SPECIALTY PHARMA
Strategies For Business Development

Contract Manufacturing

Gaining Access to Global & Specialized Services

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The global pharma industry faces numerous challenges in the form of increasing competition in generic markets, rising costs of new product development, declining research and development productivity, shrinking average patent life, and mounting governmental pressure to reduce drug prices. Given the backdrop of such a competitive landscape, the decisive factors for growth and sustainability are faster new drug development and cost containment, with pharmaceutical contract manufacturing (PCM) emerging as a strategic option offering several advantages, according to Global Industry Analysts, Inc. Thus, the global market for PCMs is projected to reach close to $40 billion by 2012, up from $26 billion in 2007.

As stated by Global Industry Analysts, Inc., the US is the single largest market for PCM, with revenues projected to be $12.8 billion in 2012. However, Asia has immense manufacturing capacity and is projected to emerge as the fastest growing region in the global PCM market. Contract manufacturing in India and China is forecast to expand at a CAGR of 20% through to 2011. Big Pharma is increasingly outsourcing manufacturing to low-cost destinations due to cost and margin pressures, and India and China offer skilled manpower and a robust manufacturing infrastructure.

The PCM sector is three tiered. Tier 1 companies offer end-to-end services ranging from clinical trials to commercial manufacturing, logistics, packaging, and marketing assistance. Tier 2 companies provide services ranging from early stage project development to commercial level manufacturing. Tier 3 companies are conventional manufacturing companies, which address the needs of the generic drugs industry.

A major factor driving the upward trend in the number of manufacturing projects being outsourced is that specialized production, ie, sterile manufacturing; biopharmaceutical manufacturing; and specialized processes, such as chiral chemistry and improvements in catalyst activity, are often not included in the core competency of pharmaceutical and biotechnology drug makers. Biopharmaceutical manufacturing is forecast to have increased by 15% in 2008, driven by sales growth of biologics.

Specialty Pharma magazine recently asked key players in the PCM market to discuss the value they offer specialty pharma companies, the unique services they bring to the table, and how they are competing in this very competitive outsourcing environment. Participants include Marc Iacobucci, Vice President, Marketing & Project Management, DPT Labs; Diana Wood, Vice President, Business Development, Stason Pharmaceuticals, Inc.; Marcelo Morales, CEO, HollisterStier-Draxis Pharma Contract Manufacturing; and Eric P. Neuffer, VP of Sales and Business Development for North America, Cambrex.

Q: What strategic opportunity does PCM offer today's Specialty Pharma company?

Mr. Neuffer: PCMs offer companies the strategic opportunity to access established assets with existing cGMP quality systems that employ a highly skilled workforce in facilities with the appropriate regulatory approvals. Contract manufacturers typically have the knowledge and experience to avoid project/product production pitfalls. In addition, Specialty Pharma can access the contractor's unique capabilities, significantly reducing cost, time, and risk versus establishing these capabilities themselves.

Mr. Morales: They can offer a combination of speed to market, lower total cost to commercialization, and enhanced quality output. CMOs that have a corporate culture dedicated to process improvements, such as Lean and Six Sigma that adhere to a "right-first-time" mentality, present the most efficient and cost-saving means of bringing a product to market. In support of a robust process improvement system, CMOs must have detailed procedures that clearly articulate executing a method, provide required training, detail necessary project management, and define effective change control management to ensure an efficient manufacturing process. Specialty Pharma companies that partner with a CMO will find a manufacturer that has an innate understanding of the entire transfer and manufacturing life cycle and possesses the ability to absorb the associated complexities at an earlier stage than has been done in the past by CMOs.

Ms. Wood: Selecting a contract manufacturer that offers turn-key services can facilitate consistency and efficiency. Identifying and formulating the API and developing the product from benchtop through large-scale production with the same contract manufacturer without the need for a tech transfer saves time and money. In addition, designing a drug up-front for manufacturability or the ability to scale up at a later time ensures that, should a tech transfer be required, the potential for issues or delays is significantly reduced.

Mr. Iacobucci: Specialty Pharma companies typically carry limited or no internal development or commercial manufacturing overhead. Historically, Specialty Pharma companies outsourced formulation development to CROs. Later, they would have to find a CMO for late-stage development and product launch. Today, the concept of a CDMO (Contract Development & Manufacturing Organization) has emerged. Such organizations have comprehensive services from preformulation through clinical and commercial manufacturing. And tying world-class development together with broad commercial manufacturing capability is a key strategic opportunity. Cost savings, time efficiencies, and access to technical

expertise are the greatest advantages Specialty Pharma companies have found working with a CDMO. The benefits include a smoother transition from development to launch, one point of contact through the entire process, and decreased regulatory complexity.

Q: What issues are driving Specialty Pharma to outsource to a contract manufacturer?

Mr. Morales: Organizations focused on specialty pharmaceutical products are likely looking for opportunities to decrease costs and invest capital into R&D efforts. In-house manufacturing operations require a substantial amount of overhead to maintain the level of training and state-of-the-art equipment necessary to uphold cGMP manufacturing suites. As a result, outsourcing the compounding, filling, labeling, and shipping of a product provides Specialty Pharma the convenience of bringing the product into a facility that is adept at running a cGMP manufacturing operation and can gain the strategic edge of having the capacity for multiple batch sizes, quicker turnarounds, and a secure supply chain. Furthermore, CMOs can complement these manufacturing capabilities with method development support, protocol development support, and related enhanced testing support, allowing Specialty Pharma organizations to focus on their core activities in research, development, patient testing, and commercialization support. Specialty Pharma recognizes that many CMOs are finely tuned facilities that anticipate demand and have the capacity to accommodate it. By looking at the entire life cycle and supply chain, CMOs become a part of Specialty Pharma's cost-management solutions.

Ms. Wood: Due to the current economic challenges, many companies have downsized, sold off certain assets, or merged, which has resulted in reduced resources and expertise, and most importantly, periods of significant distraction and questions of goals or direction. Contract manufactures can offer both expertise and resources to a Specialty Pharma. This not only includes the actual development and formulation, or manufacturing, but regulatory advice and strategy. Contract manufacturers that have expanded their services into other areas directly, or through affiliations, can assist with clinical trials, product registrations, acquisition of comparator products, and exportation/importation. This results in a turn-key operation, from discovery through registration and beyond to commercialization.

Mr. Neuffer: Specialty Pharma companies choose to outsource in an effort to minimize risk if a drug product does not make it to market or has a weaker-than-expected market penetration; minimize capital outlay for manufacturing equipment; and access large-scale specialized technology platforms (ie, high potency, chiral chemistry, highly energetic processes) without which a Specialty Pharma could not commercialize a product.

Mr. Iacobucci: As stated, Specialty Pharma companies tend not to be burdened with significant internal development and manufacturing overhead. This is in contrast to Big Pharma that historically conducted virtually all development and manufacturing internally. This is actually a good thing for Specialty Pharma as it is not laden with associated overhead and are better able to focus resources on research, business development, and marketing. So, rather than Specialty Pharma being "driven to outsource," contract manufacturers are simply an excellent complement to Specialty Pharma.

Q: What specialized processes (ie, sterile manufacturing, biopharmaceutical manufacturing, chiral chemistry) do you offer to drug makers as many of these processes are often not included in their core competencies?

Mr. Iacobucci: At DPT, we focus on semi-solid and liquid dosage forms. These types of formulae can be complex, and we have incorporated virtually every API (including biopharmaceuticals) into these platforms. We offer sterile manufacturing services, manufacturing capabilities for aerosol formulations, and metered-dose inhalers. We also offer full Chemistry and Manufacturing Controls (CMC) documentation services for these products. Customers benefit by leveraging our experience early in the development process to avoid duplicative efforts in formulating their product. We have invested substantially into niche areas that are hard to commoditize (eg, pharmaceutical aerosol). And, we have enhanced our regulatory awareness and compliance to satisfy key geographies outside the US.

Ms. Wood: Stason provides cGMP high containment manufacturing for oral products, not only on a pilot scale, but commercial scale as well, distributing products in the US and abroad. In addition, our API plants provide both pharmaceutical and biologic APIs. Stason also develops new processes for synthesizing target molecules, including biotransformation processes for the preparation of chiral molecules. We also screen biocatalysts for the resolution or asymmetric synthesis of drug molecules and development of the biotransformation process. Specific to biotechnology products, we offer services that provide advantages of conventional organic syntheses and biotransformations to design specific chemo-enzymatic approaches for the synthesis of fine chemicals and

pharmaceutical intermediates. In addition, we help develop products and technologies in molecular diagnostics for cancer and screening for anti-cancer activities.

Mr. Neuffer: Cambrex possesses a handful of key core competencies that enable drug makers to bring their products to market from a technology and value perspective. These include specialized drug delivery technology, highly potent API development and production facilities, a controlled substance license, transaminase technology, Continuous Flow Microwave Assisted Organic Synthesis, and high-energy processes (ie, nitrations, fluorinations). The large-scale heterogeneous CFMAOS lead Cambrex to develop a reactor where products are manufactured on a continuous basis, giving improved productivity, quality, and thus lowering costs.

Mr. Morales: Sterile manufacturing are core strengths of both HollisterStier and Draxis, which requires complex technology, qualified facilities, and highly-trained staff. Within our global partnerships, we offer manufacturing services for sterile injectable liquid and lyophilized products, sterile ointments and non-sterile liquids, semi-solids, and solids. To complement our parenteral manufacturing services, we have world-class laboratory capabilities. As such, we offer method validation/transfer services for chemical and biological methods. Furthermore, HollisterStier has experience in processing and testing our own dedicated line of biologic-based immuno-therapeutic agents. Ultimately, our CMO clients, especially those clients with biologic or protein-based products, benefit from this expertise.

Q: How has the growing number of biotechnology-driven protein and peptide drugs affected the amount of business you are doing, and what types of services do you offer to accommodate these types of drug products?

Ms. Wood: Alhough Stason does not offer biomanufacturing, we do have fermentation API plants. Stason has also forged partnerships with other contract manufacturers that offer biomanufacturing and expects to expand into this area in the next few years. This expansion not only includes building or acquiring manufacturing facilities, but in-licensing biotechnology products, which we plan to develop internally. To further enhance our drug development capabilities, we plan to add a new division focused on compound screening, plasma protein binding, preclinical drug metabolism, preclinical and clinical study designing, and pharmacokinetic analysis.

Mr. Morales: We are seeing an increasing number of bio-driven protein and peptide drugs, and many companies who are looking to outsource require increased flexibility in the manufacturing schedule and multiple manufacturing capabilities to accommodate several different dosage forms. HollisterStier has been fortunate to have experienced substantial growth in the past fiscal year, and protein and peptide drugs represent an increasing percentage of what we manufacture. Our recent experience shows an increased trend in Phase I, II, and III biological products. Greater than 60% of the clinical trial products being produced in the past several years have been bio-driven protein and peptide drugs, and this trend continues to increase. New product submissions are an equal mix of NDAs and BLAs, and site transfers include various categories of product.

We offer specialized pharmaceutical processes and manufacturing equipment, such as lyophilizer cold-shelf loading, use of diaphragm and peristaltic pump filling technologies, aseptic compounding capability, and cold storage capacity for API and finished product.

Mr. Neuffer: Following the successful sale of the Biopharma and Bioproducts businesses in 2007, Cambrex is completely focused on small molecule API products and development/production services. As a segment of the biotechnology-driven market is focused on enhanced delivery of very potent small molecule drugs, Cambrex has invested in capacity to support the production of HPAPIs.

Q: The highly competitive nature of the pharma industry has been driving consolidation, and companies are increasing off-shoring to emerging markets to reduce costs. As a result, players in key outsourcing destinations have been improving their manufacturing infrastructure to increase their global competitiveness. Does this speak to what is happening at your company?

Mr. Morales: Our CMO organization has anticipated the shifts in our industry and understood early on the strategic opportunity in having a global presence. Both HollisterStier and Draxis have a partnership with facilities in India and Europe, allowing us to diversify our offerings, expand our capacity, and tap into resources within our parent and sister organizations that streamline the manufacturing process. HollisterStier and Draxis Pharma Contract Manufacturing are a part of Jubilant Organosys, an Indian-based multinational pharmaceutical organization. This partnership has allowed us to expand the services our combined organizations are able to offer clients–R&D through Jubilant Drug Discovery Services, clinical trial support through Clinsys, and API manufacturing through Jubilant Organosys. Since our integration with global partners, HollisterStier has expanded its facilities to include a commercial high-speed fill line,

an analytical and microbiological lab, 1,200 sq ft of lyophilizer shelf space, and we have recently invested $2 million into an expansion project in our clinical trial manufacturing suite. CMO organizations who maintain a global footprint provide access to a broad array of services and are able to offer a single point of contact to further reduce transfer and manufacturing complexity.

Mr. Neuffer: Cambrex has increased its global competitiveness by sourcing raw materials and intermediates from Asian providers to help lower overall cost of goods to our clients. In addition, Cambrex extended its footprint into Eastern Europe in 2008 by acquiring a facility with highly skilled chemists in Estonia, providing a value-added resource to support our R&D activities across in the US and Europe.

Ms. Wood: We started out offshore, so we inherited intrinsic competitiveness from the beginning. The core company, Standard Chemical & Pharma, based in Taiwan, was established in 1967 and has become a dominant player within the Asian market. Stason was set up in 1994 as part of a global expansion plan. We have since expanded in the US to three offices, and also expanded our offices and facilities into Japan and China. We are actively pursuing expansion through acquisition and partnerships into global territories that have a significant unmet medical need for the products we currently manufacture.

During the past year, Stason expanded manufacturing facilities and developed a licensing division within both the US and Japan. This division works with companies to license products into Asia through co-development agreements, which lead to marketing/distribution agreements, and at the same time, provide our clients revenue. Through our licensing office in Japan, we are working with companies that desire co-development agreements with US-based companies. This allows us to offer our clients potential new product offerings, many NCEs within the US. Contract manufacturers have to think outside of the box and provide other services where they truly partner with clients on a global basis with a long-term vision that benefits both parties.

Q: How do you see your business evolving to keep up with the Specialty Pharma industry throughout the next 3 to 5 years?

Ms. Wood: We are actively evaluating biomanufacturing opportunities and expect this to be a growing segment within our organization. Our current goal is to continue to build on our contract manufacturing expertise worldwide and at the same time ensure quality and customer satisfaction. We are also evaluating emerging markets outside North America, Europe, and Asia to introduce current products through co-development or licensing agreements to facilitate access to medicines and products that may not be available in those territories. Stason is quite diversified offering not only contract manufacturing, but we also have divisions in APIs, brand pharmaceuticals and development, medical devices, diagnostics, nutraceuticals, and animal health. Our goal over the next 3 to 5 years is to provide additional focus and resources to grow each of these areas as manufacturing is a significant component to each.

Mr. Morales: Specialty Pharmaceutical organizations will continue to see enhancements in drug development and related delivery mechanisms. It is critical that our CMO organization monitor these improvements carefully such that we can make targeted investments in infrastructure to keep pace with the changing needs of our clients.

HollisterStier has undergone significant growth in the last 5 years, and we predict that growth to maintain over the course of the next 3 to 5 years. We will continue to be a flexible and transparent manufacturer, working through the life cycle to take costs out of the supply chain and streamline manufacturing. We are a very heavily regulated industry and take training and continual process improvements very seriously. It is our belief that these investments in time and resources ultimately present our customers with the most safe, reliable, and efficient manufacturing partnership.

Mr. Neuffer: Cambrex will continue to provide innovation and value to our commercial products and services. The evolution in the next 3 to 5 years will include further expansion and exploitation of the core competencies. As an example, Cambrex is actively working with companies to taste-mask and enhance the drug delivery aspects of APIs using our proprietary resin technology. In addition, we continue to improve our transaminase technology, increasing the yields and refining the percent of enantiomeric excess.

Mr. Iacobucci: We're seeing more and more of our work shifting to development services earlier in the regulatory process, and we are building greater flexibility to meet the needs of these products. Many of these products are 505(b)2 NDAs that are looking for new indications and even new delivery systems. As such, we will continue to enhance service, innovation, and technology. While we will remain focused on our core business of semi-solids and liquids, we'll also expand into more adjacent delivery technologies that we'll offer our customers. Our strategy isn't necessarily to become the biggest, but our goal is to be the best at whatever we tackle. ◆