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

Pierre Carlotti
Aptar Pharma: From Self-Injection to Auto-Injection

Adam Dion, MS
Financial Performance Benchmarking & Competitive Landscape Assessment of Leading CROs

Debbie Toscano
The Market for Type 2 Diabetes Therapeutics - Key Findings From a Recent Analysis

IN THIS ISSUE

INTERVIEW WITH CATALENT PHARMA SOLUTIONS' CTO & SVP INNOVATION & GROWTH

KURT NIELSEN, PHD

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November/December 2013 Vol 13 No 9

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Table Of Contents

Departments

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  - > From product feasibility to commercial supply
  - > Decreased tech transfer risk
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North American Drug Delivery Technologies Market Worth $102.2 Billion by 2017

Patent expiry of major blockbuster drugs is a prime concern for pharmaceutical companies, as developing a new chemical entity (NCE) is more expensive and time consuming than a novel drug delivery technology. Therefore, in recent years, several pharmaceutical companies have employed drug delivery technology as a life cycle management tool for some of their blockbuster drugs, the patents for which are set to expire in the near future.

The North American drug delivery market was estimated to be worth $66.7 billion in 2012, and is expected to register a CAGR of 8.9% between 2012 and 2017, according to the latest MarketandMarkets report. Based on the route of administration, the drug delivery market has been classified as oral, pulmonary, injectable, transdermal, implantable, ocular, nasal, transmucosal, and topical. In 2012, oral drug delivery segment dominated the market with a share of approximately 38%, followed by pulmonary drug delivery segment with a 20% share.

The drug delivery technologies that have recently gained importance in the North American market include orodispersible tablet (ODT), dry powder inhalers, transdermal patches, needle-free injectors, auto and pen injectors, and buccal transmucosal tablets; controlled release is the most widely accepted technology. The use of implantable devices for drug delivery is also on a rise.

Big pharmaceutical companies such as Pfizer and Merck have established in-house capabilities for the development of drug delivery technologies. On the contrary, many other companies are still relying on specialty companies engaged in the development of drug delivery technologies. High level of competition and increasing need for outsourcing has resulted in the drug delivery market to be fragmented, with several small companies developing novel drug delivery technologies for niche therapeutic applications.

The North American drug delivery market is largely dominated by the US (accounting for about 89% of the overall market). The key drivers for the US drug delivery market are the well-established pharmaceutical industry, healthcare reforms, and favorable changes in the FDA review process. Factors such as low-cost drug manufacturing and rising number of drug delivery formulations and devices are propelling the Canadian market.

British Pharmaceutical Market to Reach $31.7 Billion

A growing disease burden, universal coverage, and good access to healthcare facilities are boosting the UK healthcare market; but increasing use of generics and government cost-cutting measures to reduce expenditure are restricting further growth, says research and consulting firm GlobalData.

According to the company's latest report, the UK pharmaceutical market was worth $24 billion in 2012 and is forecast to reach $31.7 billion by 2020, at a Compound Annual Growth Rate (CAGR) of 3.5%. The segments that dominated the market in 2012 were Central Nervous System (CNS) drugs, along with cardiovascular and respiratory system drugs.

The medical device market is also forecast to grow, from $12 billion in 2012 to $17.5 billion by 2020, at a CAGR of 4.8%. In 2012, the major market shares were ophthalmic devices ($1.4 billion), orthopedic devices ($1.4 billion), wound care management ($1.1 billion), cardiovascular devices ($1.1 billion), and drug delivery devices ($1 billion).

However, increasing generic substitution and cost-cutting measures adopted by the British government and the National Health Service (NHS) have had a negative impact on market growth. In 2013, the Department of Health announced plans to cut drug prices by 10% to 20% on approximately 10% of branded medicines not covered by the voluntary Pharmaceutical Price Regulation Scheme (PPRS).

The report, CountryFocus: Healthcare, Regulatory and Reimbursement Landscape – UK, provides an analysis on the healthcare, regulatory, and reimbursement landscape of the UK; it identifies the key trends in the healthcare market and provides insights on the demographic, regulatory, and reimbursement landscape and healthcare infrastructure. Most importantly, this report provides valuable insights on the trends and segmentation of the pharmaceutical and medical devices markets. This report was built using data and information sourced from proprietary databases, primary and secondary research, and in-house analysis conducted by GlobalData's team of industry experts.

Bright Future Ahead for Biopharmaceutical Contract Manufacturing

Considerable growth opportunities lie ahead for biopharmaceutical contract manufacturing organizations (CMOs). With blockbuster biologics worth over $100 billion due to lose patent protection by 2019, the global biosimilars market is projected to grow at a robust compound annual growth rate (CAGR) of 60.4% between 2012 and 2019.

A new market insight from Frost & Sullivan, Biopharmaceutical Contract Manufacturing, finds advances in bioprocessing technologies, as well as innovation in biopharmaceuticals production with transgenic plants and animals, stem cells, and cloning, are likely to have a direct impact on the market.

Disposable technology is a key biomanufacturing trend and presents attractive opportunities for minimizing production costs, owing to its customizable design, enhanced productivity, and significant operational benefits. Disposable equipment and single-use bioreactors are considered a viable alternative to conventional stainless steel equipment, due to their flexibility, short start-up time, quick changeover between production campaigns, and absence of Clean in Place, Steam in Place, and large volumes of Water for Injection. Single-use technologies are specially designed for multi-product contract manufacturing with additional benefits, such as simple transfer of operations between sites and their ability of being easily expandable for larger volumes.

Advances in upstream and downstream processing technologies will also impact the industry. With 20% of biotech manufacturing costs accounting for upstream processing activities, and 40% for downstream ones, most companies and CMOs are gearing up to adopt new technologies to optimize efficiency. In 2011, the global industry witnessed a 6.2% budget increase for integrating new technologies in upstream processing. Reduction of quality variability in the product – impurities, such as aggregates, glycosylation variants, and so forth - and cell viability will be the key focus areas of upstream processing in biomanufacturing. Downstream processing technologies follow two different trends specific to mAbs and recombinant proteins, specifically in the purification processes. In the next 5 years, exploration of alternative purification methods will be crucial for CMOs.

Advances in lyophilization and increasing applications of process analytical technology (PAT) will also attract attention. Innovations such as automated loading processes into the dryer in place of manual loading contribute to minimizing human error and maximizing productivity. Also, manufacturers increasingly prefer the implementation of PAT and standardization of their processes, rather than relying on the validation of finished products. Near infrared spectroscopy (NIR) is one of the latest technologies that provides potential real-time control of cells in fermentation, specifically in mammalian cell culture processes. The significant enhancement of purity levels and product efficiency are expected to drive the demand for this novel technology throughout the forecast period.

Mammalian cell-based contract manufacturing is expected to sustain the industry's future expansion. This segment currently constitutes nearly two thirds of the sales revenue of the global biopharmaceutical contract manufacturing market and is anticipated to grow as high as 65% over the next 5 years, at a significantly higher rate than microbial cell-based contract manufacturing segment.

Increasing adoption of the Large Molecules model by big pharma companies will also boost prospects. Of the top 15 pharmaceutical companies, nearly 80% are expected to experience a net growth in their biologics portfolio. The big pharma shift to large molecules will likely be led by monoclonal antibodies (mAbs) and is projected to grow at a CAGR of 10.8% from 2012 to 2017.

Companies will also increasingly outsource crucial operations and will seek to adopt an integrated/risk-sharing business model. The aim is to provide a "one-stop-shop" option for the biopharmaceutical companies, where they can exploit the resources and expertise of the CMOs to reap maximum benefits, while they concentrate on their core capabilities and R&D activities.

Industry consolidation in the form of mergers, acquisitions, and strategic alliances between CMOs, biopharmaceutical companies, and technology providers are likely to increase, so as to gain access to newer geographies, niche product segments, and latest technologies. Targeting the right market niches will be crucial for long-term sustenance.

Greek Market to Show Modest Growth; Indian Market to Reach $56 billion

The growing prevalence of chronic diseases and an increasing elderly population will boost the Greek pharmaceutical market, which will increase from approximately $7.8 billion in 2013 to $8.2 billion in 2020, at a Compound Annual Growth Rate (CAGR) of 0.6%, forecasts research and consulting firm GlobalData.

According to the company's latest report, CountryFocus: Healthcare, Regulatory and Reimbursement Landscape – Greece, the Greek pharmaceutical market was valued at $7.5 billion in 2007; but, following the recent economic crisis, net public pharmaceutical expenditure saw a cumulative decline of $1.67 billion. This decline was due to amendments made to medicine prices, as well as changes to the reimbursement rates for Social Security Funds (SSFs) and to the regulation of wholesale and retail margins.

The medical device sector will also experience modest growth, from $907 million in 2007 to $1.2 billion in 2020, at a CAGR of 2.7%. The major segments in 2012 were In Vitro Diagnostics (IVD) (20.8%), cardiovascular devices (11.6%), ophthalmic devices (9.7%), drug delivery devices (7.6%), and diagnostic imaging (7.4%).

However, the Greek government has introduced several policies in order to strengthen its free healthcare system and help improve patients' health outcomes and quality of life in the long run.

Driven by the country's growing economy and population income, the Indian pharmaceutical market will increase significantly from approximately $21 billion in 2013 to $56 billion in 2020, at a Compound Annual Growth Rate (CAGR) of 15%, forecasts research and consulting firm GlobalData.

According to the company's report, CountryFocus: Healthcare, Regulatory and Reimbursement Landscape – India, the medical device sector will also experience steady growth from $7.5 billion in 2013 to $15.3 billion in 2020, at a CAGR of 11%. In 2012, the main segments were ophthalmic devices (38.3%), In-Vitro Diagnostics devices (9%), hospital supplies (8.9%), and cardiovascular devices (8.1%).

Still, the lack of transparency in the Indian drug regulatory system and weak patent laws are a major challenge for foreign multinational companies attempting to enter or expand in the Indian healthcare market.

However, there is also a need for India to improve its healthcare infrastructure in rural areas and expand its universal health coverage, since 80.6% of the population was not covered by any form of health insurance in 2012 - a factor which could hinder further growth of the market.

MARKET BRIEF

Financial Performance Benchmarking & Competitive Landscape Assessment of Leading CROs

By: Adam M. Dion, MS

Highlights from GlobalData's recently published report - PharmaLeaders: CRO Benchmark Report: Financial Performance Benchmarking & Competitive Landscape Assessment of Leading CROs

INTRODUCTION

The biopharmaceutical industry is currently facing significant headwinds. The blockbuster era is over, development costs are skyrocketing, uncertainty exists around regulatory and reimbursement, patent cliffs, generic erosion, and a sluggish global economy all have industry executives losing sleep at night. To respond to these pressures, biopharmaceutical companies have been changing the way they approach virtually every aspect of their business, including research and development. To remain competitive, drug makers are intensely focusing on generating more value and productivity out of every dollar spent on R&D. The challenge of accelerating pharmaceutical product development while controlling costs creates a difficult balancing act for industry executives. Through the use of strategic outsourcing with third-party vendors, drug makers can maximize their internal resources while at the same time entering into risk-sharing agreements with CROs to generate significant cost savings.

CRO SECTOR POSTED STRONG GROWTH IN 2012

According to GlobalData's 2013 CRO Benchmark Report, the total combined peer group revenue from these leading CRO companies increased 10.2% year-to-year, from $12.4 billion in 2011 to $13.6 billion in 2012. Largely fueling the growth in the CRO sector was Quintiles, which independently contributed approximately $397 million to the $1.2-billion peer group increase.

Quintiles' revenue grew by 12.1% year-on-year to $3.7 billion in 2012, considerably larger than its next closest rival, Covance, at $2.1 billion. Quintiles was effective at turning its order backlog into revenue, and garnering new orders in its clinical services business especially in markets abroad, in Europe and Asia. In fact, most of the companies in this report saw positive year-on-year growth rates in 2012, ranging from 4% (Covance) to 22.8% (WuXi), with the exception of Charles River, which saw a slight year-on-year revenue decline of 1.1% largely due to unfavorable foreign exchange rates. The sector posted strong growth in 2012, outpacing the 6.8% increase in aggregate corporate revenue the same peer group recorded in 2011.

Strategic acquisitions and partnerships carried out by CROs also helped to drive revenue higher for the peer group. Just before the close of FY12, Patheon completed its $269-million deal to acquire Banner Pharmacaps, one of the world's largest manufacturers of proprietary softgel capsules for the pharmaceutical and nutrition industries. The purchase of Banner fills gaps in Patheon's current product lines and also expands its geographic reach into markets in Mexico and Latin America.

Catalent Pharma Solutions made significant investments in its clinical trial business when it bought Aptuit's Clinical Trials Supplies (CTS) business in February for $410 million. The all-cash transaction transformed Catalent into one

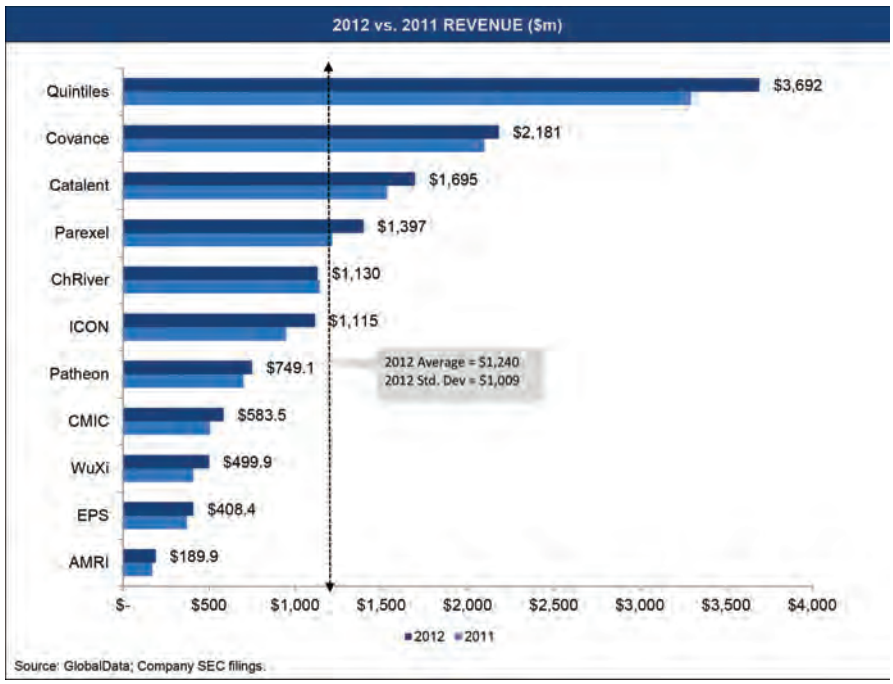
of the largest global providers of clinical supply solutions and adds analytical chemistry, respiratory product development, and regulatory consulting services to its mix. The private CRO sector also saw its fair share of acquisitions.

Clinipace Worldwide broadened its therapeutic expertise and regional footprint in Europe with its buy of Paragon Biomedical. Known principally as an oncology CRO, Clinipace will now have the talent and resources to offer its clients services for managing clinical trials in the areas of immunology, infectious disease, cardiovascular, and CNS. While traditionally known for its work in IT outsourcing, the industry giant Accenture purchased Octagon Research Solutions, complementing its data management capabilities with Octagon's proprietary software platform and deep regulatory knowledge.

CROS FOCUSING ON DELIVERING SERVICE VALUE TO SMBS

CROs are adding new capabilities specifically aimed at helping small and mid-sized biopharmaceutical companies (SMBs) optimize value and minimize risk. In a post-patent cliff world, small and mid-size pharma and biotech companies will become the heart and soul of the drug industry, and will be responsible for the lion's share of the innovation the industry will see in the future. GlobalData believes CROs are ramping up their services to meet the requirements of small and mid-size pharma and biotech companies, who tend to have varied needs and much smaller budgets compared with their Big Pharma brethren, hence requiring different outsourcing strategies.

FIGURE 1

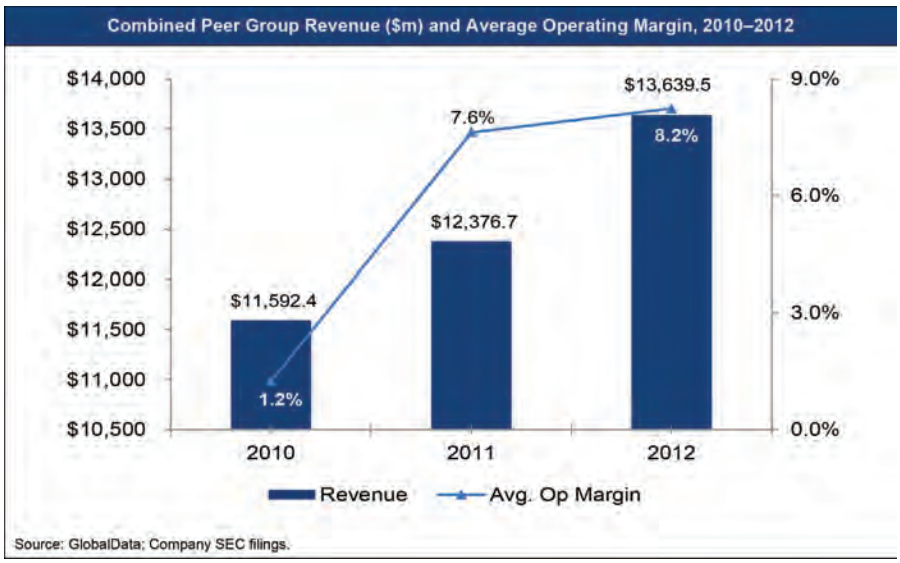


CRO revenue in 2011 and 2012. As anticipated, Quintiles remained the leading CRO based on sales revenue.

Allume is a comprehensive go-to-market service introduced by Quintiles that combines consulting, clinical services, commercial expertise, and information technology. The service helps SMBs efficiently launch new products and shorten timelines to peak sales, while retaining strategic and corporate control of their assets. Biopharma companies are looking for new ways to optimize product value, expedite market access, and mitigate commercialization risk. Allume Quintiles achieves this by simplifying and organizing the complex, resource-intensive launch planning process, leaning on Quintiles' 15 years of market entry experience. To maximize value, companies must plan product launch much earlier in the drug development process, especially when preparing to enter new geographic markets. Through Allume, Quintiles provides the strategic thinking, deep therapeutic insight, and local market access knowledge to help its customers design roadmaps to navigate a pathway to successful commercialization.

Not surprisingly, Parexel followed suit. However, instead of launching a service line, Parexel created the Parexel BioPharm Unit – a dedicated division of the company to focus solely on the unique needs of small and mid-sized biopharmaceutical companies to help them achieve their development goals. Parexel's internal research has found that 81% of all on-going development programs are originating from sponsors outside of the top 25 pharmaceutical companies – a significant growth opportunity that Parexel wants to capitalize on with its new delivery model. Under a collaborative team-based approach, Parexel's BioPharm Unit provides SMBs the opportunity to accelerate patient recruitment, increase the speed of study start-up, and

FIGURE 2



The total combined peer group revenue from these leading CRO companies increased 10.2% year-to-year, from $12.4 billion in 2011 to $13.6 billion in 2012.

improve overall efficiency for meeting critical development milestones.

EVOLVING STRATEGIC PARTNERSHIP MODEL

Throughout the past 5 years, a wave of strategic partnerships between biopharmaceutical companies and CROs has been put in place to drive more flexibility, reduce costs, and extend expertise. Collaborations have evolved from simple transactional relationships into multi-year, highly integrated strategic engagements focused on shared objectives, mutual investment, and involvement in clinical trial design and drug plan development. The growth of contract research outsourcing will primarily be driven by the need of biopharmaceutical companies to improve research and development in mature and emerging markets. Today, many biopharmaceutical companies are engaging clinical research organizations through this more integrated approach, aimed at optimizing performance and minimizing risk.

According to GlobalData's Pharma eTrack, the number of licensing deals fell slightly, from 40 in 2011 to 36 in 2012, the total licensing deal value soared to $958.9 million in 2012, a 159% increase when compared with 2011. We attribute the growth in deal value to a number of significant partnerships being struck throughout the past few years for which contract revenues are now beginning to be realized.

GlobalData believes that strategic partnerships provide companies with higher levels of integration, alignment, and collaboration that will support industry success. Merck engaged Quintiles in a 5-year clinical development collaboration to essentially reshape its entire R&D machine.

The pharma giant just announced a major shakeup to streamline its operating model and aggressively manage its cost structure. The company spent $8.2 billion in R&D in 2012 (which was down from $11.1 billion in 2010), yet has very little to show for it, as the company has a very weak late-stage pipeline. However, GlobalData expects the partnership with Quintiles will play a major role when the company reviews its R&D apparatus this year.

Covance was also busy signing deals with large pharma outfits. Throughout the past couple of years, Covance booked multi-year outsourcing deals with Bayer Healthcare, Eli Lilly, and Sanofi to conduct a variety of market access and R&D services, including discovery support, toxicology, central lab, and managing Phase I-IV clinical trials. Over the next 10 years, Covance will be paid handsomely for its work. The contracts from these three drug makers alone will add close to $4 billion to the company's coffers.

BRICS & OTHER EMERGING REGIONS REPRESENT HUGE UNTAPPED MARKETS FOR CLINICAL R&D

With lower overall costs, better recruitment and retention rates, strong investigator networks, and populations in need of novel treatments, conducting studies in the emerging markets is a strategic necessity. Biopharmaceutical companies with less experience in conducting trials in the emerging markets may need on-the-ground expertise to ensure their project is tailored to local patients and complies with regional regulations. Other drug makers that already have the experience in the region may need operational support or advice on how to ensure locally conducted trials satisfy the needs of global regulatory bodies, to mitigate costly clinical trial disruptions. CROs with the

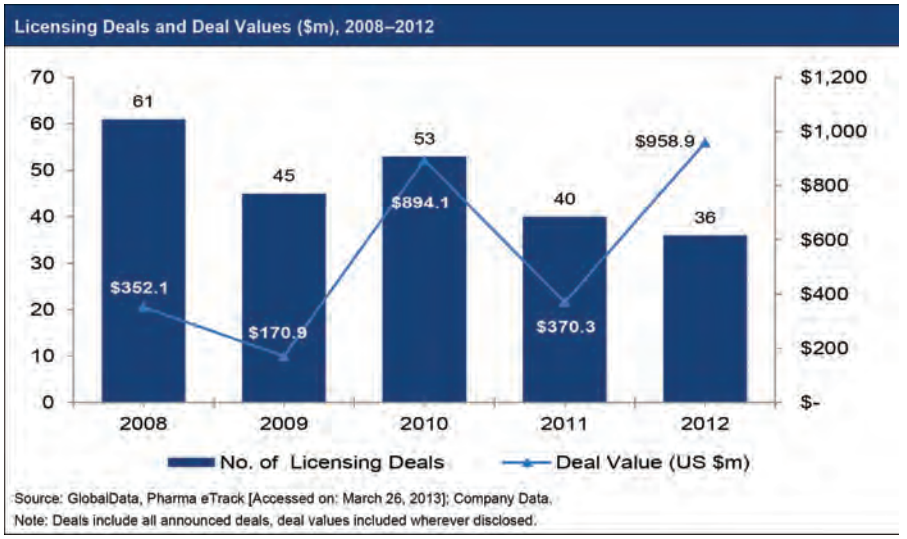
ability to deliver cost- and time-saving efficiencies to clients without compromising patient safety and data quality will be able to yield higher returns from emerging markets.

The emerging markets in Asia and Eastern Europe have become attractive regions for pharmaceutical outsourcing due to easy access to large patient pools, low labor and manufacturing costs, and highly skilled medical research talent. However, due to regional differences in commercialization and regulatory pathways, the need to partner with local expertise is a critical plank in any company's globalization strategy.

For instance, AstraZeneca (AZ) formed a strategic partnership with Beijing's Pharmaron, a provider of R&D services for the pharmaceutical and biotech industries. AZ inked the multi-year drug discovery deal with Pharmaron in October 2012 for services in the area of chemistry, drug metabolism and pharmacokinetics, and efficacy screening. Pharmaron will conduct these services with a team consisting of several hundred scientists at its newly opened state-of-the-art research laboratory in Beijing. GlobalData expects the services provided, combined with the close proximity of the Pharmaron staff, will open communication channels with AZ scientists, therefore helping them drive their drug development programs with greater efficiency and transparency.

One of the fastest-growing emerging markets for clinical trial work outside of China is South Korea. According to Outsourcing-Pharma.com, the number of clinical trials initiated in South Korea increased from 206 in 2006 to 513 in 2009, a 150% increase throughout the 4-year span. While Korea's pharmaceutical industry is competitive in terms of chemical and synthesizing technologies, it is considered less competitive in drug screening, safety evaluation, and clinical development. Therefore, companies have found partnering to be an ideal way in which to become more involved in R&D.

FIGURE 3

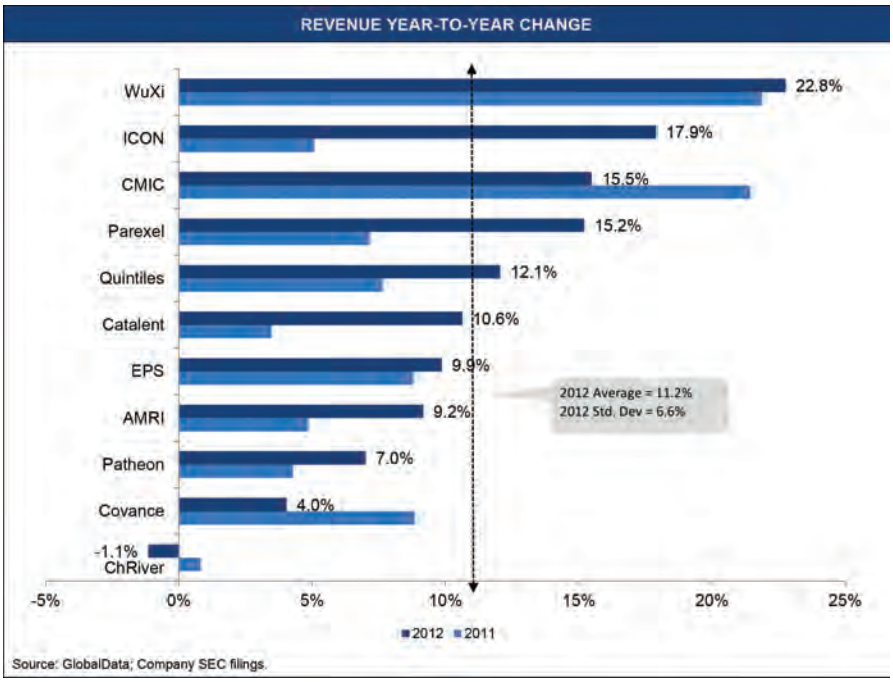


While the number of licensing deals fell slightly, from 40 in 2011 to 36 in 2012, the total licensing deal value soared to $958.9 million in 2012, a 159% increase when compared with 2011.

To enhance its bioanalytical service offerings in Korea, Quintiles announced an exclusive partnership with BioCore, a leading Seoul-based bioanalytical CRO. BioCore is South Korea's largest provider of bioanalytical liquid chromatography-tandem mass spectrometry services. BioCore was South Korea's first GLP-compliant certified bioanalytical CRO, and the first to be certified by Korea's Food and Drug Administration. Under the 2-year agreement, BioCore will provide Quintiles with liquid chromatography and mass spectrometry services. The partnership with BioCore is part of Quintiles' plan to add local capabilities as needed in order to gather high-quality bioanalytical data earlier in clinical development, which is crucial for biopharmaceutical companies making informed decisions that increase their probability of success in more expensive later-stage trials.

In March 2013, PRA announced it had acquired ClinStar, LLC, a privately held CRO that manages Phase I-IV clinical research trials in Russia. ClinStar is the largest independent, geographically focused CRO in Eastern Europe, providing clinical development services to a wide range of pharmaceutical and biotechnology companies. GlobalData believes the ClinStar acquisition illustrates PRA's dedication to support its growth in Russia and in Eastern Europe. The purchase is well-aligned with PRA's goals of meeting the needs of its clients by establishing a stronger presence with one of the most well-established CROs in the region. The acquisition will include ClinStar's stand-alone clinical trial warehousing and logistic division, IMP Logistics, which has operations

FIGURE 4



Year-to-year revenue growth by company, with Chinese WuXi AppTec leading. WuXi's net revenues increased to $499.9 million in 2012, a 22.8% increase from the $407.2 million the company reported in 2011.

in Russia, the Ukraine, and in Belarus. Through IMP Logistics, PRA will now be able to offer its clients top-quality cold chain logistics services that include the importation of investigational products, clinical supplies, laboratory kits, and storage in multiple temperature zones. GlobalData expects PRA to integrate the approximately 300 ClinStar and IMP Logistics employees, thereby augmenting its operations and expertise to create a significant competitive advantage in the region.

Two niche CROs based in the US grew their respective footprints in emerging European markets. BioRasi completed its acquisition of Sponsors Clinical Research Group (SCRG), a CRO based in the Ukraine, established in 2004. SCRG has been conducting clinical studies in various therapeutic areas, including cardiology, neurology, oncology, endocrinology, and pulmonology. The business combination enhances BioRasi's geographic footprint, addressing the ever-increasing demand for optimizing global clinical trials. The purchase will also build upon BioRasi's presence throughout Eastern Europe, which currently includes a site in Moscow, Russia.

Meanwhile, QPS a Delaware-based CRO, bought a controlling stake in JSW, Austria's largest provider of drug development services, focusing on central nervous system disorders, such as Alzheimer's, Parkinson's, and Huntington's diseases, and schizophrenia. While the financial terms were not disclosed, all of JSW's business will be conducted under the QPS-JSW moniker from here on out. QPS' acquisition of JSW added to the company's capabilities in Phase II-IV drug development and expanded its market share in Central and Eastern Europe.

SUMMARY

GlobalData believes the dynamics of pharmaceutical outsourcing and location decisions in emerging markets are changing. Cost reduction is being augmented and will gradually be eclipsed by footprint growth as a major factor shaping decisions. CROs are realizing that the ability to be on the ground closer to their customers is a key building block to establishing sustainable, long-term relationships with clients. With the economic balance shifting from mature markets in the west to emerging markets in the east, regions in Southeast Asia, like Singapore, South Korea, Taiwan, and Vietnam, have become important destinations for conducting clinical trials. Singapore, for example, is often considered the nucleus for clinical research in the Asia-Pacific region - with mainland China and the Korean peninsula to the north and Australia and Oceania to the south, Singapore is a natural hub for clinical outsourcing. The government of Singapore promotes translational and biomarker research and it has put in place laws protecting intellectual property and adheres to Good Clinical Practice (GCP) guidelines, offering a sense of security and assurance to pharma clients looking to conduct trials in the country. However, with a small patient pool, clinical trial opportunities in Singapore (and small countries like it) are limited to mostly Phase I/II trials, leaving the heavily populated countries of China and India to grab the bulk of late-stage trials where large patient numbers are required.

The Chinese CRO market has been rapidly growing throughout the past few years as Big Pharma looks to tap into the region's burgeoning drug market. However, pharmaceutical companies and service providers are entering China (and certainly India) with caution, and for good reason. Both countries have lax standards around patient safety, which is of concern to pharmaceutical companies looking to conduct clinical trials. While both India and China offer access to large pools of treatment-naïve patients and cheap labor, each country's regulatory structure lacks the transparency seen with the US and EU agencies, and both are riddled with hurdles. China and India offer byzantine regulatory regimes that make each country far more complicated than originally thought. As a result, the labor savings is China and India is commonly juxtaposed with longer approval timelines for bringing a drug to market. This is beginning to change how pharmaceutical companies and CROs do business in these regions.

REPORT DESCRIPTION

GlobalData's PharmaLeaders: CRO Benchmark Report: Financial Performance Benchmarking & Competitive Landscape Assessment of Leading CROs - applies GlobalData's proprietary ranking methodology to compare the competitive position of 11 leading CRO companies on 17 financial metrics. These companies are analyzed based on financial performance, cost-containment, capital structure, and firm utilization to illustrate the different strategies these companies are using to gain a competitive advantage.

In addition to the financial metrics, this report discusses trends impacting the CRO marketplace, along with partnering and acquisition activity, and operations strategy. This report also provides a drill-down analysis of three service lines and four geographies to examine each segment's revenue and growth leaders. Lastly, this research provides GlobalData's outlook on the CRO sector and each company's future competitive position.

GlobalData's PharmaLeaders report series is targeted to both the scientific and investor communities. Clients that have leveraged these reports come from industry R&D and strategy teams, private equity and venture capital firms, and professional and financial services consultancies.

Companies Financially Benchmarked: AMRI, Catalent, Charles River, CMIC, Covance, EPS, Icon, Parexel, Patheon, Quintiles, and WuXi

Other Companies Covered: Accelovance, Accovion, Aptuit, Asklep, BioRasi, Chiltern, Clinipace, ClinStar, CromSource, DKSH, Frontage, INC Research, Novella Clinical, Novotech, Ockham, Octagon Research Solutions, Paragon Biomedical, Pharmaron, Pharm-Olam, PPD, PRA International, PSI, QPS, ReSearch Pharmaceutical Services, Synexus, Syngene, SynteractHCR, and TFS International ◆

BIOGRAPHY

Adam M. Dion is an Analyst in the Healthcare Industry Dynamics Team at GlobalData. Mr. Dion is an author of GlobalData's PharmaLeaders benchmark reports, which rank the competitive positions of the top companies in the pharmaceutical, biotech, and CRO/CMO sectors. He is the lead author of the Pharmaceutical Benchmark Report and the Innovative Mid-Cap Biotech Benchmark Report and also provides coverage of trends in the healthcare IT space, including mHealth and cloud computing. Prior to joining GlobalData, Mr. Dion was an Analyst with Technology Business Research, a leading market research and consulting firm. In this role, he was responsible for coverage of blue-chip hardware, software, and BPO companies, such as Dell, Apple, SAP, Acer, Wipro, and Tata Consultancy, analyzing these companies' go-to-market and vertical integration strategies, financial forecasting, and competitive benchmarking. He also has been involved in a number of primary market studies in the consumer space, analyzing the market penetration of tablets, Netbooks, e-readers, and mobile devices. His analytical commentary has been quoted by leading sources, such as The Wall Street Journal, Bloomberg, Forbes, Financial Times, The Guardian, PharmaLive, CenterWatch, FierceCRO, Outsourcing-Pharma, Drug Discovery News, ComputerWorld, and eWeek. Mr. Dion earned his BS in Neuroscience from Merrimack College, and MS in Marketing from the University of New Haven. For commentary, he can be reached at adion@globaldata.com.

Management Insight

Up Against the Wall: What You Need to Know Before Digging Into Your Next Building Expansion

By: Derek Hennecke, CEO & President, Xcelience LLC

Business is booming. Customers keep coming, and you're hiring to keep up. That's great! Growth is good. I gotta warn you though, it's only a matter of time. You're going to come up against the wall. I mean that quite literally. You're going to reach a point where your walls are holding back your growth. Either you build more, or you can't grow anymore.

Maybe you'll be lucky and find a turnkey building, but in our industry, that's unlikely. If you find one, it'll be an older pharma plant that's being shorn from the series of mergers. These facilities tend not to be of the same quality as a fresh build and may not have kept up with European standards, such as having airlocks in front of the clean rooms. You're probably going to have to build.

At Xcelience, we put off that fateful moment for as long as we could. During the recession, we could only justify buying new equipment to boost capacity and capabilities. We re-arranged offices, squeezed in new rooms, and built to the outer most edges of our property rights. With the decision to launch clinical packaging and distribution in late 2011, we had to have more space. A lot of it. I scoped the property market, chose an old warehouse on Grace Street a few blocks

away, and got to work.

A few months after the ribbon cutting on Grace Street in November 2012, I came across a book I wish I'd had in my pocket in 2012. Written by the owners of Hodess Building Company, *Straight Answers to the 20 Questions Building Contractors Hope You'll Never Ask* is a nuts and bolts discussion of how the construction industry works and what you need to know to avoid costly mistakes. This column mixes my own experience with Hodess's advice, as well as providing insights into the surprising number of similarities between project management in construction and in a CDMO like ours.

CONSTRUCTION MANAGER OR GENERAL CONTRACTOR?

A Construction Manager (CM) is like a project manager. He is your decision-making partner - the one with years of construction experience. A General Contractor (GC) costs less because he reports to you. If you go the GC route, you'd better have a lot of time and experience in building. You could save money by going the GC route, but you also increase your risk. Proceed with caution.

By the time we were ready to get to work on Grace Street, we knew just enough about building to know how much we didn't know. We took the CM route. In our case, it was the right choice.

Here's an example of the difference between a CM and a GC. One of the walls of the existing shell at Grace Street turned out to not be flush and at 90 degrees. A GC would've called us to come look at it and given us a list of options. He might've offered opinions on the better option, but the decision would have been my responsibility. Because we had a CM, the site manager went directly to him, and the CM made the call. I never even saw the crooked wall; I just heard about. The CM took ownership of the problem.

GUARANTEED MAXIMUM PRICE OR COST PLUS CONTRACT?

Your CM or GC is eventually going to start talking about GMP, but he probably doesn't mean Good Manufacturing Practice. In construction, a GMP refers to a Guaranteed Maximum Price contract. If you're as green as we were, this is the best way to go. It sets a cap on how much the project can cost you, and protects you from unforeseen expenses. You can plan and budget, and you know what you're getting. This type of contract felt comfortable and familiar to us, because we offer a similar risk-capped contract option at Xcelience, which about 60% of our clients choose.

How do you set the price cap on the GMP for your construction contract? The process is fairly flowing, so by the time you set a price, both parties are generally in agreement. We got our first estimate when our documents were still pretty rough. Then, when the design was about 85% done, we got another estimate. This one was higher. I worked intensively with the CM, and we brought the costs down some. I put a few more clean rooms into the design, and we adjusted the price again. By the time the design was 95% complete, we were in agreement, and we nailed the GMP. From then on, we could be confident that there would never be overruns unless we made substantial additions.

I was glad of the GMP when, for example, the site manager discovered a mysterious and impenetrable blockage in a sewer line. He got a hold of our CM, and discussed options. They decided to dig out and replace the whole sewer line, rather than doing a short-term fix and risking the old pipes causing problems later on, which would force us to rip out fresh flooring. This was a cost I never would've foreseen. It delayed the project a week, but it was covered.

There are two other types of contracts. A lump sum contract is really only used in the public service. This is where the contractor is given a check and left alone to build. It's no small wonder that public and lump sum bidding leads to cost overruns as high as 20%, compared to only 5% to 10% in the private sector.

Sometimes, a GMP isn't possible. Let's say you're in an extreme hurry, and you need to break ground now, even though your design is only 65% done. It would be silly to peg a GMP when you barely know the scope of the project yet. Instead, you go for a Cost Plus (CP) contract. In this type of contract, you pay the CM his general conditions plus his fee on the cost of the work, and he manages the project as the design progresses. All

overruns are your responsibility with this contract. This approach is common in jobs over $50 million, or in smaller, very complex jobs.

At the risk of bringing up a sensitive topic for our biotech friends in Cambridge, MA, the Big Dig in Boston is a perfect example of a CP project. This mammoth project was ongoing for years. There was no end in sight, so no possibility of either a lump sum or a GMP contract. Certain rates were agreed upon up front, the contractor estimated the features of the job as he went along, and the design advanced a few steps ahead of the work.

SPELL OUT THE GENERAL CONDITIONS

Your CM deals with two types of costs. First, there's the cost of the contractors, subcontractors, and any self-performed work. This makes up about 90% of all costs. Then, there are the general conditions. Usually these entail direct costs for managing the project, including CM insurance, bonds, and rental, but the specific items included as general conditions can vary significantly from quote to quote.

In *Straight Answers*, Black and Brian Hodess recommend specifying general conditions when you bid out your contract, so you can compare apples to apples. You can choose one company's breakdown for general conditions and send it as a template (without figures) to other bidders. Whichever company you choose should be happy to give you its template, since it's easier to be the example than to try to match another company's format.

A detailed breakdown of general conditions will also prevent misunderstandings later on when there are changes. You'll be able to turn straight to the general conditions to see if a cost is a legitimate new cost or one that should've been covered by the general conditions.

TURN PROJECT MANAGEMENT ON ITS HEAD

Construction management teams aren't all that different from CDMO project management teams. Their functions are different, but the things you should expect from a CM or a project manager (PM) and his team are much the same.

Most clients sign a contract and then allow a CM, or in our industry a PM, to be assigned to their project. I would suggest some clients may want to turn this on its head, in both industries. You could ask to meet your CM/PM first, and then decide if you sign. In the construction industry, this is not uncommon. In the CDMO world, no client has ever asked this of me.

The first thing you want to know from your CM is that he has expertise in projects like yours. We learned this lesson the hard way with a small expansion of our main facility several years ago. The CM had never worked in pharma but was certain he could do the job. Then he wanted to design a room that used negative pressure instead of positive pressure, and we had to go back to the drawing board. We never worked with that company again.

If you're using the PM/CM-first approach, bias yourself toward companies large enough to have PM/CMs with different combined skill sets. At Xcelience, for example, we have five project managers, each with differing levels of experience in analytical, manufacturing, formulation, and packaging. This enables us to match the PM with the right combination of skills for the job. I would expect to have at least that number of CMs to choose from in a construction company.

Obviously it's possible to work with a company that has only one PM or CM, particularly if you really like that individual. Just be careful. If he's missing a skill set, who's he going to turn to? How many projects can this guy handle at once? What about turnover? Is he likely to be around for the duration of your project? Your CM/PM simultaneously weaves dozens of threads through the complex pattern of your project. If you change leaders midstream, don't be surprised if a few threads get lost.

Your CM always has the end result of your project in mind. This isn't necessarily the case in a CDMO. Many project managers see only to the end of the current contract. At Xcelience, we give our PMs the training and empowerment to see a molecule's trajectory from Phase I to launch, allowing the PM, for example, to anticipate and plan for a piece of equipment that may be needed 2 years from now. It takes a lot of training to enable a PM to envision the entire drug development pathway. We feel confident making this investment because of our low

staff turnover. Look for this kind of commitment to training and longevity whenever you must choose a project team.

Don't be afraid to ask for the resumes and references for the people on your team. Call the references and conduct interviews. Hodess suggests you get a sense of how team members will work together. Ask the site manager what he believes the CM's role is. Ask the CM what he believes the site manager's role is. Ask them how they might handle a non-performing sub. Get a feel for whether or not they can negotiate, motivate, and ultimately compel subs to do what they came to do.

WHAT MAKES A GOOD CM?

"The project management team that doesn't own the project will come to you with a problem like a retriever with a dead duck and lay it down in front of you," writes Hodess, in *Straight Answers*.

I've had plenty of dead ducks in my doorway. A dead duck is a problem handed to you. A good CM, like a good PM, never hands you a dead duck. But he might bring you duck soup.

A professional CM, like a PM, owns the project, spots problems before they arise, fixes them, and does so without cost overruns. He - I use the masculine only for convenience - takes responsibility for issues as they arise. Then he tells you about them in your weekly meetings, for your information.

A good CM handles conflict without manning battle stations. He has good relationship skills, but is firm when it comes to setting expectations for what needs to be done.

Here's a really key point: a good CM wants to understand what your business actually does. If he knows what you're trying to accomplish - the flow of products from room to room and what you're doing in those rooms - he will be better equipped to improve processes, save money, and handle problems.

A good CM is always on top of the process. He doesn't just hand off duties and trust they will be performed to standard and on time. That can be good enough, but it's rarely great. A good CM is always checking in to make sure things are progressing as they should.

When you have chosen the right CM/PM, he should feel like an extension of your own company. Hodess says he's seen some companies give their CMs ID badges and company store privileges. Why not? Anything to help them feel a part of the owner's team.

GETTING THE MOST OUT OF YOUR CM

Having the right CM is important. But what if you and everyone else love the same CM? You're going to be concerned about getting your fair share of his hours. Both in our industry and in construction, it's a good idea to get a Time and Materials quote that clearly sets out the minimum number of hours your project manager must give to your project.

CHOOSING TOP MANAGEMENT

Okay, so you can't choose the top management. Still the culture at the top is of paramount importance. Is the top guy accessible if you really need him? What is the culture at the top?

We had a fantastic project management team in our Grace Street expansion. Having worked with this one CM for over 5 years in various smaller projects, the CM took ownership of our project, understood our business, attended our meetings, saw problems, and fixed them as they arose. He worked well with the site manager, who kept the subcontractors coming and going smoothly. It would be a pity not to use them again, but if we don't, it will because the culture at the top of the company isn't the same as what we saw in the field.

This particular construction company's invoices were extremely complicated, and our lending institution was slow to release funds as a result. We came against this problem numerous times in our 5-year relationship. The company consistently complained about slow payment, and we consistently complained that there was nothing we could do about it until they simplified their invoices.

Two weeks prior to a ribbon cutting that involved DJs, cakes, ice sculptures, an attendance list of over one 100 employees, customers, press, and elected officials, we arrived at the site on Monday morning to find no one was there. We're talking crickets. We were perplexed. Why hadn't we been informed? I called the site

manager who explained that he wasn't allowed to discuss the matter, but I was to call the owner.

The owner informed me that he had ordered everyone off the job until payment was received. He explained that he did so without informing us in advance, to ensure that we got the message. Believe me, we got the message. It just didn't have the effect he intended.

I went over to his office, and managed to keep some of my cool as we contacted the lending institution. The institution verified what we had been telling them all along - that there were issues with the construction company's invoicing system, and payment would arrive within a couple of days - as previously scheduled. A couple of emails provided verification of pending payment, and construction resumed.

Five years of trust went out the window that day. I don't hold the project management team to blame. They were put in an incredibly awkward position by their owner.

Ultimately, you can have the best team in the world, but if the culture at the top doesn't line up with the rest of the team, you have a huge problem waiting to happen.

SCHEDULING: DON'T BE A HERO

This is another issue that applies equally to construction and to the CDMO world. Is your CM/PM a realist or an optimist when it comes to scheduling?

Let's say your building expansion looks like it will probably take five months, but it could be done in three if everything goes well. If your contractor promises you three, he's not doing you any favors. You'll schedule only three months of construction interest, and you'll both be in trouble when you need five. Many contactors - and many CDMOs - are tempted to fib a little about the true timeline to snag a contact. Be on the lookout for this. It's short-term thinking. If you sense your contractor is being a little optimistic, look for other signs of hard-to-believe good news in the budgeting process. Trust your instincts.

Also, be sure to ask for a detailed schedule. Hodess says they'll put a basic schedule into some RFPs, and ask his contractors to flush it out. This is a great way to gain insight into how they plan and manage a project. If you like how they think, that's a positive sign.

WALLS & MORE WALLS

Grace Street was finished on time and on budget; all in all a fantastic outcome. Since then, we've added 25% to our headcount, and are filling out the new building. It's important to us that we always have spare capacity, so we never have to turn a client away. I'll be up against the walls again soon, but this time I'll be better prepared. ◆

BIOGRAPHY

Derek G. Hennecke is President and CEO of Xcelience, a CDMO in formulation development and clinical packaging located in Tampa, FL. Mr Hennecke launched Xcelience as a management buyout in 2006, and the company has more than doubled in size. Prior to starting Xcelience, Mr. Hennecke worked for DSM as a turn-around manager in the global drug development community, managing an anti-infectives plant in Egypt, technical and commercial operations in a JV in Mexico, and a biologics facility in Montreal. He developed the formulation and business strategy of several drug compound introductions such as clavulanic acid, erythromycin derivatives and Tiamulin. A Canadian, he covets the Florida sun, but can't be kept away from the rink for long. He is an avid fan of the Tampa Bay Lightning.

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CATALENT APPLIED DRUG DELIVERY INSTITUTE: HELPING TO GET BETTER DRUGS TO WAITING PATIENTS, ENCOURAGING THE ADOPTION OF ADVANCED DELIVERY TECHNOLOGIES

Kurt Nielsen, PhD

CTO & SVP, Innovation & Growth, R&D
Founding Institute Board Member

Catalent Pharma Solutions

"Our mission is to bring better treatments to market by advancing the development and adoption of applied drug delivery technologies. By harnessing the knowledge of some of the world's leading experts in drug development, delivery, and formulation, the Institute aims to cultivate leadership and excellence in drug development through education, training, and innovation."

Headquartered in Somerset, NJ, Catalent Pharma Solutions 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 over 75 years serving the industry, Catalent has proven expertise in bringing more customer products to market faster, enhancing product performance, and ensuring reliable product supply. Catalent employs approximately 8,500 people, including more than 1,000 scientists, at nearly 30 facilities across 5 continents and generates more than $1.7 billion in annual revenue.

In 2012, Catalent launched the Applied Drug Delivery Institute to promote innovation, knowledge-sharing, and collaboration between industry leaders, academic experts, customers, and regulators to enhance understanding of available, emerging, and future drug delivery technologies and improve patient care. Kurt Nielsen, PhD, Senior Vice President of Research and Development, and Founding Institute Board Member, recently spoke with Drug Development & Delivery about the Institute, its goals, structure, and activities.

Q: What is the vision behind the Catalent Applied Drug Delivery Institute and what mission does the Catalent Institute aspire to achieve?

A: Our industry is facing an ever-increasing challenge delivering effective medicines to patients due to the increasing technical challenges of new molecules going through the development process. We believed we really needed to work more collaboratively by bringing together the best minds from across both industry and academia to share all of their combined expertise, insights, and experiences. We owe that to patients, doctors, and our shareholders.

So, we established The Catalent Applied Drug Delivery Institute in 2012, with the aim of

promoting innovation, knowledge-sharing, and collaboration between industry leaders, academic experts, customers, and regulators to enhance understanding of available, emerging, and future drug delivery technologies and improve patient care.

We believed that earlier introduction of drug delivery technology into the development process would really help advance more molecules through the development process by improving their bioavailability, therapeutic profiles, and delivery mechanisms. Our mission is to bring better treatments to market by advancing the development and adoption of applied drug delivery technologies. By harnessing the knowledge of some of the world's leading experts in drug development, delivery, and formulation, the Institute aims to cultivate leadership and excellence in drug development through education, training, and innovation.

As part of that mission, the Catalent Applied Drug Delivery Institute serves as a link between industry and academia by providing guidance, counsel, and resources on major issues pertaining to drug development, delivery, and formulation. We will continue to develop programs that facilitate mutually beneficial collaborations, increase communication, and shed light on regulatory issues affecting drug developers and researchers. The Institute also pursues a multi-tiered approach of seed funding, strategic counsel, and educational programs to advance the adoption of emerging technologies.

Ultimately, our goal is to help develop better treatments for patients by advancing the application, adoption, and innovation of applied drug delivery technologies.

Q: Who are the founding members of the executive board of the Catalent Institute, who are the advisory board members, and why were they chosen to help support the mission?

A: The Executive Board of the Catalent Institute was formed to facilitate its strategy and governance. The members include leaders from R&D, Strategy, Licensing, Marketing, and Corporate Development. We selected the members of the Advisory Board based on their broad expertise in drug delivery and experience in bringing pharmaceutical innovation to patients.

Founding members of the Board include me and some senior colleagues from the Catalent organization, including Dr. Cornell Stamoran, Vice President of Corporate Development and Strategy; Dr. Julien Meissonnier, R&D Platform Director; Terry Robinson, who is the Institute's Executive Director; Akan Oton, Director of Business Development, Technology Licensing; and Elliott Berger, Vice President of Marketing and Strategy.

We also have an Advisory Board for the Institute, which is made up of our own R&D Director Dr. Craig Davies-Cutting, plus two relatively new recruits from outside the Catalent organization, Dr. Ralph Lipp and Prof. Claus-Michael Lehr, both of whom we are delighted to have on board.

Dr. Lipp is a well-known pharmaceutical industry executive and inventor who brings over 20 years of industry and academic experience to the Institute, having previously served as Vice President, Pharmaceutical Sciences R&D at Eli Lilly and Company, and in R&D leadership roles at Schering AG.

Prof. Lehr is a world-renowned scientist in drug delivery and a Professor of Pharmaceutical Science who is actively engaged in transdermal, pulmonary, and GI drug delivery innovation as head of the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) Department of Drug Delivery (DDEL) at Saarland University in Germany.

We have also established a collaborative Key Opinion Leader network composed of leading academics from around the world to help bring diverse expertise to fulfilling our mission.

Q: How does this team plan to achieve their mission of promoting innovation, knowledge-sharing, and collaboration between industry leaders and academic experts?

A: Since the launch of the Institute in November 2012, our team has made great progress in connecting scientists from academia and industry through a number of key initiatives and programs.

First, we have begun rolling out a series of collaborative Global Symposia focused on real-world drug delivery challenges facing R&D teams today. Our initial events, which we held recently in New Jersey, and at the Royal Society of Chemistry's London headquarters, featured speakers from Catalent, 3M, Bend Research, BASF, Formac Pharmaceuticals, University of Bath and The New Jersey

Institute of Technology were very successful and generated some great feedback. Together they attracted more than 150 registrants from major pharmaceutical companies and leading universities, with attendees ranging from Vice Presidents and Directors to Principal Scientists and Graduate Students.

We believe that expanding this program of educational days in both Europe and North America, for industry professionals and academia, is crucial to achieving the Institute's objectives.

A further initiative we are employing is the publishing of educational resources and reference guides, such as our recent Oral Drug Delivery Guide, which has been extremely well received. The aim of the guide is to provide both academia and industry with an informative balance of underlying pharmaceutical sciences and insights from real-world product development experts. It covers key topics in oral drug delivery, including Predicting Drug Absorption, Solving Problems of API Degradation, Drug Delivery Technology Solutions, Criteria for Use, and Patient Population-Focused Drug Delivery Technology Strategies.

In addition to making these resources available for free download on the Institute's website, we will be printing and distributing them at our own events and also at major industry tradeshows, such as the AAPS (The American Association of Pharmaceutical Scientists) and CPhI Annual Meetings.

Our Annual Drug Delivery Landscape Survey, is now in its second year and surveys formulation scientists involved with oral product development in pharmaceutical companies in the United States, Canada, and Europe to understand their key concerns on drug delivery issues.

We are constantly looking to expand our collaborations with leading drug delivery experts, associations, and foundations like AAPS, the Geriatric Medicines Society, Faster Cures, the APGI (Association de Pharmacie Galénique Industrielle), and also academic institutions, such as the New Jersey Institute of Technology and St. John's University.

Another important initiative of the Institute is our annual Academic Competition for Future Life Science Leaders, where graduate students have the opportunity to win cash prizes and a one-year membership with the AAPS. Last year's competition drew some exceptionally high-quality original review articles, addressing a wide range of topics, including drug development, delivery technologies, improving therapeutic profiles and bioavailability, preformulation, and pediatric drugs. This year, we are delighted to announce that the Catalent Institute plans to partner with AAPS to co-sponsor the 3rd Annual Global Academic Competition and the submission site will be open later this fall in 2013. This partnership is important as it shows our joint commitment to raising awareness of drug delivery technologies as a means to improve patient care and our encouragement of the next generation of students to demonstrate their academic excellence, while creating real-world opportunities for continued advanced research and practical industry experience.

Finally, the Institute is currently focused on research efforts with clinicians to identify drug targets in need of optimization and understanding patients' unmet needs in medication delivery. We are also establishing a consortium focused on Non-Invasive Macromolecules.

Q: You mention the Drug Delivery Landscape Survey, can you share a few highlights and findings?

A: It is a fact that a high percentage of poorly soluble compounds never reach human clinical studies. Better understanding of the chemistry of the drug, solubilizers, such as polymers, surfactants, and lipids, and the various salt/crystal forms can get more drug candidates through the preclinical testing phase. Our survey results confirmed this, and the two top problems identified by respondents when working with poorly soluble drugs were optimizing the drug-release profile (71% of respondents cited) and stability (66% cited). More than half (58%) the respondents cited difficulties in identifying excipients with optimal properties, while 49% identified excipient -API interactions as a concern. As expected, permeability and absorption in the gastrointestinal tract were also key issues.

In addition, a food effect was frequently encountered (93%) by respondents. A clinically significant food effect occurs frequently with poorly soluble drugs, resulting in more complicated dosage and administration instructions for the product. Drug delivery technologies that eliminate food effects, like lipid-based systems or amorphous mixtures, can eliminate it, simplifying the dosing instructions and improving ease of use for patients.

Lastly, many respondents rated many technologies as "good" (approx. 50%).

However, for highly experienced formulators, particle engineering, amorphous mixtures, and lipid-based systems received top scores for excellent performance. A formulator's experience and expertise with the right drug delivery tool kit can help successfully develop more products and better treatments.

Q: The Academic Competition is an interesting program to reach out to future scientists, can you tell us a little more?

A: Sure. The academic competition aims to identify emerging scientific talent, foster drug delivery education, and reward academic excellence. It also reflects the Institute's commitment to fostering education, collaboration, and adoption of drug delivery technologies to develop better treatments for patients.

This year's winners were chosen from leading US and European universities with graduate programs in pharmaceutical science, including St. John's University, Rutgers University, New Jersey Institute of Technology, University of North Carolina at Chapel Hill, Purdue University, and Heinrich Heine University of Düsseldorf, Germany.

The 2012/13 grand prize of $5,000 was awarded to James Byrne of the University of North Carolina at Chapel Hill, whose winning submission focused on Treating Human Autoimmunity With Immunotherapy. His article provided a discussion of targeted immunotherapies and innovation in the form of a novel microneedle-based immunotherapy drug delivery technology strategy.

Additionally, each of the following students was awarded a first place prize of $2,000 for their thought-provoking submissions:

Shashank Jain, St. John's University: *Rationale for Selection of Solubility & Dissolution Enhancement Strategies* focused on formulation strategies to improve solubility and dissolution of new APIs, including salt formation, co-crystals, particle size reduction, amorphous solids, solid dispersions, co-solvents, and pro-drugs.

Maxim Osipovs, Heinrich Heine University of Düsseldorf: *Challenges for the Oral Delivery of Macromolecules* provided commentary on the applications of dry polymer controlled-release drug delivery technologies on the particulate scale. The major insights of the article discuss enabling a broader range of controlled-release application to dose forms, such as film strips, solid oral dispersible tablets, and liquid oral suspensions.

Maxx Capece, New Jersey Institute of Technology (NJIT): *Modified Release of Dry-Polymer Coated Active Pharmaceutical Ingredients* discussed bioavailability as the main challenge in oral protein and peptide drug delivery and a number of strategies to overcome these challenges, mainly nanoparticulate, as this option has increased versatility and could present more opportunities for marketable formulations.

Q: Finally, how can the Institute help get better drugs to waiting patients?

A: At the core of the Institute's vision is encouraging dialogue and depth of understanding of drug delivery technologies throughout industry and academia and bringing these parties together to provide optimal delivery solutions. We are taking a similar approach currently being used by universities, non-profit organizations, and industry to knock-down the collaboration and communication hurdles in translational medicine. Through collaboration, we aim to address key issues in drug delivery, such as solubility and bioavailability enhancement, to produce more efficacious drugs. By applying advanced drug delivery technologies to essential medicines, we have already witnessed significant value for patients globally.

By disseminating greater knowledge of existing delivery technologies, and creating novel technologies through collaboration, we aim to provide a significant contribution in bringing the next generation of important and effective medicines to patients more quickly. ◆

MARKET BRIEF

The Market for Type 2 Diabetes Therapeutics - Key Findings From a Recent Analysis of Global Drug Development Efforts

By: Debbie Toscano, Senior Industry Analyst, Frost & Sullivan

INTRODUCTION

Type 2 diabetes is one of the most significant global health concerns of modern times. According to the International Diabetes Federation, more than 317 million people have been diagnosed with diabetes, and an additional 187 million are living undiagnosed. No longer a disease exclusive to developed countries, type 2 diabetes is rapidly overwhelming developing countries, such as China and India, as more and more countries adopt the westernized lifestyle that largely contributes to the increasing prevalence. The global revenue earned from drugs sales to treat type 2 diabetes was approximately $36.89 billion in 2012. The rapidly increasing incidence and prevalence globally is predicated to drive this figure to approximately $68.42 billion by 2017. The market for type 2 diabetes therapeutics in China is growing rapidly and is expected to outpace Europe to become the second largest market by 2017. South Korea and Vietnam are also forecast to experience rapid growth.

The market for diabetes drugs has many barriers to entry, particularly for the insulin segment, which requires a great deal of specialization. Due to the chronic nature of the disease and the numerous co-morbidities that make this patient population particularly sensitive to long-term drug safety, the clinical and regulatory hurdles are considerable, and the inherent risks involved, including failure to receive marketing approval after a relatively large investment of time and money, limit this market to those organizations with the necessary expertise and capital. However, the immense size of the potential market has stimulated a vast and growing pipeline of potential new therapies aimed at meeting the unmet needs of tighter glucose control, improved safety profiles, and greater convenience to patients. The following summarizes key findings of Frost & Sullivan's recent analysis of the type 2 diabetes therapeutics market, which examines in detail the insulin and non-insulin segments of this market on a global level.

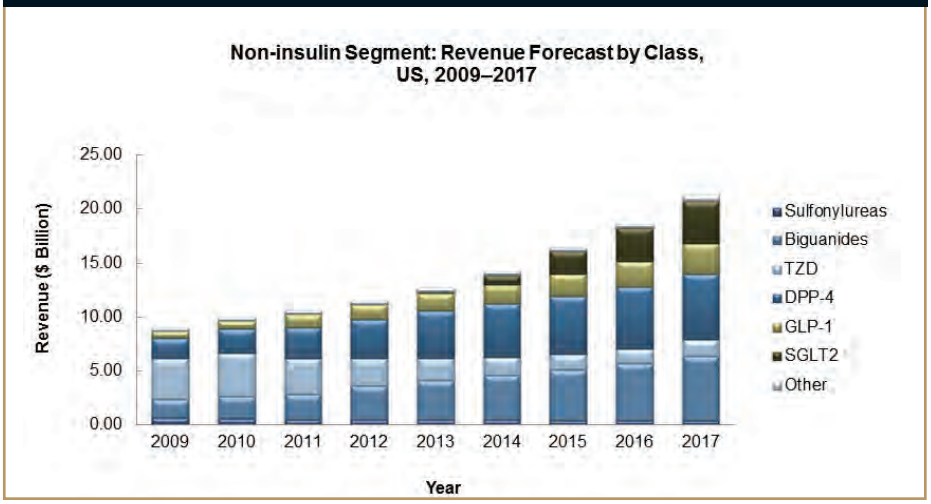
NON-INSULIN THERAPEUTICS

Non-insulin anti-diabetic drugs are mostly oral therapies and are typically prescribed as first-line therapy when diet and exercise alone are insufficient to control elevated blood glucose. Non-insulin therapeutics can be sub-segmented into standard of care (SOC) therapies and add-on to SOC. The main drug classes prescribed as SOC are all available as low-cost generics and are composed of biguanides (metformin), sulfonylureas (glipizide, glyburide, gliclazide, glimepiride), and alpha glucosidase inhibitors (acarbose, voglibose, miglitol). In the US and most of the world, metformin is the gold standard first-line therapy. Add-on therapies, which are composed of newer novel drug classes, are typically prescribed in combination with SOC when those treatments eventually fail to control elevated blood glucose on their own. Add-on therapies can also generally be prescribed as first-line or monotherapy when SOC therapies

are contraindicated or not well tolerated.

The main drug classes used as add-on therapies are meglitinides, glitazones, incretin-based therapies composed of glucagon-like peptide-1 (GLP-1) analogues or receptor agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, and the newest class, sodium-glucose co-transporter 2 (SGLT2) inhibitors. The meglitinides, of which there are two marketed drugs: Novartis' Starlix (nateglinide) and Novo Nordisk's Prandin (repaglinide), are post-meal glucose-lowering therapies and are a relatively minor portion of the market. Santarus' new diabetes product Cycloset (bromocriptine), launched in 2010, is a novel first-in-class oral antidiabetic (OAD) based on the circadian rhythm of dopamine activity. Cycloset also has a minor share of the market, but is gaining ground as physicians become more familiar with its unique mechanism. The glitazones, also known as thiazoladinediones (TZDs) or PPAR gamma agonists, represented by Takeda's Actos (pioglitazone) and GlaxoSmithKline's Avandia (rosiglitazone), were former blockbusters until the recent emergence of serious safety issues and have since seen significant declines in sales, restraining overall revenue growth for the segment. However, the segment was soon revived and stimulated by strong uptake of Novo Nordisk's Victoza (liraglutide, a GLP-1 receptor agonist) and continued strong sales of Januvia, along with the introduction of additional members of the DPP-4 class and the initial launches of a new class, the SGLT2 inhibitors. In 2012, the majority of global revenue generated for the non-insulin therapeutics segment was from sales of Januvia, as well as metformin, the most widely prescribed diabetes therapeutic worldwide.

FIGURE 1



The recent implication of increased risk of pancreatic cancer in the incretin-based therapies, such as Januvia and Victoza, has drawn considerable media attention but is not expected to have a significant impact on the market overall in light of the lack of compelling data in support of the theory. The European Medicines Agency (EMA) and the US FDA each initiated an investigation of the matter in March 2013, and both agencies have recently (July 2013) announced they have found no confirmed link between incretin therapies and increased risk of pancreatic cancer. This is good news for the manufacturers of the numerous GLP-1 therapies coming to market. While this class has been long dominated by Byetta (exenatide) and Victoza (liraglutide), several rivals are arriving to the market, the most advanced of which is Sanofi's Lyxumia (lixisenatide), currently under review by the FDA with a decision expected in December 2013 or early 2014. Lyxumia, developed by Zealand Pharma and commercialized by Sanofi, is already approved in Mexico, Australia, Europe, and, most recently, Japan. GlaxoSmithKline is also awaiting FDA approval for their once-weekly GLP-1, albiglutide, with a decision expected in April 2014. Most anticipated, however, is Eli Lilly's dulaglutide, a once-weekly GLP-1 with strong positive data that is poised to be a formidable competitor to all of the GLP-1s including Victoza. Dulaglutide could launch as early as late 2014 or 2015.

While Januvia and the DPP-4 class are expected to continue to dominate the non-insulin market for the foreseeable future, the SGLT2 class is forecast to overtake the GLP-1 class for the number two spot among add-on therapies by 2015, in light of important class-associated clinical benefits, such as weight loss and lowering of blood pressure, along

FIGURE 2

Total Type 2 Diabetes Therapeutics Market: Competitive Landscape—Non–insulin Segment, Count of Marketed and Pipeline Products by Type and Phase, Global, 2012

Drug Class	Phase 1	Phase 2	Phase 3	Pre-registration	Market	Total
DPP-4	2	0	2	0	7	11
GLP-1	13	4	4	1	4	26
TZD/PPAR	1	1	1	0	2	5
FDC	0	1	9	1	13	24
SGLT2	1	3	4	2	2	12
Miglitinide	0	0	0	0	3	3
GRA	1	1	0	0	0	2
GKA	1	3	0	0	0	4
GPR119	3	3	0	0	0	6
11β-HSD-1	2	3	0	0	0	5
Other	22	19	1	0	2	44
Total	46	38	21	4	33	142

Source: Frost & Sullivan

with convenient once-daily oral administration and potent glucose lowering. An additional benefit of the SGLT2 class is its mechanism involves increasing glucose excretion, rather than affecting glucose production or insulin sensitivity, making it a potentially important insulin-sparing drug for type 1, as well as type 2 diabetics (Figure 1).

Almost every add-on drug class can be combined with the gold standard therapy metformin, and most are offered as both stand-alone therapies, as well as fixed-dose combinations with metformin. Moreover, different drug classes can typically be prescribed as part of double or triple combination therapy, thus expanding the potential market for each, as well as stimulating partnerships between owners of complementary therapies. A recent example of such a strategic partnership is the agreement between Merck and Pfizer to co-commercialize Pfizer's SGLT2 inhibitor, ertugliflozin, as well as develop a fixed combination of ertugliflozin with Merck's DPP-4 inhibitor, Januvia.

Complementary and/or synergistic combination therapies are frequently the goal of diabetes drug developers because most diabetes patients will progress through therapeutic regimens of increasing potency. Additionally, the inconvenience of taking multiple pills can have a significant negative impact on patient compliance with their therapy, making double- or triple-fixed combinations in a single pill (while keeping the pill size manageable) an attractive option for patients and physicians.

Metformin therapy may be significantly improved in the near future with the anticipated introduction of Elcelyx Therapeutics' alternative metformin formulation dubbed NewMet™, currently in Phase II. Elcelyx has capitalized on their proprietary gut-targeted drug delivery platform to enable the targeted delivery of metformin to the gut tissues, where they believe it exerts its effect. This spares the body from systemic exposure and enabling therapeutic efficacy with a much lower dose and greatly improved tolerability, which is key as approximately 20% to 30% of patients do not tolerate metformin.

The development pipeline for non-insulin diabetes therapies is rich with potential new drugs, with more than 100 candidates identified at various stages of development. Early development compounds primarily belong to the GLP-1 class, as well as miscellaneous novel targets, such as GPR119, 11β-HSD-1, and glucagon receptor agonists, while late-stage compounds are primarily in the SGLT2 and GLP-1 classes (Figures 2 & 3).

INSULIN SEGMENT

Insulin therapy is typically reserved for the more advanced stages of the disease and is intended to compensate for the inadequate production of, or sensitivity to, endogenous insulin. In type 1 diabetes, insulin therapy is essential. The two main categories of insulin are human insulin and modern insulin. Human insulin is made by recombinant biotechnology and is molecularly identical to endogenous human insulin. Regular human insulin is a rapid-acting insulin, whereas intermediate-acting or pre-mixed human insulins have an extended pharmacokinetic profile due to formulation enhancements.

Modern insulins can be sub-segmented based on their pharmacokinetic profiles into

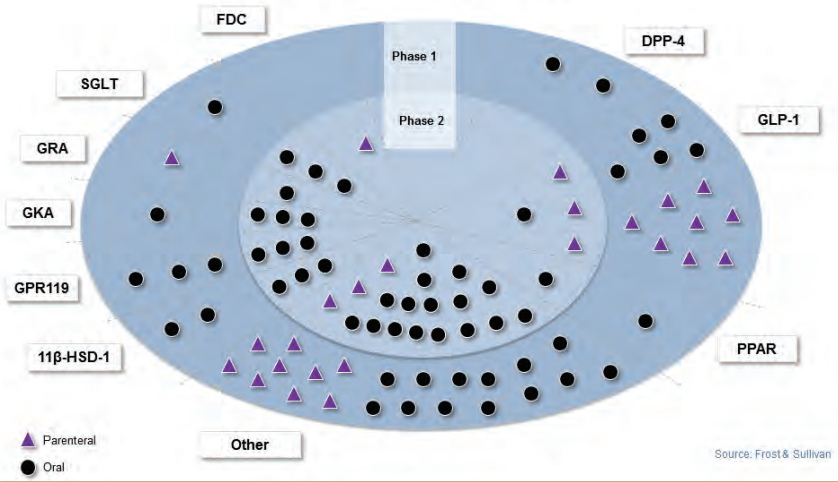
rapid-acting or mealtime insulin, pre-mixed or intermediate acting, and long-acting or basal insulin, and each serves a distinct purpose. Rapid insulin is intended to mimic and supplement the body's normal release of a "spike" of insulin upon ingestion of nutrients: hence the term mealtime insulin. Rapid and ultra-rapid insulins are insulin analogues engineered for rapid absorption via strategic substitution of one or two amino acids. This results in prevention of the formation of hexamers, a normal action of injected regular insulin, which slows the absorption. Rapid insulin is typically administered three times daily with meals.

Basal, or long-acting insulins are insulin analogues engineered for slow, continual release and are intended to provide steady 24-hour glucose control. Basal insulin is injected once daily, although longer acting once-weekly versions are in development. For many patients initiating insulin therapy, basal insulin alone might be adequate; for others, rapid insulin, in addition to basal insulin, is needed.

Intermediate-acting, or pre-mixed insulin is intended to provide mealtime control, plus control for several more hours. Pre-mixed insulins, which are composed of generally 30% rapid insulin and 70% regular or long-acting insulin, can handle glucose spikes plus additional control for a several hours. Intermediate-acting insulin, such as human insulin NPH, is regular insulin formulated for slow release over a period of 6 to 10 hours.

FIGURE 3

Total Type 2 Diabetes Therapeutics Market: Competitive Landscape—Non–Insulin Segment, Early Stage Pipeline Products by Drug Class, Global, 2012

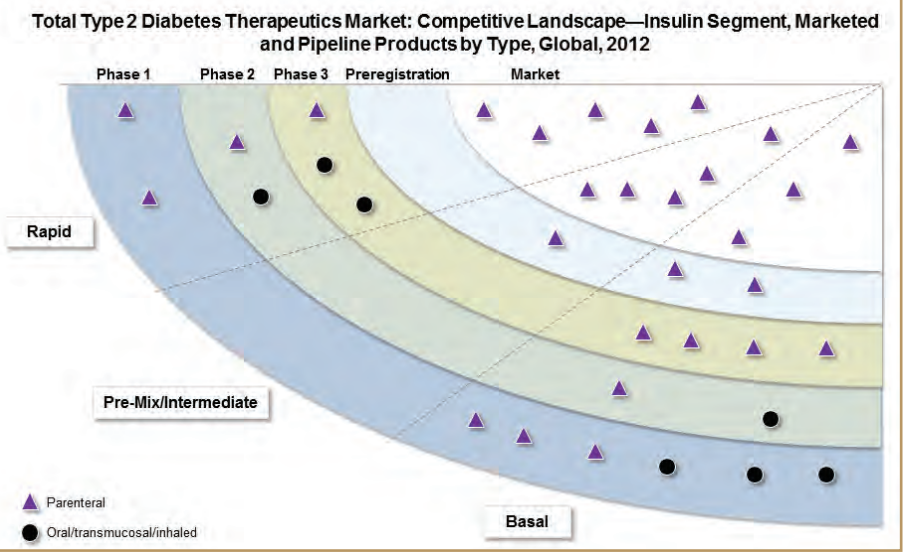


The insulin market has seen a resurgence of activity in recent years with promising new products, such as ultra-rapid-acting and liver-targeted insulin analogues, and insulin-plus-GLP-1 combinations in late-stage development. Earlier-stage candidates include several oral formulations, as well as ultra-long-acting insulin analogues. Some ultra-long-acting insulin analogues in development have the potential to greatly reduce the dosing frequency to just once weekly for basal insulin needs, as opposed to once daily (Figure 4).

Ultra-rapid-acting insulins, such as Novo Nordisk's FIAsp, which is just beginning Phase III trials in Q3 2013, promise to offer tighter glucose control and greater convenience to patients. Both Novo Nordisk and Eli Lilly are developing liver-targeted insulin analogues, which, according to the data so far, will have greatly improved efficacy profiles because they have a more physiologically relevant mode of action with subsequent benefits, such as weight loss and lower risk of hypoglycemia (dangerous drops in blood glucose). Eli Lilly's liver-targeted insulin analogue LY2605541 (insulin peglispro) is the most advanced, currently in Phase III of development.

Novo Nordisk's IDegLira, a combination product of Tresiba (insulin degludec) and Victoza (liraglutide), boasts a superior efficacy profile with its complementary action of long-acting insulin plus GLP-1 therapy, a combination long considered by many in the medical community to be the optimal therapeutic approach among all known drugs. Tresiba has been approved in Europe but has been delayed in the US due to a surprise request from the FDA to conduct a cardiovascular outcomes trial. Therefore, filing for approval of IDegLira in the US will have to wait for the green light for Tresiba; however, European approval and launch is expected in 2014 following the June 2013 application with the EMA. Sanofi is also

FIGURE 4



working with Zealand Pharmaceuticals on a similar combination product, combining Lantus (insulin glargine) with lixisenatide in a fixed ratio delivery. Phase III trials for the combination product, dubbed LixiLan, are planned to start in 2014.

The insulin market generates slightly less than half of the total revenue for the type 2 diabetes therapeutics market. However, in general, it is growing faster compared to the non-insulin market worldwide, in developed regions like the US and Europe, as well as developing markets like Korea, where younger patients in particular are becoming more cautious about controlling their blood sugar and tend to prefer insulin over OADs to avoid complications. Although oral insulin will probably not completely replace injectable insulin (at least in the foreseeable future), the availability of an insulin pill would be welcomed by both type 1 and type 2 diabetics, as both of these patient types expressed a strong desire for oral administration of their diabetes treatments in a recent Frost & Sullivan patient preference study of drug delivery methods.

SUMMARY

The market for type 2 diabetes therapeutics is uniquely characterized among therapeutic areas in its widespread global prevalence with a richness of untapped markets, diversity of established and potential drug targets, and significance of regulatory hurdles. Significant gaps in diabetes management left by currently available therapies, such as tighter glycemic control with low or no risk of hypoglycemia, greater convenience of therapy, and durable, personalized treatments that attack the root cause of the disease with disease modifying properties create a vast opportunity for innovative drug developers to successfully penetrate this lucrative expanding market. ◆

BIOGRAPHY

Debbie Toscano is a Senior Industry Analyst with the Frost & Sullivan North American Healthcare practice. Utilizing more than 20 years of life sciences industry experience, she maintains particular expertise in analysis and interpretation of scientific data as well as preparation of deliverables with attention to technical detail. Mrs. Toscano has an experience base covering a broad range of sectors, including focus on diabetes and metabolic diseases, cardiovascular diseases, and preclinical animal modeling and pharmacology. Prior to joining Frost & Sullivan, she conducted preclinical research with Novartis Pharmaceuticals. Mrs. Toscano earned her BS from Delaware Valley College in Biology and her Master's Certificate from Thomas Edison State College in Clinical Trials Management.

Modification of Silicone Chemistry & Its Influence on Release Rates of APIs

By: Brian Reilly and Nathan Wolfe

INTRODUCTION

Silicones are well known and continually used the world over for their biological compatibility and chemical stability.[1] The most researched biomaterials to date, they have been a trusted component of medical device applications since the 1950s, and popularity of their use has only increased with advancements in technology. Silicones can be found in cochlear implants, joint orthopedics, birth control devices, and pacemakers - to name a few common uses. Considering the expansiveness of the healthcare field, perhaps the most advantageous feature of silicone is that it can be designed to achieve specific performance, aesthetic, or therapeutic properties not inherently offered by relatively basic silicone formulations. Silicone is so versatile that its properties can vary greatly and even contradict each other, from one silicone to the next. For instance, basic polydimethylsiloxane (PDMS) silicone is inherently insulative at approximately 1015 $\Omega \cdot$ cm, but with the addition of certain fillers, a silicone can be made to conduct heat, electricity, or both.

A decade after silicone's auspicious advent into the medical arena, this versatile, synthetic material was first used for the controlled release of drugs, or Active Pharmaceutical Ingredients (APIs), into the body - an employment it has retained to the present time.[2] Commercial drug delivery devices that incorporate silicone are commonly manufactured for the following purposes: contraception, hormonal replacement, and infection mitigation with antibiotics.

Integrating APIs into a silicone system requires consideration of multiple factors, such as compatibility of the silicone with the API and, more generally, achievement of the prescribed dose delivery rate over the prescribed amount of time. Because different APIs can potentially alter the properties of silicone and vice versa, modification of silicone chemistry may be necessary.[3]

SILICONE CHEMISTRY

Comprising the siloxane polymer backbone of a silicone are repeating helical silicon-oxygen bonds (Si-O), with substituent, or R', groups attached to the open valences of the silicon atom. Compared to epoxies and other organic-based rubbers with Carbon-Carbon (C-C) bonds, the Si-O bonds of silicones provide larger bond angles.[1] These bond angles yield large amounts of free volume, leaving space for design or, more specifically, for managing the amount and type of substituent group and filler, including APIs, that go into a silicone system. This ability for formulation flexibility is largely what enables silicone to be so versatile.

Varying the substituent groups on the polymer chain can help optimize silicones for very specific needs. These components interact with the Si-O-Si units to cause the resulting silicone material to exhibit certain properties. Common R' groups that commend silicone for use in the medical field are methyl, phenyl, and trifluoropropyl (fluoro). Methyl, formative of polydimethylsiloxane polymers (PDMS), is most known for its water resistance and desirable surface properties, which aid in moisture retention and contribute to lubricity and gentleness in topical or more intrusive applications. This is the most common substituent group found in biomedical applications. Moreover, phenyl groups can be employed in resulting diphenyldimethylpolysiloxane polymers to increase or decrease a silicone's permeability to moisture as needed, as well as to adjust its refractive

index, or RI. As in the case of wound care dressings, external prosthetic devices, and contact lenses, silicone often needs to be permeable in order to act as a membrane through which water can be transmitted to surrounding tissue, and optical clarity is frequently required of protective encapsulants for assessment of components. Fluoro imparts swell resistance to silicone materials, which can be susceptible to size increase when in contact with common solvents, or other acidic fluids, such as stomach acids.

In addition to rendering the substituent groups on the polymer interchangeable, allowing for control of mechanical and physical properties, free volume is also one of the reasons silicone is so often made a conduit for the delivery of various actives to particular parts of the body. The other reason is silicone's chemical stability for its role in preserving the active's effectiveness at no cost to the silicone's material integrity or properties. Drug delivery applications are some of the most complex in the medical world; chemical stability is dependent upon the goals and parameters at hand. Thus, marrying a silicone formulation to a drug profile virtually always involves trial and error.

EXPERIMENTAL SECTION: BACKGROUND

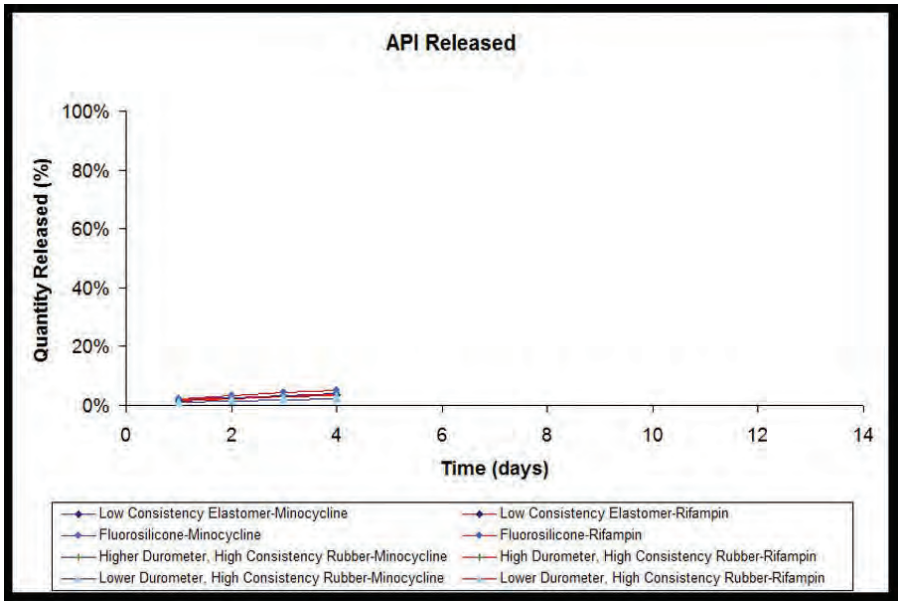
NuSil Technology conducted a study through which the antibiotics rifampin and minocycline were to be incorporated into a silicone matrix and completely released in equal portions at a steady rate by the end of 14 days.

Rifampin is best known for use against bacteria that causes tuberculosis. The human body (generally speaking) develops resistance to rifampin quickly, so the drug is partnered with one or more antibiotics for functional assistance. Rifampin's companion in this case study, minocycline, may be used to treat certain strains of MRSA infections, amoebic dysentery, cholera, and pneumonia. This

FIGURE 1

Basic Structure of Polysiloxane Chain

FIGURE 2



Results from first trial: four different silicone formulations were used, and less than 10% of the API was released after four days.

broad spectrum tetracycline antibiotic is classified as a long-acting type and so complements rifampin for coexistence in the same device.

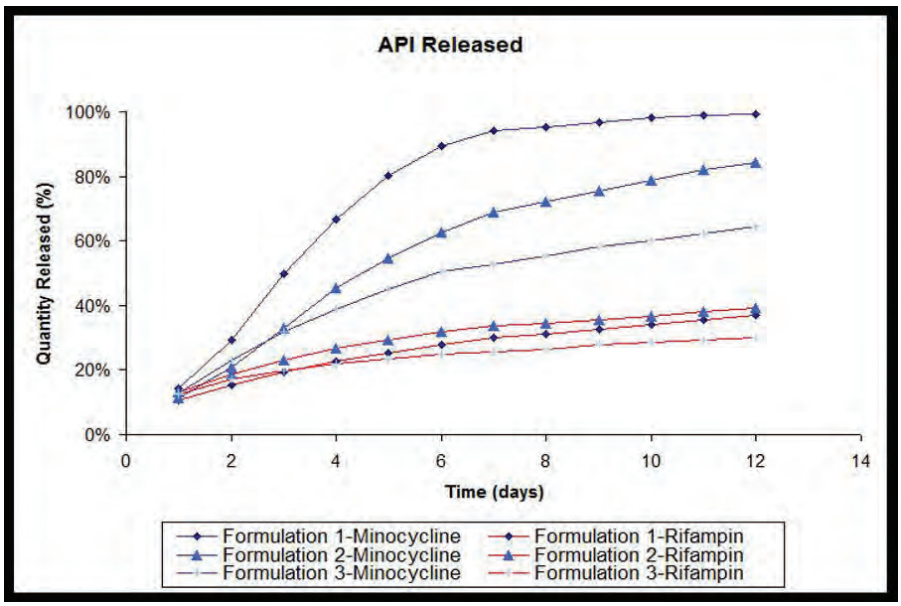
For medical device simulation, both APIs were eluted through a silicone molded component. Due to the interaction of the APIs with the silicone chemistry being a potential concern, the appropriate silicone system needed to be identified. The appropriate system would also be one that accommodated ease in processing and molding, key for effectiveness in its final form as a vehicle for eluting the APIs. Among the most common silicone types in the healthcare field are gels and elastomers.

Silicone gels are made of reactive silicone polymers and reactive silicone cross-linkers in a two-part system that yields little to no elastomeric strength. When cured, these low-viscosity materials are designed to have a soft, compliant feel which, combined with silicone's low modulus, allows them to mimic human tissue. They range from very soft for prosthetic applications to very tacky (sticky) for topical and transdermal wound care applications. Encapsulation of electronics, such as for use in certain implantable sensors, is also a common application for using silicone gels.

Silicone elastomers are similar in composition to gels but exhibit increased physical and mechanical properties due to high levels of reinforcing fillers and longer polymer chains. For instance, elastomers have higher viscosities than gels and fluids. High consistency rubbers (HCRs) are ideal for extruded tubing because their silica-reinforced, high molecular weight polymers enable them to maintain a shape when uncured; low consistency elastomers (LCEs), by contrast, are flowable and more ideal for coatings, encapsulants, and molded parts requiring optical clarity. Compared to HCRs and liquid silicone rubbers (LSRs), the high clarity and low viscosity associated with LCEs are primarily attributed to their unique base formulations, which may incorporate phenyl. Of intermediate viscosity, LSRs are used to mold high precision parts, such as gaskets, valves, O-rings, and seals. HCRs, LCEs, and LSRs are moldable materials that can be cast or injected into molds of various configurations.

Over gels, different silicone rubbers were chosen to begin the case study for their chemical makeup and consistency, imparting greater material integrity. The chosen system was modified throughout the trials so as to yield the elution results desired without compromising the mechanical strength of the silicone.

FIGURE 3



Results from second trial: three low durometer HCR formulations were used. These released a greater amount of rifampin and minocycline, but at unequal rates.

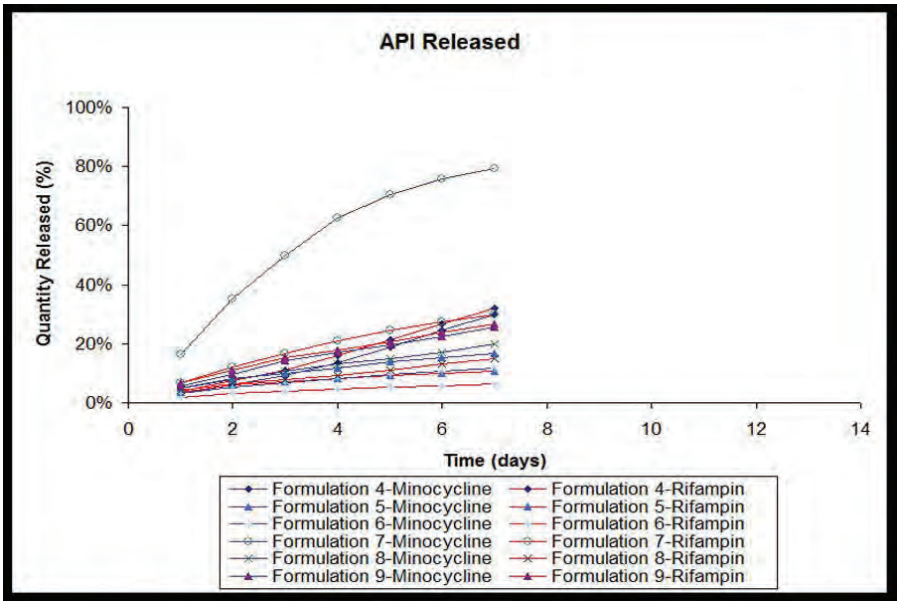
EXPERIMENTAL SECTION: RESULTS

Before the release rates of rifampin and minocycline were measured, a screening test was conducted to ensure the silicone would cure after incorporation of the APIs. This is a vital first step when incorporating any new API into a silicone system. The result may determine if additional formulating is necessary to counteract the effects caused by the API's interaction with the silicone, or if a different cure chemistry is required due to compatibility concerns. In addition, an exhaustive extraction test verified the APIs were not chemically bonding with the silicone matrix. Via elution testing, the release rates of rifampin and minocycline were tested with comprehensive evaluation a total of four times.

First attempt: An LCE, a liquid fluorosilicone rubber, a high durometer HCR, and a low durometer HCR were selected for the first elution test. The first elution test showed that per each formulation, the APIs were not being released at a sufficient rate to yield full elution after 14 days. Of the silicone materials tested, the fluorosilicone released the highest amounts of minocycline and rifampin. Further testing on the silicones and the APIs revealed that high temperatures made the actives no longer antimicrobial. To equalize the release rates and maintain the integrity of the actives, three new versions of the low durometer HCR were developed for a second elution test. To enable cure at a lower temperature, a fugitive inhibitor in the original fluorosilicone formulation was replaced with a competitive inhibitor. Inhibitors are formulary ingredients utilized to control and regulate working times (pot life) of the blended elastomer as well as their cure profiles (rate of cure at a specified temperature).

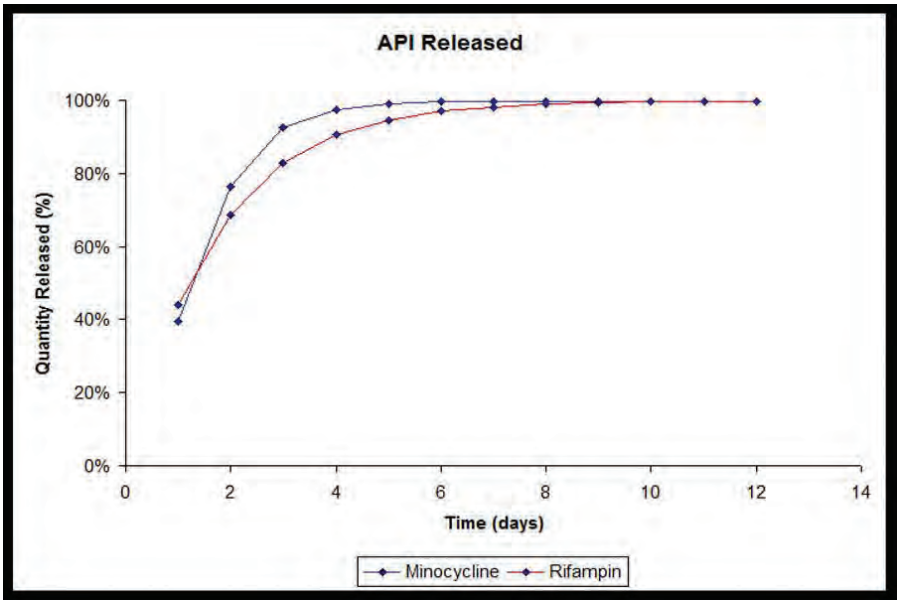
Second attempt: After some formulary adjustments were made to the silicones used in the first attempt, three low durometer HCRs were used for the second elution test. A noticeable improvement to the first trial results, the release rates of the second trial showed greater elution of the actives. However, the pharma-grade excipients intended to maximize elution diminished the physical properties of the system and produced a product difficult to process. The adjusted silicone systems were either too tacky or not tacky enough for processing on the two-roll mill. Formulary changes made

FIGURE 4



Results from third trial: equivalent release rates of the APIs were achieved with some of the six new low durometer HCR formulations used.

FIGURE 5



Final trial results: formulation 7 from the third trial was modified to meet the parameters of the study.

after these results anticipated process-friendly material and retention of uniform release rates.

Third attempt: Again, additional formulary adjustments were made in an attempt to produce better elution results. Six new formulations of the low durometer HCR were developed for the third elution test. Six formulations of low durometer HCRs were developed based on results of the second elution test. For better processing performance of the silicone, additional pharma-grade excipients were selected. Results showed that with these excipients, the silicone matrix could be more easily processed, and that some combinations promoted equivalent release of rifampin and minocycline - though no formulations fully eluted the drugs in 14 days. On some of the formulations, additional optimization required to achieve full release degraded the cured properties of the silicone. Adjustments made for the next formulation were designed to maintain the processing performance achieved in the third trial, preserve the mechanical properties of the silicone, and elude the APIs equally in 14 days.

Fourth attempt: Formulation 7 from the third attempt was redeveloped and optimized for what would be the last elution. The parameters of the study were met on the fourth trial. As is evident from Figure 5, release of the actives was uniform and occurred within the desired time frame of 14 days. Further testing showed that the cure profile for the silicone matrix was met, its mechanical integrity maintained, and its consistency compatible for two-roll mill processing.

CONCLUSION

The results discussed herein reiterate that (1) silicone chemistry lends itself to optimization and (2) formulation modification influences the release of actives. What modifications are needed for the success of drug delivery applications are dependent upon the applications' parameters and goals, including but not exclusive to the following: temperature limitations, inhibition concerns, cure profile, desired rheology, the meeting of elution profiles, and the maintenance of the physical integrity of the vulcanized silicone system. The increase in the number and kind of drug delivery applications has furthered silicone technology for the controlled incorporation and elution of APIs like rifampin and minocycline. Within the scope of assaying the release of APIs through a silicone matrix, over 100 elution studies were executed and the materials involved evaluated for mechanical, elution, and processing performance. Advancements in silicone technology are born from studies such as the one presented herein, thus augmenting through customization the ability of silicone components to meet and sustain the needs of drug delivery applications. ◆

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BIOGRAPHIES

Brian Reilly is the Marketing & Sales Director for Medical Implants at NuSil Technology LLC. He earned his BS in Biological Sciences from Cal Poly San Luis Obispo before being hired by NuSil, where he has worked for over 15 years. Mr. Reilly began his career in the R&D department formulating and developing silicone elastomers and adhesives. From there, he moved into his current role in Marketing & Sales.

Nathan Wolfe is a NuSil Technology Technical Sales Representative and Drug Delivery Market Specialist who began his 14-year career at NuSil Technology in its Regulatory Affairs department, where he supervised regulatory submissions to the FDA and oversaw contract review. As the Market Specialist for drug delivery applications, he is responsible for NuSil Technology's new Drug Delivery Silicones (DDS) Product Line as well as NuSil's expansion into targeted release and combination product applications.

The Second Quadrant

Navigating a Broad Spectrum of Solubilization Technologies: Part III of III

By: Marshall Crew, PhD, President & CEO, Agere Pharmaceuticals, Inc.

In parts I and II of *The Second Quadrant* series on solubilization technologies, the conversation revolved around current uses and untapped opportunities of today's technologies with respect to enhancing the bioavailability of poorly soluble drugs. In the final part of this series, the discussion focuses on the future. And in the spirit of the column's goal for industry-wide collaboration, we welcome another solubilization technology company that has offered to provide their views. In Part III, 10 experts representing a broad selection of technologies (amorphous solid dispersions, co-crystallization, lipid-based solubilization, metal coordination, nano-particles, particle engineering, and particle size reduction) provide their insights. The article concludes the series with opinions on recent breakthroughs and what they could mean to all of us who are committed to overcoming poor bioavailability.

RECENT BREAKTHROUGHS

Q: In the past 5 years, what have been the most significant breakthroughs that directly involve solubilization technologies or how they're used?

Dan Dobry: One breakthrough has been the development of a small-scale spray dryer that can produce small quantities of spray dried dispersion with high yield, but also produces particle properties that can be scaled up. This has enabled the application of spray dried dispersion technology into the preclinical setting. Companies that successfully use these dryers are able to enable rapid compound selection at the Med Chem/Development interface. Bend Research has provided these spray dryers and the training required to operate them to clients. This dryer was designed using computational fluid dynamics to ensure the process can be scaled up.

An exciting area of research is the design of new excipients that are specifically designed for application to solubilization problem statements. Bend Research's collaboration with Dow Chemical is an example of where new breakthroughs in excipient science can impact the throughput of the spray drying process. Stay tuned for future developments.

Tom Dürig: In the past 5 years, we have seen significant improvement in understanding how different polymers work in solid dispersions, as well as in the fundamental understanding of limitations and the mechanism of how different solubilization technologies, such as amorphous dispersions, lipid, surfactant, and self-emulsifying systems, affect absorption. Additionally, we are on the cusp of a new era with several companies developing purpose-designed excipients for solubilization, for instance, new versions of AquaSolve™ HPMCAS with improved extrudability and solubilization power.

Dr. Joan Feixas: In the past 5 years, advances in design strategies and characterization of cocrystals have

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Tom Dürig,
Senior R&D Director - Pharmaceutical & Nutrition Specialties,
Ashland Specialty Ingredients -
tdurig@ashland.com

continued to increase significantly within the crystal engineering field. Crystal engineering has been improved by better understanding of known synthons (combinations of hydrogen bondings) and the discovery of new ones. Hence, the rational design approach has grown at the expense of high-throughput screening. Furthermore, cocrystal structure prediction software has also progressed, although predicting these crystal structures is still a major challenge. Single crystal X-ray diffraction (SCXRD) remains the most common method to confirm the structure of a cocrystal although other techniques like X-Ray Photoelectron Spectroscopy (XPS), 15N CP-MAS NMR and 13C CP-MAS NMR are also used.

Dr. Filipe Gaspar: More than significant breakthroughs, I believe there has been a continuum of knowledge gathering in areas such as polymer and material science, solid state characterization, formulation design, IV/IV correlations, and mechanistic understanding of processes. This, together with the existence of technology providers from early research up to commercial reality has, in my view, accelerated the use of these advanced technologies.

Dr. Robert Hoerr: Expanded uses of innovative processes and new excipients have allowed the preparation of amorphous solid dispersions or solutions. These stable amorphous forms are rapidly emerging as one of the most useful methods of enhancing the solubility and bioavailability of BCS class II/IV drugs. Electrospray technology is now being developed to achieve that goal. In particular, electrospraying offers fast processing times, scalability, and the ability to process thermally sensitive drugs.

Keith Hutchison: The improvements in bioavailability using lipid-based formulas is impressive for many APIs throughout the past 5 years, evidenced by the significant increase in the number of compounds in development using lipid-based formulas, particularly liquid and semi-solid compositions in hard capsules. The equipment and processes used to develop, evaluate, and manufacture liquid and semi-solid hard capsules have also advanced in terms of scale-up, commercial scale, process efficiency, and versatility.

Dr. Dave Miller: The understanding of drug-polymer interactions and the identification of the most effective concentration enhancing polymers toward maximizing and stabilizing supersaturation from amorphous solid dispersion systems has increased substantially in recent years. This has been critical to the advancement of amorphous dispersion technologies and their application for bioavailability

"…new breakthroughs in excipient science can impact the throughput of the spray drying process."
Dan Dobry,
VP, Bend Research-
Dan.dobry@bendresearch.com

enhancement. Also, I believe the advent of the KinetiSol technology will significantly expand the application of amorphous solid dispersion systems because it increases the space of compounds and compositions that can be viably processed into amorphous dispersions by non-solvent processing. It will relieve the current burden on commercial GMP spray drying technology and create new possibilities for advanced amorphous dispersion compositions that will yield better drug products.

Dr. Tom Piccariello: Due to poor aqueous solubility, 40% of newly approved drugs and over 60% of drugs under development have oral bioavailability issues. Ideally, a drug substance possesses both adequate aqueous solubility and hydrophobic properties. This combination remains difficult to achieve, but recent breakthroughs in solubilization technologies appear promising. These breakthroughs include advances in modeling systems to better understand bioavailability issues, as well as developments in novel excipients and new processing techniques, in innovative methods to modify drug properties, and in new reformulation techniques. Synthonics addresses the latter two areas through its application of its metal coordination chemistry. Metal coordination has the capacity to very effectively address API oral bioavailability issues of impaired drugs by enhancing both water and lipid solubility simultaneously.

Dr. Mark Mitchnick: Perhaps the biggest advance is simply the increasing acceptance that bioavailability can be impacted in a predictable way. If one really studies the currently available, scalable technologies, it's clear there have been only incremental technical advances, but the real improvements have come from better execution.

WHERE WE'RE HEADING

Q: Where do you see the size and direction of the industry over the next 5 years, and the role solubilization technology innovation providers will play?

Dan Dobry: The overwhelming trend in the industry (including large pharma, mid-size, and small companies) shows high use of low-solubility compounds, especially in many specific therapeutic areas. For other targets, some researchers are steering their chemistry to more soluble compounds. Because the development timeline is lengthy, only

"The customer is looking to key partners to provide the scientific depth and range of technology options to address solubility…"
Keith Hutchison,
Senior VP of R&D Dosage Form Solutions, Capsugel -
keith.hutchison@capsugel.com

"…the industry will be relying more on external providers to develop solubility enhanced formulations."
Dave Miller, PhD,
VP of R&D, Dispersol Tech -
Dave.miller@dispersoltech.com

time will tell in which philosophy enables the best new medicines. For now and the foreseeable future, low-solubility compounds will be an important part of small molecule drug development.

Tom Dürig: The industry is rapidly morphing from highly specialized niche drug-delivery applications into main stream practice. We are already seeing the second wave of solubilization demand coming from generic companies.

Dr. Joan Feixas: More and more poorly soluble drugs emerge from contemporary drug discovery programs, and this trend may increase in the future. Development of these drugs is subject to significant risk of new products demonstrating low and erratic bioavailability with consequences for safety and efficacy. Pharmaceutical cocrystallisation can certainly expand the possible solid forms available for development and should become a routine objective with relatively low cost and limited incremental risk to improve solubilization for poorly soluble APIs, especially when the formation of salts is not possible. Some drug candidates that were rejected in the past for poor solubility or poor solubility profile could certainly be reassessed using this new solubilization technology approach.

Dr. Filipe Gaspar: The vast majority of oral drugs are poorly soluble, and this will continue to foster the application of solubilization platforms not only for new entities but also in reformulations. The size of the market will certainly grow with the increased usage of current solubilization technologies and with new ones coming along. There will be specialized niche players, and contract manufacturing organizations will have a greater responsibility not only in providing a timely pathway for development and commercialization of products needing novel solubilization technologies, but also in contributing, together with academia, sponsors, and regulators, to key advances and innovations.

Dr. Robert Hoerr: Because of the new solubilization technologies, including particle engineering, the pharmaceutical companies will improve the yield of their discovery programs and have more potential compounds to develop. ENS is applicable from early screening during drug discovery for processing compounds in quantities ranging from mg to commercial scale.

Keith Hutchison: Solubilization technology providers are playing an increasing role, globally, and across all market segments, including specialty NDA 505(b)2 application. Bioenhancement is critical in both nutraceutical and pharmaceutical applications, to enhance the efficacy of existing formulations or advance new small and large molecules to market. The customer is looking to key partners to provide the scientific depth and range of technology options to address solubility, and other formulation challenges, and meet their target product profiles. Combine this with the steady flow in the number of poorly soluble compounds and the industry is set for more commercial products utilizing solubility and permeability enhancement technologies.

Dr. Dave Miller: I envision less formulations R&D and specialized formulations expertise in-house particularly in the solubilization technology space; therefore, the industry will be relying more on external providers to develop solubility-enhanced formulations. As the percentage of poorly water-soluble compounds in development pipelines continues to increase, the demand for solubilization technologies will grow. Hence, companies providing novel solubility-enhancement solutions and services will be in greater demand and will become an increasingly more value-added component of the pharmaceutical development chain.

Peter Nelson: As was stated in Part II of this multi-part series, the need for solubilization technologies will continue to grow. Service providers, excipient and

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Joan Feixas, PhD,
CEO, Enantia -
jfeixas@enantia.com

equipment suppliers, and the pharmaceutical companies themselves will be required to operate more efficiently and at lower cost while simultaneously reducing risk. I envision the need for further collaboration between equipment and excipient suppliers, service providers, and the pharmaceutical innovators to steadily increase. The requirements, objectives, and milestones associated with projects need to be more transparent at the onset. The more all involved parties understand, the faster the desired result is attainable.

Dr. Tom Piccariello: The role of solubilization technologies will grow as products incorporating them enter and succeed in the market. Throughout the next 5 years, we see the industry growing in size and moving in directions that are validated by success. In addition to their traditional role in drug development, these new solubility technologies could provide a rescue function for previously marketed drugs or for drug candidates that were not marketed but perhaps could be when helped by the new technology. Metal coordinated pharmaceuticals have the potential to be a significant component of this expansion.

Dr. Mark Mitchnick: We like to think of it as BA providers and solubilization being one large portion of that space. Clearly, the field will expand. Our jobs aimed at increasing BA have more than doubled in the last 12 months alone.

"It may surprise some of us to realize that solid dispersions are the fastest growing solubilization platform.."
Filipe Gaspar, PhD, Director of Drug Product Technologies, Hovione - fgaspar@hovione.com

OTHER INSIGHTS

Q: Is there any information about solubilization technologies, their applications, or the benefits they can deliver you believe DDD readers would find surprising?

Dan Dobry: Some readers may find it surprising how rapidly and efficiently, spray dried dispersion technology can be applied to compounds in all phases of development. Specifically, how little API is required to produce spray dried dispersions. In some cases, only tens of milligrams are necessary to produce enough dispersion to test the feasibility in vitro or in an animal model. Readers may also find that using innovative analytical methodologies, it is possible to be very fast and quite inexpensive to complete a feasibility study. Additionally, spray drying is ideally suited to compounds that may require high containment. As long as formulators partner with companies that have the experience and know-how to scale up their formulation, it can be a rewarding experience.

Tom Dürig: I believe the power of solubilization technologies and amorphous dispersions can be truly illustrated by a recent case our scientists worked on, where we developed an amorphous drug dispersion that enhanced bioavailability 15-fold and reduced the dose from 15 capsules to 1.

Dr. Joan Feixas: Pharmaceutical cocrystallization can be used not only for solubilization, but also to improve other properties of the API, such as hygroscopicity, flowability, handling (higher melting point, easier filtration…) and tabletability. Cocrystals can also be used for chiral resolution of racemates or in purification processes of APIs or intermediates.

Dr. Filipe Gaspar: It may surprise some of us to realize that solid dispersions are the fastest growing solubilization platform. Ten years ago, such approach was generally seen as a last resort, and today is for many formulators the first or second option in their tool box.

Dr. Robert Hoerr: One of the key challenges in solubilization technologies is to produce uniform nanoparticles. Electrospray is a liquid atomization method that uses electric forces to overcome surface tension during the breakup of a liquid jet. Compared with current technologies, such as ball milling, bulk mixing, high pressure homogenization, and double emulsion techniques, electrospray has many potential advantages. First, electrospray

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Robert Hoerr MD, PhD, Co-Founder, Chief Scientific Officer,Nanocopoeia, Inc. - Bob.hoerr@nanocopoeia.com

can generate monodisperse particles. The size of particles can be varied from a few nanometers to micrometers by adjusting operational parameters. More importantly, by using different nozzle designs, structured nanoparticles with complex composite structures can be produced in a controlled way, such as for high-efficiency drug particle encapsulation. Furthermore, unlike mechanical spray techniques, electrospray is a gentle method operated at ambient conditions. As a result, the particles' chemical or biological properties are preserved without degradation due to heat or mechanical stresses. In addition, all the particles generated by electrospray carry charges with the same polarity. Particle agglomeration can be minimized using charge repulsion. Such monodisperse, non-agglomerated particles, especially particles in the nanometer range, can provide new approaches for designing high-performance drug formulations.

Keith Hutchison: Lipid, liquid, and semi-solid fill approaches are often utilized to address a range of formulation challenges in combination with bioenhancement, eg, high potency, low dosing, food effect, and API stability. And while some customers often perceive soft gel capsules as the one and only "liquid" dosage form, Capsugel has pioneered filling and sealing of liquid and semi-solid formulations in Licaps® hard capsules, and today manufactures several billion units per year commercially at US, European, and Japan-based manufacturing facilities. Combined with our SGcaps® soft gel and solid lipid pellet technology, a range of final dosage formats can be evaluated in parallel for the development of optimized bioenhanced finished dosage forms.

Dr. Dave Miller: Solubilization technologies are often thought of as being applied later in clinical development; however, these technologies are frequently employed very early in preclinical development to enable the establishment of safety and efficacy for new chemical entities. These solubilization concepts are then typically incorporated into the drug product design to support clinical studies and ultimately commercialization. In this context, solubilization technologies are enabling new molecules as they facilitate advancement at every phase of development.

Dr. Tom Piccariello: One surprising aspect of metal coordination is the degree of solubility improvement conferred upon the API relative to the low cost of synthesizing what are new compositions of matter. Once the optimized form of the drug-metal coordination complex is defined, it can be relatively simple to manufacture. The cost-effectiveness of producing patentable molecules through this approach contrasts sharply with previous efforts to accomplish similar changes with more expensive technologies. Another aspect that may be surprising is the extent to which metal coordination can be combined with other techniques to find solutions to difficult technical barriers.

Dr. Mark Mitchnick: There are several unique drug delivery approaches to enhance bioavailability by "in use" solubilization technologies, but each has different caveats. It is in the appropriate selection from the full arsenal of approaches and then excellent execution that the products with best bioavailability are developed.

CLOSING REMARKS

This concludes our interviews of the solubilization experts from the provider side of the industry. Clearly, we are gaining significant knowledge regarding the various issues that are required to develop and commercialize "enabled" formulations. As more products progress through the development stages and are launched with nanoparticles, solid dispersions, lipids, and other vehicles, strong precedence is being set that will give those with less experience the confidence to advance more compounds that have historically been viewed as "challenging." There were many

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Mark Mitchnick, MD CEO, Particle Sciences, Inc. - mmitchnick@particlesciences.com

"Metal coordination has the capacity to very effectively address API oral bioavailability issues by enhancing both water and lipid solubility simultaneously."

Tom Piccariello, PhD, Co-founder, President & CSO, Synthonics - tpiccariello@synthonicsinc.com

interesting and important points made by the column contributors in 2013, and from their input, we observed much agreement on the following points, the first about our collective success, and then two key remaining challenges:

- Significant progress is being made in new and old technologies, new and re-purposed excipients, and in the collaboration among providers and the clients they serve;
- There is broad recognition that we need to have a deeper understanding of the chemistry, functional relationships, and molecular interactions between insoluble APIs and excipients; and
- Even when new excipients and technologies emerge, lack of familiarity, and the cost of proving the safety and effectiveness can significantly slow their adoption.

Insights provided by excipients and technology experts have been a catalyst for additional thought about the solubilization formulation design stage. Probably one of the greatest needs is closely related to the second bullet point, the need for better predictability. For example, given a specific poorly soluble compound, it is still difficult to predict which technology and combination of excipients will result in the desired pharmacokinetic profile. In fact, to arrive at a suitable formulation, the typical process involves significant iterations between formulation and IV/IV testing. Improvements on this process will require advances in our understanding of the key factors governing bioavailability, how to manipulate those properties using materials science, and the interplay of those materials with the biological systems to which we intend to deliver these drugs.

As the technologies to deliver poorly soluble molecules mature, standardization will become increasingly important. Examples of this could be algorithms for screening delivery platforms, testing methods, and the nomenclature used. Standardization of the best practices for developing, characterizing, and manufacturing solubilized formulations will become an increasingly important aspect as this segment of the industry moves forward. This will enable improvements in development cycles, reduction of risk due to false starts, and better communication amongst colleagues and regulators. These benefits of standardization could also positively impact our ability to more quickly adopt new and emerging technologies and excipients.

LOOKING FORWARD TO 2014

So where do we go from here? As it relates to the column, we plan on covering additional important topics in solubilization in 2014, including the state of the academic research environment for delivery of poorly soluble molecules and the materials science that is enabling better understanding and platforms. We want to explore the views from companies that have successfully commercialized solubilized formulations. We will see what lessons have they learned and what they believe are the unmet needs? We will take a deeper dive into the key scientific drivers behind why such a large percentage of compounds are coming from discovery with poor solubility.

In conclusion, I'd like to thank again the experts who took time out of their busy schedules to contribute insights to the dialogues on excipients and solubilization technologies in the inaugural year of this column. To ensure The Second Quadrant serves as a forum for interactivity and collaboration, I invite you to send your reactions, thoughts, and suggestions so we can continue our conversation. New topic ideas are always welcome. As this is the last column of 2013, I'd like to wish all readers and colleagues success and good health in 2014. ◆

Marshall Crew
President & CEO
Agere Pharmaceuticals, Inc.
crew@agerepharma.com
LinkedIn: https://www.linkedin.com/profile/view?id=17815140

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DRUG DEVELOPMENT Executive

Aptar pharma

APTAR PHARMA: FROM SELF-INJECTION TO AUTO-INJECTION

Pierre Carlotti

Vice-President, Marketing & Communication

Aptar Pharma Prescription Division

"Designing and developing a novel auto-injector that meets all stakeholders' criteria is a fascinating and complex journey. The one-size-fits-all approach is not realistic as there are many criteria to take into account beyond user needs and preferences, due to the range of drugs, drug formulations, therapies, and patient profiles that can be catered to."

The global market for injectable drugs is valued at US $240 billion, representing some 28% of the global drug market, with an annual growth rate of +4% in 2012. In addition, the pipeline of new injectable drugs is very healthy, with more than 3,500 ongoing projects, of which the vast majority are for generics with very few biosimilars (generics of off-patent biopharmaceutical drugs) so far.

Pierre Carlotti, Vice-President of Marketing and Communication for Aptar Pharma Prescription Division, recently spoke with Drug Development & Delivery about the market for auto-injectors and some relevant market trends, and explains how his company went about designing and developing a novel auto-injector.

Q: How did Aptar Pharma become interested in the injectable drug delivery devices market? Could you tell our readers more about this new strategy?

A: Aptar Pharma is the Aptargroup business segment dedicated to meeting the needs of biotechnology, healthcare, and pharmaceutical companies with innovative and patient-focused drug delivery solutions. Our core technologies and businesses have traditionally been non-invasive spray and aerosol drug delivery devices, including electronically assisted devices. We are world leader in the pharma spray and aerosol market, manufacturing more than 1 billion proprietary devices per year, which are regulated as combination drug products, in our facilities in Asia, EU, Latin America, and North America.

Recently, we reoriented our strategy to also increase our market presence in the large and fast-growing biopharmaceutical market in which injectable devices are the gold standard dosage forms. In 2011, we sealed a strategic partnership with Oval Medical, a cutting-edge parenteral technology company based in

Cambridge, UK. In 2012, we acquired the French company Stelmi (now rebranded as Aptar Stelmi), a world-leading supplier of premium quality elastomeric closures for parenteral primary packaging. These deals will allow us to combine Aptar Pharma's recognized experience, industry leadership, and global presence with Oval Medical's expertise and Aptar Stelmi's 50-year track record, to become a leading player in high-quality injectable devices and components.

Q: Could you tell us more about the specific auto-injector segment of the injectable drug market that Aptar Pharma is targeting?

A: Auto-injectors are spring-loaded devices holding a prefilled syringe (the primary drug container) that are easy to use by design and intended for self-administration of a fixed dose by the patient, even if in some cases they are used by less trained personnel (eg, relatives of the patient).

They represent a tiny niche of the injectable drug market because they are used in only a few drug categories designed to treat selected chronic diseases. These include rheumatoid arthritis, lupus, psoriasis, spondilarthritis, multiple sclerosis, hepatitis C, anemia, and emergency/crisis treatments, such as anaphylactic shock and migraine attacks. Given the ageing of the global population and other pathophysiologic factors, the prevalence of these diseases is growing. There are also other diseases that could benefit from auto-injectors in the future, including specific indications in asthma, cancer, and cardiovascular therapies.

Currently, this small niche represents a device market worth US $130 million in 2012 - disposable and reusable auto-injectors combined - with a very dynamic annual growth rate of more than 20%.

The drug delivery device is key because it defines the user interface: there is no "good drug" without a "good device." As a consequence, self-injection requires an adapted device-user interface (the "one-size-fits-all" device technology platform does not exist), and proper training and instructions for use. This is particularly true in the case of non-chronic diseases, or when the treatment regimen dictates infrequent drug administration (eg, once every 2 or 4 weeks).

In addition, as novel injection devices are sophisticated pieces of technology with strong intellectual property protection, they are "enabling drug delivery technologies". They enhance ease of delivery in the hands of the patient (if cognitive, perceptual, and physical abilities are not too impaired by the disease) and thus reinforce patient compliance. They also sustain market differentiation, which is strategic for pharmaceutical companies to gain or protect market share. Self-injection devices are also more cost effective for the healthcare system.

FIGURE 1

Q: Pro-Ject™ (Figure 1) is Aptar Pharma's new auto-injector: can you tell us how it was designed and developed?

A: It is essential that all key stakeholders involved in the decision-making process are consulted early on in the development of a novel auto-injector. Patients and healthcare professionals are pivotal partners because they are the interface with the drug product and the device. Although pharmaceutical and biopharmaceutical companies are the natural partners of device manufacturers, it is essential for the latter to listen to, understand, and take into account the "voice of patients and healthcare professionals" so as to capture user needs, preferences, and potential misuses as early as possible. Human Science Engineering is now part of the device development process to define and refine the User Requirement Specifications in accordance with the latest regulators' guidelines.

The healthcare professional's point-of-view: Physicians are not device specialists, but they are the main prescribers. Training nurses have a pivotal role in informing, assisting, and training patients to best use the prescribed device, especially when it is used for treating chronic diseases, such as rheumatoid arthritis. Their job is complex given the variety of device technologies and operating modes, user interfaces, look and feel, as well as the variety of patient and therapy profiles. Ideally, they contribute their professional advice, training, and monitoring to reinforce patient adherence, which in the end is essential for the success of the therapy.

The patient's point-of-view: Patients are not device specialists either, but they are the regular users in the case of self-administration. Self-injection is not an easy experience, especially when the drug is painful; and it is dependent on the drug regimen. A variety of improper uses of auto-injectors have been reported, including upside-down firing, premature device firing, and removal that have significant safety and efficacy consequences. Usability is often reported as a main issue given the variety of unlocking (cap removal or push-on-skin) and firing mechanisms (activation button or slider or push-on-skin), which may confuse patients, especially when they shift from one drug product to another, which can involve a change of auto-injector. The feedback provided by the device to the patient may vary as well, with single-click and double-click audible cues, see-through control window for visual cues, and various other visual and tactile indicators.

Pro-Ject™ integrates all the identified user-preferred features. It has all the attributes of a "modern" disposable auto-injector designed around a standard glass prefilled syringe (PFS). These include two simple handling operations (Figures 2 & 3), a large and clearly visible control window and multiple safety and patient compliance features. In addition, Pro-Ject™ is very compact in size and light in weight, which is a real benefit in terms of transport, storage, and environmental footprint. Given its unique design, Pro-Ject™ can be easily adapted or tailored to specific therapy needs because the core technology provides design freedom to optimize the user interface.

Pro-Ject™ also has unique visual and acoustic feedbacks for needle insertion and end-of-injection that allow for strong product differentiation. Pro-Ject™ design and development benefit from Aptar Pharma's long experience of a Quality-by-Design approach, which translates into robust design, successful manufacturing scale-up, and flawless fast-track to market.

FIGURE 2

Q: What are the major design challenges that companies are likely to experience when designing and developing a novel auto-injector?

A: Designing and developing a novel auto-injector that meets all stakeholders' criteria is a fascinating and complex journey. The "one-size-fits-all" approach is not realistic as there are many criteria to take into account beyond user needs and preferences, due to the range of drugs, drug formulations, therapies, and patient profiles that can be catered to.

Because the relationship between the drug, the prefilled syringe, and the auto-injector is highly complex, the design and development of the optimal solution present a number of technical and scientific challenges. This requires strong project management, which must allow experts to communicate and work together effectively.

Having recognized this, the objective of device designers is to create platform technologies that can leverage the robustness of proven technical building blocks. Designers want to improve effectiveness and safety while seeking manufacturing synergies to avoid high up-front investments during development and scale-up. Minimizing R&D expenses and capital expenditure are welcome in any project but become essential for generics and emerging markets in which cost effectiveness is a major priority.

FIGURE 3

Q: What are the market trends that are particularly relevant to self-injection?

A: New drugs and reformulations of existing drugs (in the case of life cycle management of existing drug products or biosimilars/generics) often provide a set of initial challenges. The injected drug volume and the drug viscosity, which may be interrelated, both influence the selection of the prefilled syringe format and specification (materials for the barrel, stopper and needle shield components, injection volume, needle size and profile, silicon lubrication, etc) and therefore the design of the auto-injector.

Optimization of current device designs and the search for patent-protected product differentiation are strong market drivers, together with specific needs related to therapies and patient profiles. Recently, we have seen some degree of technical convergence between prefilled syringes, safety-engineered syringes, pen injectors, auto-injectors, and needle-free injectors. There is no clear demarcation line between a traditional prefilled syringe and an "automatic" device anymore, and this allows a wide range of new designs to be developed. This explains the wide variety of the devices on offer as well as the number of patents referring to injectable devices or means, which is in excess of 3,000.

Given the emergence and penetration of smart devices in the medical sector, it is natural to see novel electronic injection devices flourishing and getting close to being used on the drug market. They offer almost unlimited possibilities in terms of user feedback, monitoring, and training, with devices talking to patients and/or data being transmitted to patients and physicians. They can incorporate programmable dosing of large injectable doses (between 1 and 2 ml, or even more in the case of micro infusors and patch injectors) and high-viscosity drugs to help the patient control the rate of injection. Given the complexity of these "edevices" and the fact they incorporate electronic components and batteries, they are also faced with specific regulatory and environmental challenges compared with any conventional mechanical device. ◆

Company Profile

DISCOVERY RIDGE RESEARCH PARK
ABC Labs, Inc.
4780 Discovery Drive
Columbia, MI 65201

ORIGINAL CAMPUS ON ABC LANE
ABC Labs, Inc.
7200 E. ABC Lane
Columbia, MO 65202

T: (800) 538-5227 F: (573) 777-6033
E: info@abclabs.com
Website: www.abclabs.com

Established in 1968, ABC is a privately held company of about 400 scientists and support personnel. We provide a broad array of GLP- and CGMP-compliant product development and analytical testing services to the pharmaceutical, biotech, animal health, and medical device industries. Our approach to doing business promotes relationships beyond a simple transaction. It facilitates collaboration, promotes quality, makes better use of resources, and helps us plan to have the right talent and resources when and where our clients need them. It also improves decision-making, which can save time, money, and reduce risk. In other words, better insight, better outcomes.

Company Background

For more than 4 decades, ABC has been delivering analytical expertise in support of product development. But like the industries we serve, our company has changed. Today's ABC offers more than superior science and quality data. Through development know-how, cross-disciplinary technical expertise, and applied experience with multiple regulatory frameworks, ABC delivers the kind of scientific insight that drives better outcomes.

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Company Profile

ADHESIVES RESEARCH, INC.
400 Seaks Run Road
Glen Rock, PA 17327
T: (717) 235-7979
Toll-Free: (800) 445-6240
F: (717) 235-8320
Website: adhesivesresearch.com

ADHESIVES RESEARCH IRELAND LTD.
Raheen Business Park
Limerick, Ireland
T: +353 61 300 300
F: +353 61 300 700
Website: adhesivesresearch.com

It all starts with a partnership approach to product development.
With decades of experience formulating and manufacturing high-performance pressure-sensitive adhesive (PSA) systems for the pharmaceutical industry, Adhesives Research is known for its specialty adhesive and film components for transdermal, oral, and topical drug delivery systems. We are one of the world's leading independent developers of high-performance custom PSAs, tapes, coatings, specialty films, dissolvable films, and laminates.

Our mission is to innovate.

Adhesives Research offers custom polymer synthesis, adhesive mixing, compounding, coating, and release liner design supported by comprehensive analytical capabilities. It's through the flexibility of these capabilities that we have pioneered the use of many adhesive and coating technologies to enable the world's leading pharmaceutical and drug delivery companies to launch innovative products for applications in:

- Transdermal delivery systems
- Device-assisted drug delivery systems
- Oral drug delivery

Quality and compliance come first.

Our cGMP-segregated manufacturing and ISO 9001 and 13485-compliant quality systems help us manufacture world-class adhesive tapes and coated products. We offer diverse manufacturing capabilities to produce pharmaceutical and medical device components under the appropriate Code of Federal Regulation requirements and ISO standards to support our customers in their FDA approval process, including:

- More than 20 coating lines in our state-of-the-art US and European manufacturing facilities.
- Five isolated manufacturing lines for the production of components used in pharmaceutical, medical device, and consumer applications under ISO 9001 and 13485.
- Two manufacturing lines dedicated to our ARx, LLC subsidiary incorporate APIs into dissolvable films and adhesive coatings under 21 CFR 211.

Custom formulations for each application.

Based upon proven PIB, acrylic, and silicone polymer technology platforms, Adhesives Research's skin-friendly adhesives are available with conductive, porous, occlusive, hydrophilic, hydrophobic, gentle, or long-term wear adhesion functional properties to meet the unique needs of our clients' applications.

Where to find us.

Founded in 1961, Adhesives Research is headquartered in Glen Rock, PA. Our global expansions have included the opening of a manufacturing facility in Ireland; sales and marketing offices in Great Britain and Singapore; a representative office in Shanghai, China; and sales representation in Japan, Korea, and Taiwan. Additionally, Adhesives Research operates two technical centers for the design and development of custom adhesives, coatings, and film components; one in Pennsylvania, and the other in Ireland.

AGERE PHARMACEUTICALS, INC.
62925 NE 18th Street
Bend, OR 97701
T: (541) 318.7115 F: (541) 318.7082
E: info@agarepharma.com
Website: www.agerepharma.com

Leveraging best practices for superior results. Agere is a CDMO committed to Quality-by-Design (QbD) principles and focused on enhancing the bioavailability of poorly soluble drugs. Clients choose Agere for API-customized formulations and comprehensive cGMP manufacturing and analytical services. Our modern approach to solubilization formulation is enabled by our Quadrant 2™ platform, which encapsulates expertise and fundamental science. Adhering to a QbD-based discipline from the earliest stages empowers Agere scientists to focus on achieving results to meet the ultimate goals for each client's drug product.

Modern solubilization formulation. Agere's formulation platform, Quadrant 2, embodies a new approach that enables efficient, scientifically sound, and unbiased exploration of solubilization alternatives tailored to achieve business and efficacy objectives for each drug product. Quadrant 2 adopts best practices to inform and discipline the formulation process from inception. By isolating promising solubilization approaches earlier, we can then invest rigorous effort on formulations that have a higher probability of achieving the requisite performance, stability, and manufacturability. Each client's goal is to ultimately achieve an efficacious, safe, and profitable drug product. Agere's Quadrant 2 incorporates these goals from the beginning to navigate the best path to a predictable and successful outcome.

Formulation development. Agere's drug product development services leverage our Quadrant 2 platform, and our extensive process, analytical and manufacturing capabilities. They also benefit from the systematic approach intrinsic to the QbD methodology as we evaluate, define, analyze, and refine the manufacturing process and procedures. Agere applies our broad formulation knowledge base, analytical support, and unique computational tools to produce capsule and tablet forms suitable for IND-enabling studies and clinical trials. Throughout each project, we develop the appropriate critical process parameter information and comprehensive drug product specifications. This information is then packaged in technology transfer documents for our clinical trial manufacturing team.

cGMP manufacturing and analytical. Clients often start with Agere in formulation, and then rely on us for cGMP manufacturing and analytical through Phase III. Agere's commitment to a rigorous and systematic approach continues into CTM, where we support clients using our versatile cGMP manufacturing suites, a fully compliant cGMP analytical lab, and ICH stability storage facilities. Our integrated team of specialists provides efficient transfer of formulation development programs into clinical trial campaigns and beyond. Combined with Agere's solubilization formulation design and development services, our cGMP expertise also facilitates applications for IND/IMPD.

Please contact us and see why we're one of the fastest-growing solubilization CDMOs in the industry.

Company Profile

Aptalis Pharmaceutical Technologies
100 Somerset Corporate Blvd.
Bridgewater, NJ 08807
T: (908) 927-9600
Website: www.aptalispharmaceuticaltechnologies.com

Aptalis Pharmaceutical Technologies is your trusted oral drug delivery partner for overcoming even the most demanding delivery challenges. We enable our partners to successfully bring valuable patient-optimized products to market through our commitment, expertise, and proprietary technologies. Our comprehensive portfolio of oral drug delivery technologies for *bioavailability enhancement, custom release profiles, and taste-masking* for orally disintegrating tablets (ODTs) and other dosage forms are employed in a customized approach to meet our partners' needs.

As an experienced oral drug delivery partner to the global pharmaceutical industry, Aptalis is focused on delivering high-value products with robust, defensible proprietary positions for our partners that grow the commercial value of their portfolio. We are committed to our partners' success, providing flexible and tailored co-development and product out-licensing agreements for value-added Rx and OTC products across multiple therapeutic categories.

We have integrated R&D and manufacturing facilities in the US and Europe, where our teams of experts apply a rich array of development, manufacturing, and regulatory skills to successfully deliver patient-optimized medicines to our partners in various regions around the world.

Microcaps® and AdvaTab® for Taste-Masking and Orally Disintegrating Tablets (ODTs)

The Aptalis Pharmaceutical Technologies portfolio of proprietary taste-masking technologies has been validated in numerous products commercialized around the world. These technologies can also be used in combination with our customized drug release technologies to develop unique product formulations, with pleasant taste, excellent mouth-feel, custom release profiles, and multiple administration options.

Diffucaps® and Diffutab® for Customized Drug Release

The Aptalis Pharmaceutical Technologies portfolio of customized drug release technologies provides a wide variety of customized release profiles that can be tailored to optimize a drug's therapeutic performance. For example, a particular drug may require both rapid onset of action and sustained release within a single dosage unit, while a different drug may require escalation of physiological drug levels rapidly after a defined delay. Other drugs may be part of a combination product that requires different release profiles for each active ingredient. Our proprietary technologies can be used alone or in combination with taste-masking technologies to develop customized release profiles to address a variety of therapeutic needs.

Biorise™ for Bioavailability Enhancement

Our patented, and proprietary Biorise™ technology enables and improves the bioavailability of drugs with low solubility. Biorise™ can improve the rate and extent of drug solubilization, which can result in faster onset of action, improved bioavailability, equivalent therapy at lower doses, and/or effective oral dosing of poorly soluble drug candidates.

To learn how a partnership with Aptalis can advance your product toward commercial success, contact us at:
www.aptalispharmaceuticaltechnologies.com

Ashland — your pharmaceutical technology resource

Controlled-release Formulation Solutions

With over 60 years of experience, Ashland can meet your controlled-release formulation needs by providing the broadest range of excipients and technologies, as well as polymer expertise and technical support from benchtop to commercialization.

Our products for modified- and sustained-release formulations include:

- **Introducing directly compressible Benecel™ DC hypromellose (HPMC) for:**
  - **Increased content uniformity**
  - **Improved flow**
  - **Lowered manufacturing costs**
  - **Reduced development time**
- Custom-molecular weight Benecel™ HPMC grades for matrix tablets
- High-viscosity grades of Klucel™ HPC for sustained release and diffusion control in matrix tablets
- Delayed-release (enteric) grade Aquarius™ coating systems based on methacrylic acid/ethyl acrylate copolymer
- Extended-release Aquarius SRX coating systems (based on Aqualon™ EC) for use with organic solvents

Ashland can also provide starting formulations based on desired tablet properties or predict tablet properties using formulation information, thus reducing customers' time to market and development cost.

For more information, please contact your local Ashland Specialty Ingredients representative or visit us at ashland.com/ddd/pharmaceutical.

ASHLAND

With good chemistry great things happen.™

ASHLAND INC.
8145 Blazer Drive
Wilmington, Delaware 19808
T: (877) 546-2782 E: pharmaceutical@ashland.com
Website: ashland.com/pharmaceutical

General Company Description

Ashland Specialty Ingredients, a commercial unit of Ashland Inc., offers an unparalleled range of products to meet the needs of the pharmaceutical and nutraceutical industries. Our products offer a variety of functions as described in this brochure. Because Ashland's products are based in both cellulosic and vinyl pyrrolidone polymer manufacturing, we provide innovative solutions through a broad range of chemistries to meet our customers' formulation needs. Our global manufacturing plants are held to strict cGMP standards, meaning our customers can depend on high-quality products, regardless of manufacturing site.

Ashland is your full-service pharmaceutical technology resource for tablet binding, film coating and disintegration; as well as excipients for controlled release and drug solubilization.

TECHNICAL SERVICES

Analytical Capabilities

- Advanced powder flow and segregation testing
- Dissolution USP I, II and III
- Differential scanning calorimetry and thermogravimetric analysis
- Melt rheology
- Microscopy - scanning electron, polarized light and high resolution digital
- Kinetic dissolution
- Advanced mechanical testing
- Size exclusion chromatography
- Karl Fischer titration
- Coulometry
- Nuclear magnetic resonance
- High-performance liquid chromatography and gas chromatography
- Infrared and ultraviolet spectroscopy
- X-ray powder diffraction
- Laser diffraction

Pilot Manufacturing/Testing Capabilities

- Fluid beds with capacity up to 300 liters
- Several sizes of tablet coaters
- Numerous tablet presses and a MEDELPHARM Stylcam compaction simulator
- Extrusion/spheronization
- Hot-melt extrusion
- Spray-dried dispersions
- Formulation design
- Oral solid dosages
- cGMP manufacturing for clinical trials

FACILITIES

Ashland offers a formidable variety of technical capabilities to meet the needs of the pharmaceutical and nutraceutical industries. Through our global network of technical service laboratories we offer assistance with formulation development, problem solving and analytical support. Our facilities are located in Wilmington, DE, Hyderabad, India; Istanbul, Turkey; São Paulo, Brazil; Shanghai, China; Mexico City, Mexico; and Buenos Aires, Argentina.

MAJOR PRODUCTS/SERVICES

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

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

MARKETS SERVED

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 Specialty Ingredients offers comprehensive and innovative solutions for today's demanding consumer and industrial applications.

TRANSDERMAL TRANSCENDENCE

A higher level of performance

Delivers new possibilities

- **Global Production Capabilities**
- **Turnkey GMP Operations**
  - > From product feasibility to commercial supply
  - > Decreased tech transfer risk
- **AVEVA Offers**
  - > Proprietary pipeline and approved product licensing
  - > Co-development & Joint Venture opportunities
  - > Full range of R&D and manufacturing

AVEVA
DRUG DELIVERY SYSTEMS

That's the promise of Aveva Drug Delivery Systems, combining innovation and unparalleled industry experience to advance drug delivery and pioneer new frontiers in transdermal drug delivery for new chemical entities and life cycle management opportunities to enhance existing products.

As a global leader of transdermal patches offering a full range of research, development and manufacturing capabilities, Aveva transcends traditional limitations of patch technology and business partnerships to achieve new levels of product and corporate performance.

- > Customizing solutions to the unique characteristics of each drug
- > Masterfully balancing the patch properties of adhesion reliability and gentleness that lead to an enhanced patient experience
- > Transdermal candidate assessment of APIs in as little as four weeks

A flexible, customer-oriented business philosophy that adds value to projects and exceeds customer expectations

To license a product or to see how we can add value to your project, call Robert J. Bloder, Vice President Business Development, at **954.624.1374** or visit **www.AvevaDDS.com**

AVEVA DRUG DELIVERY SYSTEMS, INC.

TRANSDERMAL PATCH EXPERTS

3250 Commerce Parkway
Miramar, FL 33025
T: 954-624-1374
Website: www.avevadds.com
Contact email: Robert.bloder@avevadds.com

AVEVA Drug Delivery Systems Inc. is a global leader in transdermal drug delivery located in the United States. The company has an extensive history of providing pharmaceutical partners with fully integrated, controlled-release transdermal products that fulfill unmet market needs or supply high-quality, affordable brand equivalents. By leveraging this experience, AVEVA offers a full range of research, development, and manufacturing capabilities to produce transdermal pharmaceutical products that can improve the quality of life, usage, and compliance rates for patients.

A Higher Level of Performance

That's the promise of Aveva Drug Delivery Systems, combining innovation and unparalleled industry experience to advance drug delivery and pioneer new frontiers in transdermal drug delivery for new chemical entities and life cycle management opportunities to enhance existing products.

Aveva transcends traditional limitations of patch technology and business partnerships to achieve new levels of product and corporate performance.

- Customizing solutions to the unique characteristics of each drug
- Masterfully balancing the patch properties of adhesion reliability and gentleness that lead to an enhanced patient experience
- Transdermal candidate assessment of APIs in as little as four weeks

Aveva implements a flexible, customer-oriented business philosophy that adds value to projects and exceeds customers' expectations.

For more information, please contact Robert J. Bloder, Vice President, Business Development for:

***Product & Pipeline Licensing Opportunities**
***Joint Ventures & Co-Developments**

Battelle
The Business of Innovation

BATTELLE
505 King Avenue
Columbus, OH 43201
T: (800) 201-2011
E: solutions@battelle.org
Website: www.battelle.org

As the world's largest independent research and development organization, Battelle's Health and Life Sciences Global Business delivers comprehensive innovations to support the development of significant advances in medical devices, biopharmaceuticals, public health, and next-generation diagnostics and therapeutics. Battelle's integrated approach combines several science, technology, and engineering disciplines in its biopharmaceutical non-clinical and drug delivery research and development businesses. These capabilities offer unmatched interdisciplinary expertise from discovery through post-market support.

PHARMACEUTICAL & MEDICAL DEVICES

Accelerating Innovation for the Healthier World

Let Battelle help you accelerate your medical product development timeline, from ideation to evaluation to commercialization. Our multidisciplinary teams advance innovation by integrating world-class expertise across a wide range of science and engineering disciplines. We are redefining the possible in drug delivery, Human Centric Design (HCD), molecular imaging, in vitro diagnostics, and neurotechnology.

Drug Delivery: Bring innovative new drug and biologic delivery systems to market safely and effectively. Battelle provides risk assessment, sustaining engineering support or complete end-to-end development solutions for autoinjectors, combination injection devices, patch-pumps, infusion pumps, contrast media injectors, inhalation delivery systems, skin-permeation delivery systems, and emerging drug delivery innovations.

Human Centric Design (HCD): Translate ambiguous end-user needs into specific technical and engineering requirements. Battelle has applied Human Centric Design principles to medical device development for more than half a century. Our cross-disciplinary HCD teams combine cognitive psychology, behavioral science, industrial design, materials science, and engineering.

Molecular Imaging: Translate scientific discovery into innovative molecular imaging applications. Battelle applies expertise in biomarkers, medical device development, and molecular probes to deliver real-world solutions for our clients. Our scientists work on the leading edge of nuclear medicine and imaging across a broad spectrum of specialties, including radiopharmaceutical delivery, power injector systems, radiopharmaceutical and radioisotope generation, gamma imaging, and PET/SPECT technology.

In Vitro Diagnostics: Minimize your risks, reduce time to market, and provide a smooth transition from R&D to manufacturing with Battelle's diagnostic product development services. We integrate product development and engineering; advanced materials development; bioinformatics; biologics development; biomarker research, development, discovery, and validation; chemistry development; optics development, and engineering; FDA regulatory compliance; and manufacturing solutions.

Neurotechnology: Find new applications for the latest discoveries in neurotechnology. Battelle scientists and engineers are applying the latest technologies and neural decoding methods to develop pioneering neurotechnology applications, from wheelchair control to brain cancer detection. We integrate expertise across multiple disciplines, including control systems, automated and robotics systems, sensor development, electrical and electromechanical device design, and electrophysiological signal processing.

3D Printing/Rapid Prototyping: Mitigate risk and improve cost-effectiveness with Battelle's 3D printing/rapid prototyping service. We utilize the latest, leading-edge technology to quickly create product prototypes that help you identify potential deficiencies early in the developmental process.

CRODA

Croda Health Care
North America
marketing-usa@croda.com
Europe, Middle East, Africa
hc-europe@croda.com
Latin America
marketingla@croda.com
Asia
hc-asia@croda.com
www.croda.com/healthcare

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™
  - 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

MORE TECHNOLOGY.

MORE SOLUBILITY.

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

SOLVE PROBLEMS WITH CAPTISOL SOLUTIONS.
VISIT US AT AAPS 2013 AT BOOTH #3910.

CAPTISOL®
A Ligand TECHNOLOGY

CAPTISOL.com

Company Profile

CAPTISOL®
A Ligand TECHNOLOGY

Captisol, a Ligand Technology
11119 North Torrey Pines Road
Suite 200
La Jolla, CA 92037
Website: www.captisol.com
E: orders@captisol.com

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

The CAPTISOL® technology is used to address solubility and stability limitations in drugs. Six FDA-approved, CAPTISOL-enabled® medications are marketed by: Pfizer, Zoetis, Bristol-Myers Squibb, Baxter Healthcare and Onyx Pharmaceuticals. CAPTISOL® also has agreements in place with a number of pharmaceutical companies worldwide with CAPTISOL-enabled® product candidates. Routes of administration investigated include parenteral, oral, ophthalmic,nasal, topical, and inhalation.

The regulatory acceptance of CAPTISOL® is supported by extensive safety studies demonstrating its excellent systemic safety profile. In 1999, a Type V Drug Master File (DMF) was 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.

Catalent®

optimized delivery technologies. better outcomes.

Every molecule has a challenge. We have a solution. From orphan drugs to blockbusters, our development expertise, delivery technologies and reliable supply deliver better outcomes for payers, patients and innovators.

INNOVATIVE DELIVERY OPTIONS

Solutions for more molecules with versatile, proven RP Scherer softgel technologies.

- OPTISHELL™ FOR COMPLEX FILL FORMULATIONS
- OPTIGEL BIO™ FOR MACROMOLECULES
- OPTIGEL LOCK™ FOR ABUSE DETERRENCE

ENHANCED BIOAVAILABILITY

Improved solubility and permeablity. Optimized final dose forms. Integrated services from development to supply.

- RP SCHERER SOFTGEL TECHNOLOGIES
- OPTIMELT™ HME TECHNOLOGY
- ZYDIS® NANO TECHNOLOGY

OPTIMIZED CONTROLLED RELEASE

Better outcomes with improved regimens and target release profiles. A wide range of dosing options: combination, dividable and pulsed release.

- CONTROLLED RELEASE TECHNOLOGIES
- OSDrC® OPTIDOSE™ TABLETS

SOLUTIONS FOR TARGET POPULATIONS

Better adherence and patient outcomes. Ideal for pediatric and geriatric populations, specific conditions and disease areas.

- ZYDIS® FAST-DISSOLVE TABLETS & GRANULES
- OPTIGEL MICRO™ TECHNOLOGY

DEVELOPMENT DELIVERY SUPPLY

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

+1 888 SOLUTION solutions@catalent.com www.catalent.com/betteroutcomes

Company Profile

Catalent Pharma Solutions
14 Schoolhouse Road
Somerset, NJ 08873
T: (888) SOLUTION or (888) 765 8846
E: solutions@catalent.com
Website: www.catalent.com

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 over 75 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 85 of the top 100 pharmaceutical and 41 of the top 50 biotech marketers. Our team of over 1,000 talented scientists has supported more than half of innovative drug and biologic approvals since 2004, 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.

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

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

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. Our robust GPEx® mammalian cell line engineering technology accelerates large molecule drugs 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.

OUR CAPABILITIES JUST WENT FROM

BROAD TO BROADER

FROM SEMI-SOLIDS TO LIQUIDS TO SOLIDS

FROM NON-STERILE TO STERILE

FROM CONCEPT TO COMMERCIALIZATION

FROM VIRTUAL TO LARGE PHARMA

The integration of DPT Labs and Confab expands our capabilities and expertise in dosage forms from semi-solids and liquids to include solid dose.

Learn more about what our integration can do for you.

www.dptlabs.com
www.confab.com

DPT®

Confab

A DPT COMPANY

Company Profile

DPT Laboratories
318 McCullough Ave.
San Antonio, TX 78215
T: 1-866-Call DPT
Website: www.dptlabs.com

Company Background: Date Founded: 1938
Number of Employees: 1,000

Company Description: With a specialized focus on semi-solids and liquids, DPT offers pharmaceutical companies the broadest range of capabilities in the industry. From R&D formulation to commercial-scale manufacturing, small batches to large, liquids to emulsions, sterile or non-sterile, we offer clients of all sizes the most effective resources for meeting challenges. When it comes to the development and manufacturing of semi-solids and liquids, DPT has unmatched level of scientific and engineering expertise

In 2013, DPT and Confab Laboratories integrated businesses and solidified the leadership position in semi-solids and liquids while broadening our offering to include a wide array of solid dosage forms.

Separately, DPT and Confab were leaders in the development and manufacturing of semi-solids, liquids, and solid dose forms. With integration, we've not only broadened our service offerings but we've also expanded our access to a greater number of skilled and knowledgeable employees across both organizations. Integration allows us to better serve the needs of our clients in North America and around the world with high quality pharmaceutical development and manufacturing services.

Whether you're a start-up operation or Big Pharma, we can take your project all the way from lab to production. Just as important, we continue to invest heavily in our capabilities, including centers specializing in semi-solid and liquid manufacturing, aseptic manufacturing, solid dose manufacturing and R&D.

Services & Capabilities

Development

- Formulation Services
- Analytical Services
- Packaging
- Process Development
- Stability Studies
- Microbiology
- Clinical Trial Materials
- Regulatory Submission
- Inhalation Product Testing

Manufacturing

Capabilities	DPT San Antonio	DPT Lakewood	Confab Montreal
Sterile			
Injectables	✓	✓	
Ophthalmics		✓	
Nasal Sprays		✓	
Ointments		✓	
Non-Sterile			
Aerosol foams & Sprays	✓		
Rectal/Vaginal applications	✓		
Extrusions	✓		
Tablets			✓
Capsules			✓
Liquid FFS			✓
Suppositories			✓
Plastic Ampoules			✓
Creams	✓		✓
Emulsions	✓		✓
Gels	✓		✓
Lotions	✓		✓
Ointments	✓		✓
Solutions	✓		✓
Suspensions	✓		✓

Facilities

San Antonio, Texas

- The Center of Excellence for Research and Development offers comprehensive development services and customized solutions or sterile and non-sterile semi-solid and liquid dosage forms.

- The Center of Excellence for Semi-Solids and Liquids provides solutions for both clinical and commercial-scale manufacturing according to current Good Manufacturing Practice (cGMP) guidelines. This center also includes a dedicated aerosol and pressurized Metered-Dose Inhaler (pMDI) manufacturing facility.

Lakewood, New Jersey

- The Center of Excellence for Sterile and Specialty Products specializes in the development and aseptic manufacturing of clinical trial materials and commercial-scale products that meet the most stringent sterile pharmaceutical requirements.

Montreal, Quebec

- Specializing in the manufacturing of solid, semi-solid and liquid dosage forms. Our 140,000 sq. ft. facility is one of the most respected cGMP compliant facilities in Canada. In addition to being licensed by Health Canada Therapeutic Products Directorate, our facility has been inspected, accepted and licensed by the U.S. Food and Drug Administration (FDA), Anvisa and other international markets.

18th Annual

DRUG DELIVERY PARTNERSHIPS™

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January 27-29, 2014
Boca Raton Resort & Club
Boca Raton, FL

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Driving True Innovation in Life Sciences by Defining and Meeting the Unmet Need

Alfred Mann
Chief Executive Officer and Chairman of the Board
MANNKIND CORPORATION

The Future of Drug Delivery Technologies

Fernando Sallés, PhD, CLP
Executive Director, Strategic Licensing and Acquisitions Lead, Ophthalmics and Drug Delivery Technologies
MERCK RESEARCH LABORATORIES

Plus!

- Human Factors
- Connected Health
- Informatics
- And more!

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*valid after November 15, 2013 and only applicable to the standard registration rate

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NEW!

Delivering Drugs Beyond the Blood-Brain Barrier

Madhavan Nair, PhD
Professor and Founding Chair, Dept of Immunology, Director,
INSTITUTE OF NEURO-IMMUNE PHARMACOLOGY;
Associate Dean, FIU COLLEGE OF MEDICINE;
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Sesha Neervannan
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Co-Founder and Co-CEO, SHEEX, INC.;
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Formex is a leading specialty contract development and manufacturing organization (CDMO) offering pharmaceutical dosage form development and cGMP manufacturing. Formex is privately owned by the Biotech Investment Group of San Diego, California.

Formex science specializes in bioavailability enhancement solutions for pharmaceutical and nutraceutical APIs.

Formex is the recognized world leader in Hot Melt Extrusion (HME) expertise for bioavailability enhancement and manufacturing. Formex is also a scientific leader in addressing amorphous dispersion development via Spray Drying Dispersions (SDDs).

Our scientists have decades of experience developing HME and SDD formulations.

The legacy of formulation development at Formex was the foundation that grew to our modern day capabilities to support clinical trial and larger scale cGMP manufacturing.

Formex has performed work for numerous pharmaceutical and biotechnology companies throughout the world while complying with the Food and Drug Administration.

In addition, Formex is licensed by the DEA to handle controlled substances (Schedules III-V).

All of our services are performed according to FDA-ICH guidelines, client- approved protocols and Standard Operating Procedures.

Formex operates an 80,000-sq-ft facility in the Torrey Pines region of San Diego California. With over 25,000 sq ft of cGMP clinical and commercial manufacturing space, including 17 separate and dedicated cGMP suites, Formex has suites qualified and dedicated for cytotoxic compound handling as well as potent compound handling.

The Formex facility has over 40,000 sq ft dedicated to R&D, analytical labs, and cGMP ICH stability storage.

With temperature-controlled cGMP warehouses and the entire facility on a dedicated backup generator system, Formex operates a world-class facility of cGMP and R&D labs that is among the best for a contract development and manufacturing organization (CDMO).

Formex performs a wide range of contract pharmaceutical services including:

- Formulation Development
- Bioavailability Enhancement
- Analytical Testing
- Hot Melt Extrusion
- Spray Dried Dispersions
- ICH Stability Testing
- cGMP Manufacturing of Clinical Trial Materials
- cGMP Commercial Manufacturer (small scale)

Dosage form capabilities include but are not limited to:

Tablets
- Immediate, Sustained, Enteric, Controlled Release
- Chewable, Effervescent, Fast Dissolving
- Film Coating (aqueous and solvent based
- Pulsatile Release
- Taste/Odor Masking
- Molded Tablets

Capsules
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  - Powder, Pellets, Granules, Tablets
- Liquid-Fill
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Company Profile

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219 Changebridge Road
Montville, NJ 07045
T: (800) 724-2372
Contact: Anthony Galasso (agalasso@lifesciencepr.net)
Website: www.lifesciencepr.net

LifeSciencePR, a spin-out of well-established SGW Integrated Marketing & Communications, is a full-service lifescience marketing and communications agency specifically assembled to address the unique challenges, issues, and opportunities of emerging and innovative life science companies. Our experienced staff knows what it takes to break through with your breakthroughs! Whether it's capital, co-development partners, a step up in valuation, etc., we can power your engine in your continued drive toward your financial and corporate objectives.

Public Relations/Media Relations

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

Investor Relations

IR is a strategic management responsibility that integrates finance, communication, marketing, and securities law compliance to enable the most effective two-way communication between a company, the financial community, and other constituencies, which ultimately contributes to a company's securities achieving fair valuation. We can help, whether it's capital raising, financial community meetings and contacts, and traditional or internet corporate communications.

Social Media Development/Management

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

Multimedia/Interactive/Web Design

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

SEO/SEM

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

Advertising Design

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

Traditional/Online Media Planning & Placement

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

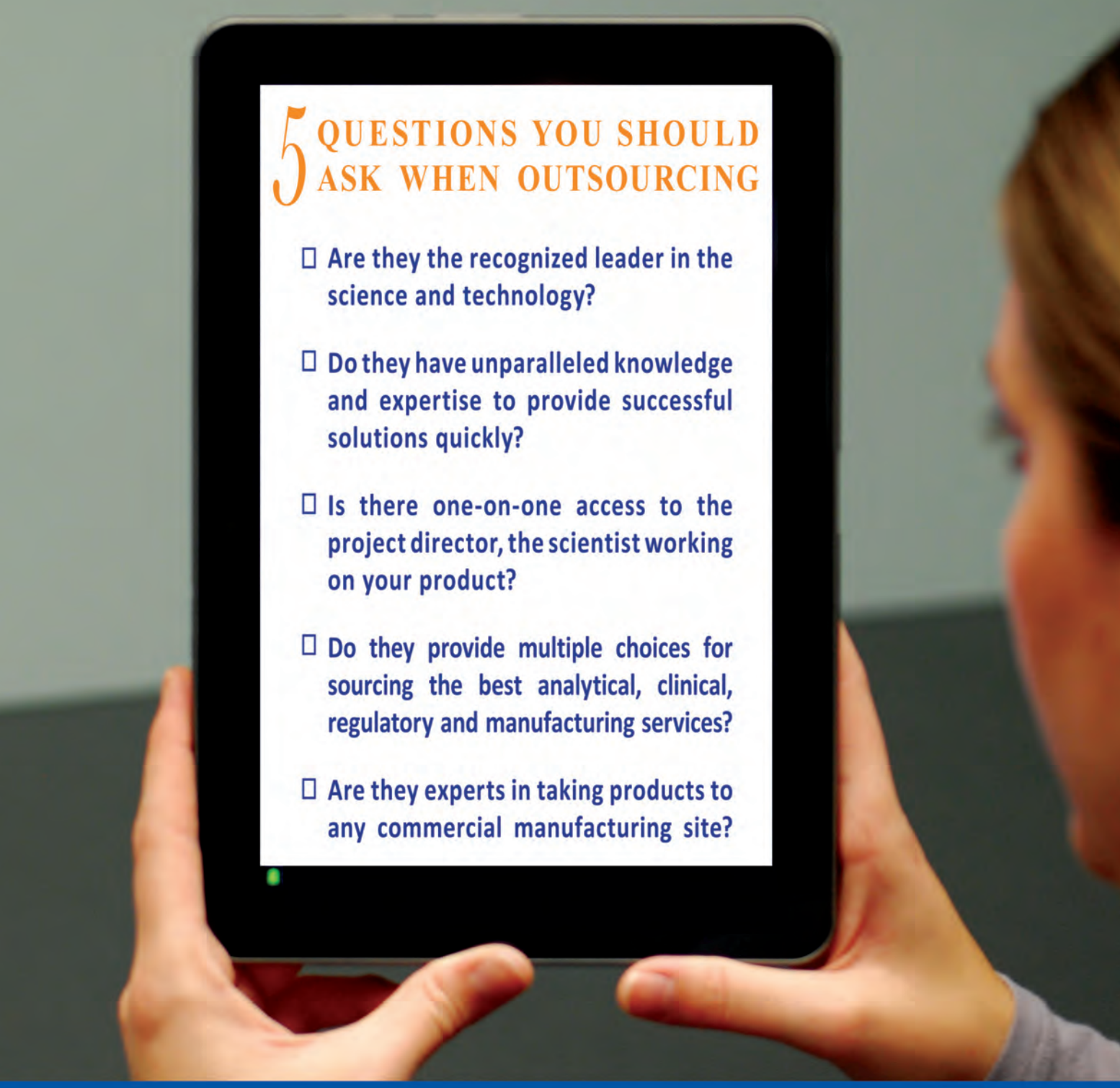
Tradeshow/Event Planning

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

Research & Focus Group Services for:

- Brand Development
- Client Perception

Building a world-class brand and a positive effective perception doesn't happen by chance. It's a purposeful endeavor that is rooted in the fusion of disciplined, strategic thinking and execution. The result is an asset that drives your business ahead. Our strategic platform and architecture will get you there!



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Company Profile

Lyophilization Technology, Inc.
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

A Contract Development and Manufacturing Organization focused on all aspects of Lyophilization. A talented and dedicated staff, skilled through experience, is coupled with in-house capabilities in product development, process engineering, clinical manufacturing, and technical support. Recognized as an industry leader, the company has a proven reputation in providing innovative solutions, achieving desired results, and exceeding client expectations.

MAJOR PRODUCTS/SERVICES

LTI has successfully developed formulations, manufacturing processes, and prepared material for clinical trials for over 384 diverse products. Gain the benefits of the experience and capabilities for creating solutions for the unique needs of lyophilized products.

- Anti-infectives
- Human/Recombinant Biologics
- Vaccines
- Oncolytics HPCs
- Small Molecules/Therapeutics
- Diagnostics

Capabilities

- Pre-clinical to Phase II Clinical Materials, lyophilized and liquid products
- Dedicated/disposable product contact items/equipment
- Containment capabilities for handling cytotoxic/high potent APIs
- Lyophilizers ranging from 0.2 m2 to 4.5 m2
- Praxair ControLyo™, Nucleation On Demand ***New***
- Vials from 2 to 160 mL and novel delivery systems
- Cartridges/syringes from 1 to 50 mL ***New***
- Bulk Lyophilization or Drying
- Batch sizes to 75L
- Drug and Device Registration/DEA license
- US/EU compliant

Development Sciences

Development services are conducted with a product quality and manufacturing mindset. This entails considering product administration, stability, and processing requirements from the start. Distinct development and process laboratories provide ample capacity for small-to-medium scale formulating through fill and finish activities. Filling, stoppering and loading the qualified pilot-scale lyophilizers are completed in certified Class 100 clean rooms to emulate aseptic manufacturing conditions.

- Thermal Analysis
- Product Design
- Formulation Development
- Cycle Design/Refinement
- Product Characterization
- Toxicology Material

Clinical Manufacturing

The Clinical Manufacturing Area (CMA) is flexible for preparation of products with unique requirements, adheres to aggressive project timelines, and is fully cGMP compliant. The dedicated CMA includes separate controlled areas for warehousing, preparing materials, compounding, fill/finish, and inspection. The aseptic processing suite features containment and isolation technology. The operation has been inspected and approved for handling BSL-2 material.

- Pre-clinical
- Phase I
- Phase II
- Liquid Fills

Technical Services

The broad range of experience in a wide variety of products provides a specialized expertise from which you can capitalize. Technical services are available providing support for all aspects of lyophilization.

- Customized Training
- Validation
- Investigations
- Quality/Compliance

MAJOR MARKETS

LTI has provided lyophilization-focused Development and Clinical Trial Material Manufacturing services to more than 296 biotechnology and pharmaceutical clients spanning from virtual, small to large multi-national companies over 20 years.

The **TECHNOLOGY**

The **INTELLIGENCE**

The **STRENGTH**

TO

MAXIMIZE YOUR PRODUCT'S POTENTIAL

Improving your product's bioavailability, taste and controlled release options can have significant therapeutic and convenience benefits to patients. They can also provide additional lifecycle opportunities for your existing products. Metrics is now sharing its new proprietary specialty technologies with clients through a range of partnering options, including licensing and co-development. Ask how our innovative drug delivery technologies can help you find your product's true potential. Or learn more at www.metricsinc.com.

Metrics INC.

Improved Bioavailability.
SUBA™ is our novel drug delivery technology for enhancing the bioavailability of poorly water-soluble drugs.

Taste Masking.
Cleantaste™ is a proprietary technology to mask the taste of liquids and tablets, which can improve patient compliance and potentially reduce dosage frequency.

Controlled Release.
Our proprietary pellet technologies enable a range of controlled release of active pharmaceutical ingredients (API).

Metrics is a full-service CDMO that adds value to its clients' product portfolio through innovative, proprietary technologies.

Metrics / Greenville, NC / 252-752-3800 / www.metricsinc.com

Company Profile

Metrics, Inc.
1240 Sugg Parkway
Greenville, NC 27834
T: 252-752-3800
Website: www.MetricsInc.com

Contacts: Jeff Basham, Vice President, Marketing & Sales, jeff@metricsinc.com,
Tom Salus, Director of Sales, tsalus@metricsinc.com

Company Description

Metrics Inc. is one of the most respected contract pharmaceutical research, development and manufacturing companies in the United States today.

Started as an analytical laboratory in 1994, Metrics has evolved into a full-service provider of:

- Quality pharmaceutical formulation development
- First-time-in-man (FTIM) formulations
- Clinical material manufacturing (CTM) for Phase I, II, and III trials
- Commercial manufacturing
- Analytical method development and validation services
- Specialty technologies for controlled release, bioavailability enhancement, and taste-masking

Metrics proudly operates as a subsidiary of Mayne Pharma Group Limited, a publicly traded pharmaceutical company in Melbourne, Australia.

Areas of Expertise

Metrics has developed expertise in a number of key areas, including:

- **Formulation development.** Averaging 17 years of career experience, our formulation development scientists offer expert recommendations on insoluble and unstable actives, potent and toxic actives, and small molecule delivery.
- **Potent & cytotoxic products.** Our cGMP-dedicated and segregated facility features custom-engineered total containment. With no open processes or PAPRs, and one-way material flow, containment is achieved at <=30 nanograms cpm.
- **Fast-track development.** With our industry-leading ratio of four analytical chemists for every formulator, Metrics can meet accelerated timelines and deliver from NCE to first-time-in-man within 6 months.
- **Analytical methods development & validation.** With 130+ analytical chemists on staff, Metrics' services include chromatography (LC and GC), dissolution (UV and LC finish), moisture, particle size, ion chromatography, AA/ICP, FTIR, titrations, particulate matter (HIAC), cleaning methods (LC and TOC), and LCMS.
- **Clinical trial manufacturing.** Whether it's teacup-size batches or 450-kilogram batches, Metrics has the expert personnel, facilities, and equipment to deliver materials for Phase I, II, and III clinical trials. In the past 5 years, Metrics conducted more than 75 FTIM projects for different chemical entities and simultaneously developed 700-plus batches of CTM.
- **Specialty Technologies.** Metrics offers product development that leverages proprietary technologies in the areas of customized controlled-release drug delivery; bioavailability enhancement for poorly water-soluble drugs; and improved palatability for liquid and solid presentations. Metrics scientists also can formulate non-sterile liquids, creams, and gels, or manage technology transfer for manufacturing and packaging.

Facilities & Additional Services

Housing the latest development and analytical equipment within a state-of-the-art and cGMP 92,000-sq-ft facility, Metrics also provides:

- Commercial manufacturing
- Stability storage and testing
- Raw materials testing
- Trace materials analysis
- Microbiological testing

Worldwide Regulatory Excellence

Globally, Metrics provides a broad spectrum of services to support IND, NDA, and ANDA submissions to the FDA and worldwide regulatory agencies for clients ranging in size from internationally renowned corporations to small virtual companies.

Company Profile

MEGGLE USA, Inc.
50 Main St.; 10th Floor
White Plains, NY 10606
T: (914) 682 6891 F: (914) 682 6896
E: customer.service@meggle.com
Website: www.meggle-pharma.com

MEGGLE Excipients & Technology is a leading lactose manufacturer for the global pharmaceutical industry. MEGGLE provides supply chain security with manufacturing facilities in Europe and North America, and offers a broad product portfolio, including milled, sieved, spray-dried, and agglomerated alpha-lactose monohydrate, beta-anhydrous lactose, and DPI lactose grades.

MEGGLE Excipients & Technology is a pioneer in co-processing technologies allowing simple, yet robust formulation development and manufacture. By co-processing lactose with other excipients, MEGGLE has developed high-performance excipients having unique qualities with applications in directly compressible immediate- and sustained-release pharmaceutical solid dosage forms.

MEGGLE also possesses extensive knowledge in the manufacture of other excipient products and provides contract manufacturing services to several well-known global excipient companies wanting to enhance their excipient performance and product quality.

Company Background

Founded in 1887 as a small dairy in Wasserburg near Munich, Germany, MEGGLE is a privately held, third-generation, family owned business. With an emphasis on quality and innovation, the company is a global leader and premiere manufacturer of dairy products. The company is represented by more than 2,200 employees worldwide.

Markets Served

MEGGLE Excipients & Technologies serves the pharmaceutical and biotechnology markets with a global network of offices and authorized agents. As an innovator in co-processed technologies, MEGGLE also provides contract manufacturing services to several other global excipient companies.

MEGGLE's broad product portfolio, multiple manufacturing locations, technical centers in major markets, and innovative technologies make MEGGLE the preferred supplier and valued partner by large and small pharmaceutical product manufacturers.

Products, Services & Capabilities

MEGGLE Excipients & Technologies Excipient Products:

- Lactose monohydrate
- Anhydrous lactose
- Co-processed excipients
  - MicroceLac®
  - Cellactose®
  - StarLac®
  - RetaLac®
- Lactose for inhalation
- Lactose for lyophilization and parenteral applications
- Custom lactose products

MEGGLE Excipients & Technologies Services:

- Spray-drying
- Co-Processing
- Agglomeration
- Blending
- Product Customization

Company Profile

Novozymes Biopharma US Inc
One Broadway, 14th Floor
Cambridge, MA 02142
T: (617) 401 2500 (US sales office) T: +45 4446 2896 (EU sales office)
E: biopharma@novozymes.com
Website: www.biopharma.novozymes.com

Novozymes Biopharma develops and manufactures high-quality, animal-free, and regulatory-compliant recombinant ingredients and technologies to provide pharmaceutical and medical device manufacturers with the knowledge-based solutions needed to address their challenges and develop innovative, safer, and more consistent products.

With over 25 years' experience in the pharmaceutical industry, Novozymes is the world leader in the supply of recombinant products and technologies for drug delivery applications. Novozymes' large-scale manufacturing facilities worldwide are run to cGMP/Q7 quality standards, ensuring customers receive product quality and consistency, as well as the security of long-term supply. The company's customer-integrated approach combines Novozymes' scientific know-how with the specific needs of customers to deliver improved products and performance.

Novozymes' Half-Life Extension Technology - Tailored to Deliver

Novozymes' tunable half-life extension (HLE) technology can flexibly extend half-life to reduce the dosing frequency of drugs from days to weeks. Based on albumin, Novozymes offers HLE by genetic fusion, Albufuse® Flex, or chemical conjugation, Recombumin® Flex, enabling half-life to be modulated to meet the needs of a particular disease or application. Leading the way in improving patient quality of life and reducing healthcare costs, Novozymes' technology is already being widely used in the fields of diabetes, hemophilia, and neutropenia.

Drug Delivery - Facilitating Drug Delivery With the Use of Recombinant Albumin

Whether it is to improve the half-life of the active molecule or to increase the drug retention time for controlled release, Novozymes can help drug manufacturers with a solution suited to the desired application. As the purest and most homogenous rAlbumins available, Novozymes' Albucult® (suited to drug, vaccine, and device manufacturing), and Recombumin® (ideal for drug delivery and formulation) are ideal for stabilizing drug formulations.

Novozymes' Hyaluronic Acid - Hyasis®

Novozymes Biopharma's cGMP-grade hyaluronic acid (HA), Hyasis, has been designed to fill a gap in the market for biomedical and pharmaceutical manufacturers looking for Q7 regulatory compliant ingredients with superior performance benefits. Superior heat stability permits autoclaving without significant loss of product viscosity, and tight control of molecular weight during production allows for excellent control in formulations. Hyasis can also dissolve five times faster than other sources, reducing processing times by up to 50%.

Produced using a fermentation process of the safe bacterial strain, *Bacillus subtilis*, Hyasis is free of animal-derived components and organic solvents, ensuring superior purity and reducing contamination risks. Hyasis can be customized using Novozymes' proprietary crosslinking technology to achieve a specified viscosity. This enables the product, Hyasis® Link, to be adapted for drug delivery and medical device applications across ophthalmology, dermal fillers, and osteoarthritis.

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With a commitment to quality, scientific excellence, and exceptional customer experiences, Patheon is a leading global provider of contract drug development and manufacturing services. Our integrated network consists of 8 development centers and 13 manufacturing facilities across North America and Europe.

Patheon provides pharmaceutical and biotechnology companies of all sizes with direct access to the expertise and full range of solid, sterile, and softgel dosage forms to bring drug candidates from preclinical stages through production to launch products anywhere in the world.

CONTRACT DRUG DEVELOPMENT & COMMERCIAL MANUFACTURING

Dose Forms & Technologies

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- Powder-Filled Capsules
- Powders/Granules/Coated Beads

Sterile
- Liquid-Filled Vials
- Lyophilized Vials
- Prefilled Syringes & Cartridges

Solid – Specialized
- Multilayer Tablets
- Fast Dispersible Tablets
- Controlled-Release Tablets
- Liquid-Filled Capsules

Highly Regulated Products
- Controlled Substances
- High Potency

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- Twist-Off Softgels
- EnteriCare® Enteric Softgels
- LiquiSoft™ Chewable Liquid-Filled Softgels
- Versatrol™ Controlled-Release Softgels
- Solvatrol™ Enhanced Solubility Softgels
- Soflet® Gelcaps
- Chewels® Chewable Gels
- EcoCaps™ Non-Animal Softgels

Comprehensive Services

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- Analytical Method Development & Validation
- Formulation Development
- Clinical Trial Material Manufacturing

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- Tech Transfer/Scale-Up Management
- Risk Mitigation Services

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PharmaCircle LLC, Encinitas, CA 92024
T: +1-760-436-1199 E: contact@pharmacircle.com
www.pharmacircle.com

PharmaCircle™ is the leading online knowledge management company provider serving pharmaceutical sciences professionals. PharmaCircle provides critical data and analysis on all aspects of the pharmaceutical business with global coverage of research, development, regulatory, clinical, and business activities. Our clients include almost all of the top 20 pharmaceutical companies as well as numerous commercial stage and emerging biopharmaceutical companies and suppliers. We work closely with Science, Business, Clinical and Regulatory professionals folks as well as Information/CI specialists to provide answers to challenging questions related to their business needs.

What makes PharmaCircle different?

A combination of unique data and analysis along with proprietary know-how in search and display technologies makes PharmaCircle much more than a database.

- PharmaCircle's senior management team brings you more than 25 years of first-hand experience in the field.
- Unmatched content in the areas of drug delivery, formulation, excipients, delivery device and other important product/pipeline details and information.
- The tools to search hundreds of important company, product and technology attributes and display them dynamically in tables or charts to help you make important product, technology and service decisions.
- PharmaCircle's customer support, provided by its top management, is unmatched in the business.

PharmaCircle's PharmSci Searchable Databases and Analyses Include:

DD Technology (>4,800 Technologies)	**How Supplied Injectable (>4,400 Products)**	**How Supplied Non-Injectable (>11,900 Products)**
Drug Delivery Patent (>75,000 Patents)	**FDA Excipient (>11,700 Excipients)**	**FDA Package (>143,500 Packages)**
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PharmaCircle's 35+ Searchable Databases Include:

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EU:HMA	UK:EMC	New Zealand Medsafe	Japan: PMDA	Health Canada

Company Profile

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

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

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

Specific capabilities include:

- Silicone molding - transfer, liquid injection, insert, and compression molding
- Plastic injection molding - biomaterial options, such as ethylene vinyl acetate (EVA), polyurethanes, and poly (lactide co-glycolide) (PLGA)
- Experience with steroids, hormones, anti-proliferatives, and microbicides
- Micro-molding of parts as small as 0.001 g, minimum shot size of 0.05 g
- Design assistance, tooling, molding, and assembly
- Dedicated presses and mixing equipment for APIs
- Class 10,000 clean rooms, Class 5 isolators
- More than 10,000 square feet of available manufacturing space for new manufacturing operations

ProMed utilizes both in-house testing and partnerships with state-of-the-art analytical facilities to ensure that drug content, drug elution, purity, mechanical strength, and dimensional specifications are consistently met. ProMed Pharma's Quality Assurance is dedicated to delivering drug-eluting components of the highest quality that can be used in implantable pharmaceutical products and/or life-sustaining medical devices. Our Quality System was designed using the 21 CFR 820 Quality System Model and supplemented with applicable sections of 21 CFR 210 & 211 GMPs. ProMed Pharma has also elected to be compliant with ISO13485 standards.

Company Profile

ResearchDx
5 Mason
Irvine, CA 92618
T: (866) 225-9195 F: (949) 297-3983
Website: www.researchdx.com

ResearchDx is the leading Contract Diagnostics Organization (CDO) for the biopharmaceutical and diagnostic industries. We provide integrated, turnkey, flexible services that are focused on our customers' objectives. We manage the entire diagnostic development process - from initial assay concept and discovery through clinical research to regulatory approval. At ResearchDx, we take contract R&D for diagnostics to the next generation.

The founders of ResearchDx have a passion for the advancement of personalized medicine. In founding the first-ever CDO, they help biopharmaceutical companies overcome the barriers to developing diagnostic products. ResearchDx has extensive experience in genetics, clinical research, and clinical laboratory services.

Experience You Can Trust

The ResearchDx management team has unparalleled experience in managing clinical laboratories, designing and managing clinical research, and navigating the complex regulatory environment specific to diagnostics.

Integrated Services

Trust ResearchDx to provide independent and unbiased guidance, expert analysis, and seamless integration of all the services you need to develop a diagnostic product - including assay development, clinical laboratory services, clinical trial design and conduct, project management, manufacturing, regulatory guidance and submissions, and consulting. In the era of personalized medicine, ResearchDx is forging a new path as the first-ever CDO. Biopharmaceutical companies need diagnostics partners that can easily and readily adjust to meet new or unexpected challenges during the development process. The traditional Contract Research Organization (CRO) simply cannot meet all the demands of developing companion diagnostics. As a CDO, ResearchDx offers integrated, flexible services that you can trust to stay on track.

Flexibility

ResearchDx can adapt to meet your complex and constantly evolving needs for diagnostic development. We can build, validate, and perform any assay that your business demands, or alternatively work with competing technology vendors to ensure the best fit for your application.

Focus On Your Business

Your diagnostic development is ResearchDx's sole focus. You can rest assured that we have the experience and dedication to ensure the fastest possible path to commercialization for your diagnostic product needs.

Game Changers.

Prefilled Syringes | Reconstitution Systems | Auto-Injectors | Wearable Injectors | Ocular Systems | Novel Systems

A Market-Driven Portfolio of Innovative, Differentiated and Customizable Product Platforms to Enable and Enhance Injectable Therapies

UNILIFE®

www.unilife.com

These products have not been evaluated by the FDA.

Company Profile

Unilife
250 Cross Farm Lane, York PA 17406
T: (717) 384 3400
E: info@unilife.com
Website: www.unilife.com

Unilife Corporation is a US-based developer and commercial supplier of innovative, highly differentiated injectable drug delivery systems. Unilife's extensive portfolio of game-changing products includes prefilled syringes, reconstitution systems, auto-injectors, wearable injectors, ocular delivery systems, and novel delivery systems. Products from each platform can be customized to address specific customer, drug, and patient requirements.

Pharmaceutical customers can leverage Unilife's visually distinctive, high-quality products to differentiate their injectable biologics, drugs, and vaccines to improve patient care, maximize user preference, and build market share within competitive therapeutic areas.

Prefilled Syringes

The Unifill® range of ready-to-fill syringes is the world's first and only prefilled platform with integrated, automatic, and user-controlled needle retraction. Unifill syringes feature USP-compliant materials in the primary container and can be integrated with standard filling and packaging processes. They are designed for intuitive use and compact, convenient disposal by healthcare workers or patients.

Reconstitution Systems

The EZMix platform of dual-chamber syringes represents a safe, simple, and efficient system for the reconstitution and injection of liquid-liquid or liquid-dry combination therapies. Users can intuitively mix together a combination of liquid or dry drugs with minimal steps. Reconstitution is ventless and orientation-free to maintain sterility and minimize the risk of drug wastage. Integrated, automatic needle retraction virtually eliminates the risk of needlestick injuries.

Auto-Injectors

Unilife has developed a broad platform of disposable and smart reusable auto-injectors that are compact in size, intuitive to use, and customizable to customer, drug, or patient needs. RITA™ is a sleek, disposable auto-injector with true end-of-dose indicators, no visible springs or mechanisms, and automatic needle retraction. LISA™ is an electromechanical reusable auto-injector that completely automates the removal of the needle shield, the injection of the dose, and automatic needle retraction. In addition to the user being able to select the speed of injection, LISA is the only reusable auto-injector that enables disposal of a used syringe without risk of needlestick injury.

Wearable Injectors

Unilife has developed a flexible portfolio of wearable injectors for large dose volume or long duration therapies. Prefilled, pre-assembled, and ready-to-inject, Unilife wearable injectors utilize standard materials, are compatible with standard filling processes, and require no terminal sterilization. This highly customizable platform can be programmed to control the duration, rate, and volume of dose delivery to address the specific customer, drug, and patient requirements.

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 becomes an integral part of your product offering, and any delays or issues in 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.

Company Profile

UPM Pharmaceuticals, Inc.
6200 Seaforth St.
Baltimore, MD 21224
T: (410-843-3738)
F: (410-633-4438)
Website: www.upm-inc.com

UPM Pharmaceuticals®, Inc. can provide customized preformulation and formulation development, clinical trial manufacturing, commercial manufacturing, and analytical services to pharmaceutical, biotechnology, government, and university clients. UPM's new Bristol, Tennessee, facility is an approximately 500,000-sq-ft campus that can provide clients needing a large-scale commercial manufacturer for tablets and capsules, as well as semi-solid creams and ointments. Fully appreciating that flexibility and time-to-market are critical; utilizing these two facilities, UPM can be highly responsive to clients' program changes and specializes in developing creative solutions to unique challenges. Every step of the way, UPM Pharmaceuticals works to advance and optimize products through up-to-date resourceful approaches while adhering to the highest quality standards. Through the years, our staff and systems have been consistently challenged by FDA, DEA, QP, and client audits, and we have passed these rigorous inspections repeatedly.

Scientific Expertise – Access to some of the industry's best formulation design scientists, manufacturing professionals, and analytical chemists, who are known for developing innovative solutions to difficult challenges.

Rapid & Responsive Turnaround – Our Scientists and senior managers utilizes daily planning meetings and a master scheduling process that provides for timely and responsive project management.

Quality Assurance & Document Control – Our highly experienced quality assurance personnel implement complete cGMP quality and regulatory systems that support formulation development, clinical batch and commercial manufacturing, and analytical work-up.

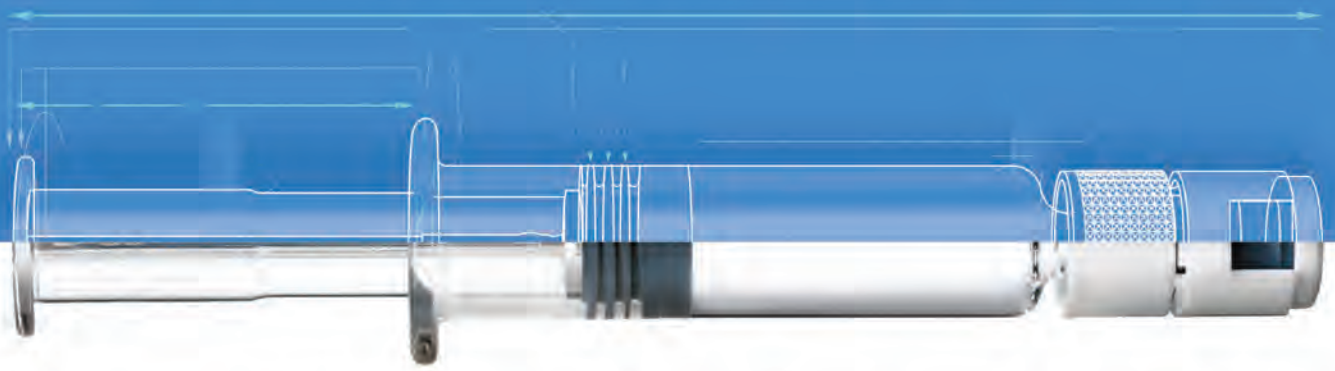
Capital Investment – Recent equipment acquisitions have increased our capabilities for solid dose formulation development. These capabilities include mini-scale R&D proof-of-concept manufacturing (BREVI-BATCH™), low-solubility compound processing, uHPLC sample analysis, head-space analysis, and bi-layer tableting. UPM's purchase of the Bristol site has demonstrated our commitment to providing our clients with a complete manufacturing solution from concept to commercialization.

Manufacturing Facilities – The expansion of UPM includes a low-humidity/high-potency suite, direct API filing suites, and expanded packaging line suite. Increased annual manufacturing capabilities of up 3.5 million tablets, 700 million capsules, 138,000 kg of creams/ointments, and up to 43 million packaged bottles and 5 million packaged tubes/jars.

Services Offered

- Preformulation & Formulation Development
- BREVI-BATCH™ Mini-Batch Proof-of -Concept Studies
- Direct API Fill Into Capsules for Proof-of-Concept Studies
- Low-Solubility Processing
- Wet Granulation
- Dry Granulation/Roller Compaction
- Single & Bi-Layer Tableting
- Tablet & Particle Coating
- Capsule Filling
- Blinding of Clinical Supplies Commercial Packaging
- CTM Packaging
- Analytical Services
- uHPLC Processing
- Particle Size Analysis
- USP Micro Testing
- USP Stability Testing
- Head-Space analysis
- Solid Oral Dose cGMP Commercial Manufacturing
- Semi-Solid cGMP Commercial Manufacturing
- Commercial Packaging

From clinical development to commercial production



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

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

- More than 25 years of experience in aseptic filling
- Expertise with many compound classes, including biologics
- Highly trained experts in key technical areas
- Integrated life cycle management
- Innovative drug delivery options
- State-of-the-art cGMP manufacturing
- Excellent global regulatory support

Vetter Development Service | Vetter Commercial Manufacturing | Vetter Packaging Solutions

VETTER

Answers that work

For US inquiries please contact infoUS@vetter-pharma.com • For EU, Asia and other international inquiries, please contact info@vetter-pharma.com

www.vetter-pharma.com

Company Profile

VETTER
Vetter Pharma International
Eywiesenstr. 5
88212 Ravensburg, Germany
T: +49-(0)751-3700-0 - F: +49-(0)751-3700-4000
E: info@vetter-pharma.com
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.

NOVAguard SA™

Needle Safety for Care Givers and Patients

A prefillable syringe safety system can help reduce needlestick injuries. With an easily deployed needle shield, West's NovaGuard SA technology platform* is ideal for use in any health care setting. Trust West to be by your side with patient-focused drug administration solutions.

West®

By your side
for a healthier world

Contact West today.

North America	+1 800-345-9800
South America	+55 11 4055 6061
Europe	+49 2403 7960
Asia Pacific	+65 6860 5879

www.westpharma.com
www.westpfssolutions.com

Company Profile

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
E: webmaster@westpharma.com
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® SA[2] 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.

[1]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.

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

AT LAST

Early drug development made easy.

Xcelience® is your premier source for formulation development and clinical supplies manufacturing and packaging solutions.

Since 1997, Xcelience has been renowned for reliably expediting drug product development and clinical manufacturing for oral solid, semi-solid and liquid dosage forms. Our formulation development scientists have considerable experience overcoming challenges associated with physical and chemical properties of drug substance, or limited quantities of active pharmaceutical ingredient, in a manner that results in compounds with improved solubility and bioavailability.

Services include preformulation, analytical method development/validation, formulation development, clinical supplies manufacturing, clinical supplies packaging and distribution.

Partnering with a specialist like Xcelience for early phase oral dosage form development can accelerate drug development timelines and reduce risk. To learn more contact us at info@xcelience.com or call us at 813.286.0404.

Xcelience® Formulation Development

www.xcelience.com

Contact us today at 1.813.286.0404 or info@xcelience.com

Company Profile

Xcelience, LLC
5415 West Laurel Street
Tampa, FL 33607
T: (813) 286-0404 - F: (813) 286-1105
E: Info@Xcelience.com - W: www.Xcelience.com
Contact: Sharon Burgess, Senior Vice President

Xcelience is your premier provider for formulation development and clinical supplies manufacturing and packaging solutions.

Xcelience has one responsibility - getting your molecule through the stages of development quickly and cost effectively. With our scientific expertise, our extensive capabilities, and our flexibility, we will accelerate your drug to clinical trial. Since 1997, Xcelience has been known for reliably expediting drug product development and clinical manufacturing for oral solid, semi-solid, and liquid dosage forms. Services include preformulation, analytical, method development/validation, formulation development, clinical supplies manufacturing, and clinical supplies packaging and distribution. We are more than just a service. We are formulation development, clinical manufacturing, clinical supplies packaging, and distribution made easy - at last.

XCELIENCE ADVANTAGE

- A three-phase facility expansion completed in 2012 increased capacity and processing speed for formulation development, analytical, GMP manufacturing, and packaging and distribution.
- Extensive clinical trial supplies manufacturing capabilities to increase overall capacity, improve production times, and expand existing capabilities for production, coating, and encapsulation.
- Global access to five Xcelodose® precision powder micro-dosing systems, allowing clients to fill very small amounts of powder into capsules and accelerating time to first-in-human studies.
- Liquid-in-capsules services to improve aqueous solubility and increase compound bioavailability.
- Small-scale batch production for companies with limited API.
- A new 24,000-sq-ft, FDA-approved clinical supplies facility dedicated to primary and secondary packaging in support of Phase I-III clinical projects.
- Fully-automated packaging lines for primary bottling of tablets and capsules to increase the speed of batch packaging shorten timelines and package larger batches.
- Complete primary packaging services for solid dosage forms; including thermoform and cold form blistering.
- Provide secondary packaging, labeling, and assembly service for all drug product dosage forms.

SERVICES & CAPABILITIES

Preformulation

- Salt screen
- Polymorph screen
- Drug substance characterization
- Excipient compatibility
- Accelerated stability
- Chiral stability

Analytical Services

- Method development
- Qualification & validation
- Raw material testing
- Stability sample analysis
- Dissolution testing
- Residual solvent analysis
- Chiral determination
- Cleaning evaluations
- Technical packages for drug substances

Formulation Development

- Solids (tablets, gelatin, or HPMC capsules, sustained release & coatings)
- Semi-solids (ointments, creams & gels)
- Oral liquids (solutions, suspensions & emulsions)

GMP Manufacturing

Clinical supplies manufacturing capabilities include:

- Tablets
- Capsules
- API into capsule
- Liquid to capsule
- Semi-solids
- Non-sterile liquids

Clinical Supplies

- Primary & secondary packaging
- Global distribution
- Storage
- Returns, retains, reconciliations & destruction
- Clinical supplies project management

FACILITES

Xcelience West Laurel Street headquarters is a GMP-compliant, DEA-licensed facility. A new 24,000-sq-ft, FDA-approved clinical supplies facility, located on West Grace Street, is dedicated to primary and secondary packaging in support of Phase I-III clinical projects.

Technology & Services Showcase

Innovative Platforms

Adhesives Research, Inc. has over 20 years of experience developing and manufacturing custom pressure-sensitive adhesive tapes, specialty coatings, films, and laminates for the for the world's leading pharmaceutical companies. We offer the pharmaceutical industry a wide range of coating technologies and adhesive capabilities for transdermal, oral, and topical drug delivery. Based upon proven PIB, acrylic, silicone, and dissolvable film technology platforms, Adhesives Research's skin-friendly adhesives are available with conductive, porous, occlusive, hydrophilic, hydrophobic, gentle, or long-term adhesion functional properties to meet the unique needs of our clients' applications. For more information, contact Adhesives Research at (800) 445-6240 or visit **www.adhesivesresearch.com.**

Solid Dosage Forms

Agere Pharmaceuticals offers clients formulation design and development, cGMP analytical, and solid oral dosage form services. Solid dosage forms supported include tablets, capsules, powder for inhalation, and alternative dosage forms. We can select excipients, drug excipient ratios, and process development, as well as prepare immediate and sustained-release forms for the clinic. In addition to characterization of unit operations, Agere offers a broad spectrum of analytical and physical measurement capabilities. All services are offered on a fee-for-service basis. For more information, please contact Agere at (541) 639.8397 or info@agerepharma.com or visit **www.agerepharma.com.**

Oral Delivery Technologies

Our proprietary AdvaTab® technology is an advanced orally disintegrating tablet (ODT) enabling rapid disintegration in the mouth, generally in less than 30 seconds, without water. AdvaTab can be combined with the Microcaps® taste-masking technology and the Diffucaps® customized-release technology to create robust tablets with high-dose capacity, customized release, and superior taste-masking. Aptalis Pharmaceutical Technologies is your trusted oral drug delivery partner for overcoming even the most demanding delivery challenges. We enable our partners to successfully bring valuable patient-optimized products to market through our commitment, expertise, and proprietary technologies. Our comprehensive portfolio of oral drug delivery technologies for bioavailability enhancement, custom drug-release profiles, and taste-masking for ODTs and other dosage forms are employed in a customized approach to meet our partners' needs. For more information, visit Aptalis Pharmaceutical Technologies at **www.AptalisPharmaTech.com.**

Specialty Ingredients

ASHLAND

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 HYPERLINK "www.ashland.com/ddd/pharmaceutical" **www.ashland.com/ddd/pharmaceutical.**

Technology & Services Showcase

Licensing & Capabilities

Aveva has a number of products for license from its development pipeline along with a full complement of R&D capabilities to produce transdermal drug delivery systems that fortify pipelines and maximize product life cycles. Aveva Drug Delivery Systems is one of the world's largest manufacturers of, and a pioneer in, transdermal drug delivery systems with a rich history of providing pharmaceutical partners with fully integrated, controlled-release transdermal products that fulfill unmet market needs. Products for licensing include Sufentanil, Fentanyl, Clonidine, and Nicotine. For more information, contact Robert Bloder, VP of Business Development, at (954) 624-1374 or visit **www.avevadds.com.**

Medical Devices

Let Battelle help you accelerate your medical product development timeline, from ideation to evaluation to commercialization. Our multidisciplinary teams advance innovation by integrating world-class expertise across a wide range of science and engineering disciplines. We are redefining the possible in drug delivery, Human Centric Design (HCD), molecular imaging, in vitro diagnostics, and neurotechnology. For more information, contact Battelle at (800) 201-2011 or visit **www.battelle.org.**

Gum Base Supplier

Cafosa, part of the Wrigley/Mars group of companies leading the chewing gum market, is the world's leading Gum Base supplier for confectionery, nutraceutical, and pharmaceutical applications. Gum Base is the main ingredient used to produce chewing gum, a combination of polymers, resins, and softeners plus an inorganic filler that gives different textures and chewing properties to chewing gum depending on its composition. Cafosa has developed an innovative concept for the pharmaceutical industry: Health in Gum is an excipient, a directly compressible powder gum containing a mix of Gum Base and polyols to which you can add your API, so you can create medicated chewing gum by adding your APIs to Health in Gum powder. Health in Gum offers an innovative drug delivery system for your products. There is no need for specific chewing gum production equipment. For more information visit Cafosa at **www.healthingum.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 **www.catalent.com/index.php/development/biologics/overview.**

Technology & Services Showcase

Super Refined® Excipients

CRODA
Health Care

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.croda.com/healthcare.**

Development & Manufacturing

DPT®
COUNT ON US™

DPT is a contract development and manufacturing organization (CDMO), specializing in semi-solids and liquids for biopharmaceutical and pharmaceutical products since 1938. From virtual to large pharma, from concept to commercialization, from sterile to non-sterile - DPT offers the broadest range of capabilities in the industry. Drug development services include pre-formulation, technology transfer, formulation and biopharmaceutical development, analytical development, CMC preparation, and validation through process development, and regulatory support. DPT has a solid regulatory history, with production capabilities that include five world-class cGMP facilities, clinical trial materials, full-scale commercial production, controlled substance registration Class II-V, complete supply chain management, and expanding sterile product development and aseptic manufacturing facilities. Packaging services include packaging identification, specifications development, engineering, and procurement resources necessary for conventional and specialized packaging. For more information, contact DPT Labs at (866) 225-5378 or visit **dptlabs.com.**

Leading CDMO

Formex
The Formulation Experts

Formex LLC is a leading contract development and manufacturing organization focusing on oral and topical dosage forms. Formex specializes in bioavailability enhancement and controlled-release technologies, such as hot-melt extrusion and spray-drying. Formex provides preformulation, formulation development, analytical method development, analytical testing, preclinical manufacturing, cGMP clinical trial manufacturing for Phase 0-III, and small-scale commercial manufacturing. Formex currently occupies 45,000 sq ft of our 80,000-sq-ft facility with 25,000 sq ft of cGMP manufacturing space, including 17 separate and dedicated cGMP suites, including suites qualified and dedicated for cytotoxic compound handling as well as potent compound handling. For more information, contact Formex at (855) 436-7639 or visit **www.formexllc.com.**

Innovative Syringe Systems

The Gerresheimer Group is a leading global partner for the pharma and healthcare industries with expertise in both glass and plastic. Our product offering ranges from standard pharmaceutical containers to customized drug delivery systems, such as syringe systems, insulin pens, and inhalers for safe medication dosage and application. Gerresheimer Bünde is known for its excellence in the area of RTF® syringes (Ready-to-Fill), which are supplied completely washed, siliconized, assembled, nested, packed in tubs, and sterilized to the customers. A range of proprietary accessories, such as the rigid needle shield with thermoplastic elastomer (TERNS) and the tamper-evident Luerlock closure with twist-off motion (TELC®), facilitate safety and convenience for the end-users of these syringe systems. Gerresheimer partners with customers worldwide to meet specific market needs. For more information about prefillable syringes, contact Dr. Arno Fries at +49 5223 164-401 or visit **www.gerresheimer.com.**

Technology & Services Showcase

Insulin Management System

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.**

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.**

Development/Clinical Trial Manufacturing

LYOPHILIZATION TECHNOLOGY, INC.
Integrating Science and Technology

Lyophilization Technology, Inc. (LTI) provides Development and Clinical Trial Material Manufacturing services to more than 296 biotechnology and pharmaceutical clients spanning virtual, small, and large multi-national companies. Experience with over 384 diverse 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 Lyophilization Technology, Inc. at (215) 396-8373 or visit www.**www.lyotechnology.com.**

Technology & Services Showcase

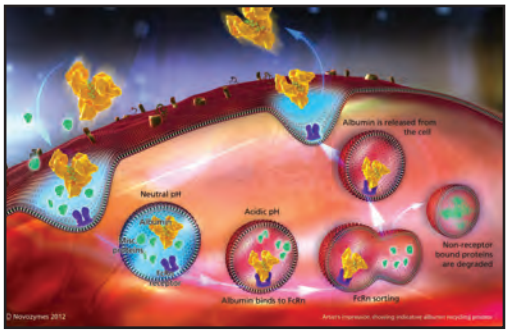
Excipients & Technology

MEGGLE Excipients & Technology is a global leader in the manufacture of lactose for the pharmaceutical industry. MEGGLE provides supply chain security with manufacturing facilities in Europe and North America, and offers a broad product portfolio comprising α-lactose monohydrate, β-anhydrous lactose, and DPI lactose grades. MEGGLE Excipients & Technology is a pioneer in co-processing technologies allowing simple, yet robust formulations. Through co-processing lactose with other excipients, MEGGLE has developed high-performance ingredients having unique qualities with applications in directly compressible immediate- and sustained-release pharmaceutical solid dosage forms. MEGGLE also possesses extensive knowledge in the manufacture of other excipient products and provides contract manufacturing services to several well-known global excipient companies wanting to enhance their excipient performance and product quality. For more information contact the MEGGLE Group at (914) 682-6891 or visit **www.meggle-pharma.com.**

Full-Service CDMO

Metrics is a full-service global contract development and manufacturing organization (CDMO) specializing in oral and topical dosage forms. A subsidiary of Mayne Pharma Group Limited, Metrics also offers clients an impressive portfolio of advanced proprietary delivery methods for controlled release, bioavailability enhancement, and taste-masking. Founded as a contract analytical laboratory in 1994, Metrics has evolved into a provider of quality pharmaceutical formulation development, analytical testing services, and commercial and CTM manufacturing for Phase I-III. For more information, contact Metrics at or visit **www.metericsinc.com.**

Tunable Half-Life Extension Technology



Novozymes' albumin-based half-life extension (HLE) technology can flexibly extend drug half-life to reduce the dosing frequency of drugs from days to weeks. Novozymes offers HLE by genetic fusion, Albufuse® Flex, or chemical conjugation, Recombumin® Flex, enabling the tunability of HLE to meet the needs of a specific disease or application. Leading the way in improving patient quality of life, Novozymes' technology is already being widely used in the fields of diabetes, haemophilia, and neutropenia. Through the optimization of drug half-life, dosing frequency and healthcare costs can be reduced significantly whilst increasing patient compliance. Long patents until at least 2030 provide manufacturers with a unique competitive edge in current challenging markets. For more information on Novozymes' HLE technology, please visit **www.daytoweeks.com.**

Development & Manufacturing

With a commitment to quality, scientific excellence, and exceptional customer experiences, Patheon is a leading global provider of contract drug development and manufacturing services. Our integrated network consists of nine development centers and twelve manufacturing facilities across North America and Europe. Patheon provides direct access to a full range of solid, sterile and softgel dosage forms, as well as world-class expertise in highly potent compounds and lyophilization. With Patheon, pharmaceutical and biotechnology companies of all sizes can bring drug candidates from preclinical stages through production to successfully launch products anywhere in the world. For more information, contact Patheon at (888) PATHEON or visit **www.patheon.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.**

Contract Diagnostics

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ResearchDx is the leading Contract Diagnostics Organization (CDO) for the biopharmaceutical and diagnostic industries. As a CDO, ResearchDx integrates in vitro diagnostics (IVD) non-clinical and clinical research, CAP/CLIA laboratory assay discovery, development and testing, GMP manufacturing of test kit components, and end-to-end consulting to achieve the fastest path to market for your IVD/companion diagnostic. With experts managing the entire development process from initial assay concept and discovery through clinical research to regulatory approval, ResearchDx employs a proactive project management approach with the availability of resources to ensure appropriate attention to timelines every step of the way. By offering the complete range of CDO services without owning a proprietary testing platform, ResearchDx ensures its clients' diagnostics are developed with the methodology and platform that best optimize its characteristics and commercialization strategy. For more information, contact ResearchDx at (866) 225-9195 or visit **www.researchdx.com.**

Child-Resistant Closure

Rexam Healthcare, a global leader in healthcare rigid plastic packaging and medical devices, will launch the latest version of its industry reference child-resistant closure (CRC) - the Clic-Loc® 4. Clic-Loc is the first and only CRC available to combine more than 40 years of demonstrated safe and effective oral dose protection, adult-friendly operation, and multiple manufacturer benefits. The Clic-Loc delivers superior ergonomics, is easily used on production lines, and creates an audible warning click to alert parents and caregivers. Like the current Clic-Loc, the new edition is shrink-wrap friendly, and offers unsurpassed capper flexibility and variety. Importantly, with an aging worldwide population, the Clic-Loc is designed for secure and frustration-free use by seniors and those with disabilities. The new Clic-Loc 4 will provide enhanced functionality and aesthetics, for industry-leading protection, production efficiency, and product differentiation. For more information, visit Rexam Healthcare at **www.rexam.com.**

Technology & Services Showcase

Intranasal Delivery

The Teleflex VaxINator™ is an easy-to-use and cost-effective solution for intranasal drug delivery. It employs the same technology as the clinically proven LMA MAD Nasal™ and enables standardized positioning in the nasal cavity for broad deposition across the nasal mucosa. 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 Teleflex VaxINator is a syringe and atomizer-based system, and a range of accessory items are available to meet your intranasal drug delivery needs. Applications include vaccines, pain medications, anaesthetics, antimicrobial, and many other possibilities. For more information, contact Teleflex at (801) 281-3000, LMAOEM@teleflex.com, or visit **www.lmaco.com.**

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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.**

Development Services

UPM Pharmaceuticals® is an independent provider of contract formulation development, analytical services, and cGMP manufacturing. We continue a legacy of intellectual distinction and uncompromising performance with every new project. The talent and experience of our team, our dedication to science-based formulation design, and our commitment to communication and timeliness enables us to offer the highest level of customized drug development services. Our 40,000-sq-ft main facility in Baltimore features cGMP pharmaceutical manufacturing and packaging suites as well as analytical and R&D laboratories staffed by industry veterans. Whatever form your product takes, we ensure rigorous and technically sound product characterization, methods development, and QC release. Our clients enjoy service that is highly responsive and fast with total quality management characteristic of a customer-focused business. For more information, contact UPM Pharmaceuticals at 410-843-3738 or visit **www.upm-inc.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.

Technology & Services Showcase

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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.**

Development & Manufacturing

Xcelience® Formulation Development

Xcelience is a premier provider of formulation development and manufacturing solutions with a solid reputation for accelerating early phase small molecule development. Our outstanding quality record, significant drug development expertise, willingness to customize, and disciplined project management enable us to deliver real advantages to clients needing to speed potential drugs to clinical trials. Since 1997, Xcelience has been renowned for reliably expediting drug development. Our formulation development scientists have considerable experience overcoming challenges associated with physical and chemical properties of drug substance, or limited quantities of API, in a manner that results in compounds with improved solubility and bioavailability. Partnering with a specialist like Xcelience for early phase development can significantly reduce product risk and accelerate development timelines. For more information, contact Xcelience at (813) 286-0404 or visit **www.xcelience.com.**

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Hormone Delivery Technology

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OraSorb™ hormone delivery technology provides the convenience of a pill with a metabolic profile similar to a patch. CIMA's new delivery system combines solubilization and permeation enhancing technologies into one buccal tablet. The solubilization technology ensures the hormone is in solution when it comes in contact with the buccal mucosa. The buccal permeation technology provides for rapid absorption. The high bioavailability of the buccal delivery means that efficacious drug levels can be obtained with lower doses. Buccal delivery also reduces first-pass hepatic metabolism, which results in reduced hepatotoxicity. This resulting formulation has a more favorable "patch-like" metabolite profile with the convenience of a buccal tablet. If you would like to learn more about OraSorb, please contact CIMA Labs at (763) 488-4975 or visit **www.cimalabs.com.**

November/December 2013

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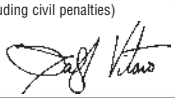

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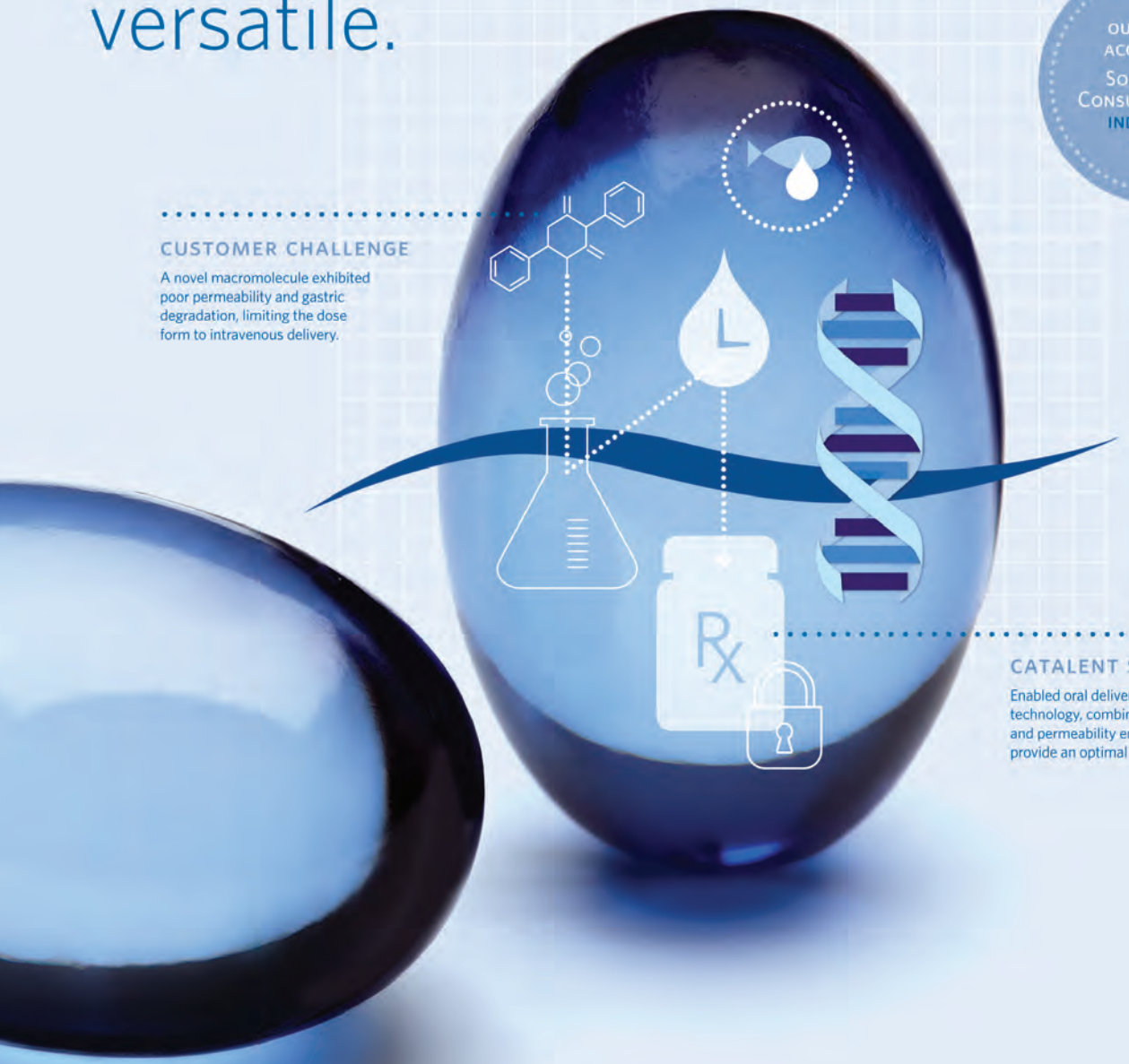

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