. You need the management, expertise, and support of a manufacturer capable of creating systems and components that will mitigate risk and differentiate your product. Pharmaceutical and biopharmaceutical customers trust West to provide prefillable syringe systems and components that help bring products to market safely, reliably, and with the integrity you've come to expect. West works side-by-side with top pharmaceutical and biotechnology companies to design and manufacture drug packaging and delivery systems that bring injectable drugs from concept to the patient efficiently, reliably and safely. Our global technical expertise and services provide solutions that are true to our core goal of reducing regulatory risk while ensuring quality and patient safety. So you can rest easy. Pictured above is West's prefillable syringe solutions that include the Daikyo Crystal Zenith® 1-mL long insert needle syringe system. For more information, contact West at (800) 345-9800 or visit **www.WestPFSsolutions.com**.

CDMO Services

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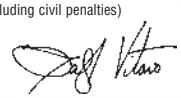

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