RIGOROUS INTEGRATION IN A SCALABLE DEVELOPMENT & MANUFACTURING ENTERPRISE TO SUPPORT CONTINUED GROWTH OF BIOPHARMACEUTICALS

→ BY **SYED T. HUSAIN**, ALCAMI

The pharmaceutical and biopharmaceutical development and manufacturing market continue to experience significant expansion as the development of small molecule drugs and more complex large-molecule biologics rival for attention. Small and midsize pharma/biotech companies are leading drug discovery and the engagement of contract development and manufacturing organizations (CDMOs) helps them to improve capabilities and enable companies to compete in this dynamic market.

To attract and keep customers, competitive CDMOs are bolstering their offerings by expanding areas of expertise. In recent years, some of these expanded capabilities have been organic, while others have been achieved through strategic partnerships and mergers with strong, capable partners.

One example is "Alcami", the alliance of AAIPharma Services and Cambridge Major Laboratories, which through rigorous integration and improvements formed a full-service CDMO offering drug substance and drug product development, manufacturing, testing and packaging services. The development of biopharmaceuticals – often in the form of parenteral or injectable medications – requires unique expertise, facility specialization, and an understanding of the entire development process. Current outsourcing trends in this market are prompting companies like Alcami to increase recognition of how significant aseptic processing is to customers' success – and how important it is to engage contract partners with the best capabilities, finishing parenteral medications aseptically.

A REASON TO RELY ON OUTSOURCING

According to the 2016 Nice Insight CDMO Outsourcing Survey of over 500 outsourcing-facing pharmaceutical and biotechnology executives, outsourcing partners are being engaged for every phase of development, with over 50% of all respondents outsourcing every phase with the exception of phase IV / Post-Launch.[1] Additionally, overall engagement increased for phase II, III, and IV by as much as 25 percentage points (phase III) since 2015.[2] However, some of the newest numbers are even more significant in specific segments.

Phase IV / Post-Launch services, for example, are outsourced to CDMOs by nearly half of all big pharma respondents (47%) while 69% of emerging pharma / biotech companies engage CDMOs as outsourcing partners for preclinical services. Overall, the annual outsourcing expenditure on CDMOs was $51M or greater for 71% of survey respondents with 28% exceeding $100M. With that, 75% of total respondents expect that number to grow over the next five years[1], indicating a steadily increasing reliance on outsourcing partners.

Even more noteworthy, however, is the percentage of services outsourced for biopharmaceutical drugs and associated manufacturing processes. As the world's population ages, the middle class continues to swell and treating chronic conditions becomes more prevalent in developing countries, the demand for biopharmaceuticals rises; this increase is clearly visible in outsourcing practices.

Large molecule new biologic entities (NBEs) and biosimilars accounted for 26-50% of all outsourced services for 16% and 13% of all respondents, respectively. Additionally, microbial cell line and mammalian cell line based development and biomanufacturing were outsourced or will be outsourced by 62% and 55% of survey respondents.[1] Some of this outsourcing is due to traditional pharmaceutical companies increasing their focus on biologic drug development and seeking cost effective ways to make this investment.

EXPERTISE FOR BIOPHARMACEUTICALS

Biopharmaceuticals and parenteral drugs in general require aseptic processing at nearly every stage of the production process. These processes require advanced controls and optimal packaging materials to meet regulations and guarantee patient safety. Like many pharma/biotech companies, contract service providers are beginning to form scalable enterprises to reduce costs while bolstering their services to offer a more complete suite of options to support the drug development and manufacturing cycle.

Most of today's biologic drug products – including monoclonal antibody drug products that have been on the market for over 20 years – are designed for parenteral

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administration[3] but considerable challenges exist in liquid drug development, including quality concerns and close regulation. These drugs also require advanced primary and secondary packaging materials and technology due to the complexities associated with administration, high development costs and increasing patient demand.[4] Protecting the sterility of the product as it moves through each phase of formulation, filtering, filling, and packaging is mission critical. Full-service CDMOs have been investing in advanced containment and process technologies to mitigate these risks at all stages. With the right CDMO partner, it's even possible to follow the processes as far as distribution services.

Alcami is leading by example. In 2014 Cambridge Major Laboratories, a full-service CDMO providing active pharmaceutical ingredient (API) development and manufacturing, combined with AAIPharma, an experienced, long-term provider of pharmaceutical analytical testing, drug product development and drug product manufacturing and packaging services. The result? Alcami, a supplier of integrated chemistry, manufacturing, and controls (CMC) services with centers of excellence in solid-state chemistry and formulation development services and a U.S.-based drug product sterile manufacturing facility. In fact, they recently announced the completion of clinical trial material from API manufacture to Drug Product (sterile) release in 79 days which is a 65% reduction in timeline in comparison to a non-integrated approach.

Over the last several years, Alcami has produced millions of parenteral fills in its small- and large-molecule sterile parenteral product manufacturing facilities that also support lyophilized products, suspensions, emulsions and terminal vial sterilization. The combined operational matrix allows seamless integration of services covering development, testing and manufacturing from API, and on to finished packaging.

THE PACKAGING IS THE PRODUCT

While the outsourcing of biopharmaceuticals is noteworthy in all four respondent segments in the 2016 Nice Insight CDMO Outsourcing Survey – Emerging, Small, Mid-Size, and Big Pharma/Biotech – the outsourcing of packaging materials is also significant, with over half of all respondents outsourcing both commercial (58%) and clinical (60%) scale primary packaging.[1] Though packaging has not typically be considered in the early stages of drug development, packaging materials can significantly impact a biopharmaceutical drug product and the growth in biopharmaceuticals is heightening the need for unique containment and delivery systems.[5]

Most understand the fill-finish process of aseptically prepared drug products requires sophisticated equipment in a highly controlled cGMP environment to ensure product quality and patient safety. The complexity of most biopharmaceuticals also prevents easy identification or characterization with many products being heat sensitive and susceptible to microbial contamination. These conditions necessitate the use of aseptic principles at every step, potentially illustrating why controlled room temperature (CRT) packaging and cold-chain packaging services were outsourced to 47% and 36% of respondents, respectively.[1]

Single-unit dosing is reducing medication non adherence and helping assure the promised therapeutic benefits of biopharmaceutical drug products; however, for these benefits to carry through from the manufacturing process, fill-finish processes have to meet stringent requirements to ensure flow path sterility and integrity, operational safety, and fill-volume accuracy. Additionally, all the requirements of a drug, including shipping, storage, and the dose form, as well as ease of administration, should be considered during drug development. The expertise of an experienced and integrated CDMO partner will help speed the evaluation of options and the execution of final packaging processes.

When the product is the process, the process is everything, and that process does not end with drug development or production, it ends with the patient. When the process can be contained and monitored by one company with expertise at every stage, all production processes can remain consistent, aseptic, reliable, and cost effective for all parties involved. P

→ ABOUT THE AUTHOR

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Syed Husain, the commercial leader for Alcami, leverages in-depth experience in sales, business development, marketing and operations for the development and manufacture of small molecules, antibody drug conjugates (ADCs), peptides, and large molecules covering drug substance and drug product. Syed earned a BS in chemical engineering from New Jersey Institute of Technology in 2003 and an MBA from Cornell University in 2009.

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MARCH 2016

→ **REVIEWED**

NEW NAME, LOGO FOR **ALCAMI**

ALCAMI represents a rebranding of AAI Pharma Services and Cambridge Major Laboratories (CML), creating a world-class supplier of comprehensive pharmaceutical development and manufacturing services.

NEW NAME

The Alcami name is an anagram of AAI-CML, so it pays homage to the legacy. It also serves as a reference to "Alchemy," the forerunner of modern chemistry, based on the transformation of matter, particularly converting base metals into gold, and also refers to a process of transformation, creation or combination.

AAI-CML
ALCAMI.

→ **ANAGRAM**

TAGLINE

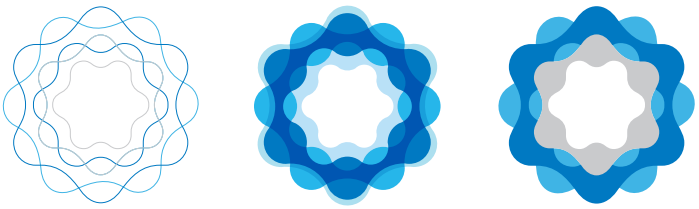
The aim for the tagline was to communicate a message of seamless transition with reference to the additional capacities and capabilities that would support the clinical progression and commercialization of medicines for their customers.

THE RESULT IS "CONNECTED AT EVERY LEVEL."

This communicates the integration and the connection between a CDMO and customer, and AAI/CML's strategy to be focused on end-to-end service for the right audience.

The tagline establishes a connection from drug substance to drug product and the multi-layering of relationships between the new entity and the marketplace. It is a connection through science and philosophy – a true partnership.

→ LOGO MARK PROCESS



→ EXPLORATION OF TYPEFACE

ALCAMI All caps / Curved strokes

alcamiii Hand-drawn / Optical kerning

alcami Lower case / Increased height

→ BEFORE

AAIPHARMA | CAMBRIDGE MAJOR LABORATORIES

→ AFTER

alcami™

LOGO

The direction is further progressed in the logo. The connection of the multi-layered hexagonal shapes alludes to elements of processing complexity and relationships that are sophisticated.

The symmetry of the logo suggests a connected relationship between Alcami and its customers; it brings their personality forward.

The primary color palette meets industry expectations and brings continuity from the legacy organizations.

There is a delicacy and refinement to the visual, which conveys continuous partnership. The concept can be used in multiple forms, adapted and evolved. Derivative messaging keeps the "connected" theme fresh and relevant.

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