Successful Biosimilar Development Requires an Outsourcing Partner with the Right Experience

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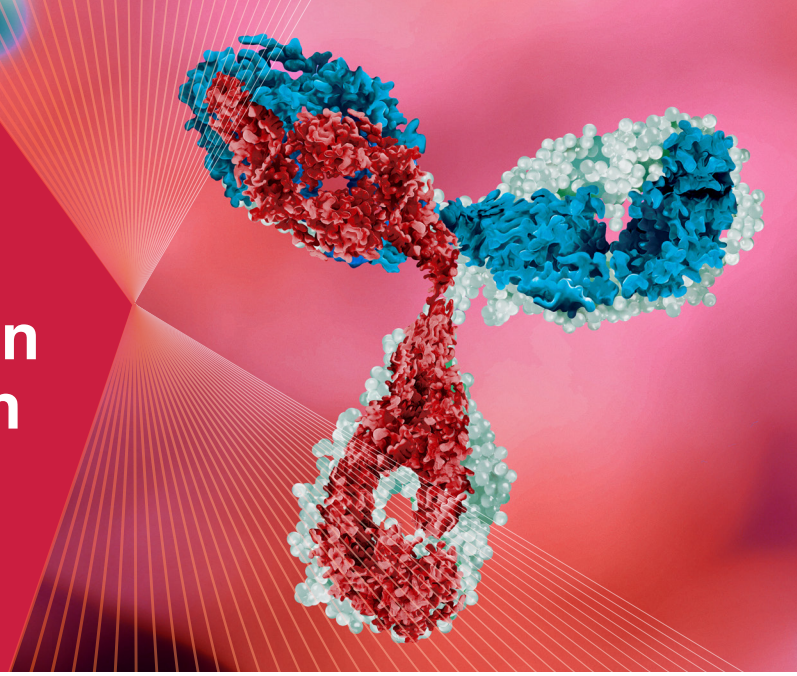

Demand for biosimilars is expected to increase significantly in the coming years, particularly in the United States. Developing new biosimilar candidates is a challenging endeavor that requires partnerships with outsourcing partners that have deep protein science, analytics, and process engineering expertise. Avid Bioservices has successfully supported biosimilar development for nearly a decade and is further expanding its capacity to provide manufacturing services from the bench through larger-scale commercialization.

Anticipating Strong Growth in Demand for Biosimilars

The value of the global biosimilars market is predicted to expand at a compound annual growth rate of 24.7% from $11.8 billion in 2020 to $35.7 billion by 2025.[1] The market is segmented into insulin, monoclonal antibodies (mAbs), recombinant human growth hormone (rhGH), granulocyte colony-stimulating factor, interferon, erythropoietin, etanercept, follitropin, glucagon, calcitonin, and teriparatide and enoxaparin sodium, with mAbs dominating. Europe accounted for the most biosimilar sales in 2019, followed by Asia.

Due to the considerable time it took to establish an approval pathway for biosimilars and complex patent barriers, the United States has lagged behind Europe and Asia in the number of biosimilar approvals.[2] As of October 2020, over 60 biosimilars had been approved by the European Medicines Agency (EMA), while the U.S. Food and Drug Administration (FDA) had only approved 28, 18 of which have actually launched commercially.[3] Uptake of approved biosimilars is also lower in the United States than in Europe or Asia, largely due to payer reluctance and existing reimbursement practices.

That situation is changing, however.[2] Between November 2019 and mid-March 2020, 6 (six) of those 28 biosimilars have reached the U.S. market, which further validates that the current U.S. biosimilars pipeline is growing strong. Five biosimilars to AbbVie's Humira will reach the market in 2023, which should lower the price significantly for the biosimilars and the originator drug, as well. Proposed legislation could help drive adoption with financial incentives for prescribers treating Medicare patients, while state governments and private insurers are also introducing policies to encourage biosimilar use. Doctors and patients are also becoming more educated on the nature of biosimilars.

The pressures placed on the overall healthcare system by the COVID-19 pandemic have also increased interest in high-quality biosimilars.[4] By the third quarter of 2020, biosimilars were being recognized by advocates of low-cost healthcare as important to achieving cost savings, and some biosimilars in the U.S. market have claimed a significant share of their markets.[3,5]

The First Challenge: Reverse Engineering

Developing a biosimilar is not an easy task. The formulated drug product must be bioequivalent to the original drug. While – operationally – the work involved for biosimilars is the same as that for branded drug products, biosimilars must meet a specific set of target properties. If the innovator drug presents 99% purity, then the biosimilar must as well; anything less is unacceptable. Achieving that kind of goal is incredibly difficult without possessing specific information about the process used to manufacture the original drug.

Typically, biosimilar developers know the strength of the innovator product and the formulation. Detailed analysis of samples of the marketed drug provides necessary information on the physicochemical characteristics (e.g., sequence, posttranslational modifications). Those data describe the endpoint that must be reached.

Because biologics are produced via cell culture, however, without specific information about the culture conditions and the downstream purification operations, attaining a bioequivalent product is extremely challenging. In essence, particularly for highly complex biologics, the process is the product. Successful reverse engineering of a process for which little information is available beyond the general knowledge pertaining to biologics manufacturing is required. And even the smallest differences – such as the bioreactor size – can have a significant impact on the structure of the drug substance.

As a result, developing biosimilars in not for the faint of heart.

Extensive Process Science and Engineering is Essential

From an execution standpoint, the same procedures and checks and balances are used for biosimilars and branded drugs, but the ability to develop a robust, scalable process that will reliably provide a biologic with a highly specific set of properties is unique to biosimilars. A greater emphasis is thus placed on the first few at-scale or engineering batches.

The key to success is leveraging the appropriate expertise to execute such complex projects, including experts with the right sets of knowledge and capabilities to interpret results and design further experiments that will continuously build upon previous data. They must have a deep understanding of protein chemistry, cell culture, and the impact of process conditions on protein structure down to the smallest detail, including changes in scale. Overall, process science, analytics, and engineering expertise applied early in process development are crucial.

Understanding the CQAs

Biosimilar developers must also have a deep understanding of the critical quality attributes (CQAs) of their biosimilar candidates. They must know in great depth the nature of the branded products they are targeting and the structure, purity, and other characteristics required for their biosimilars.

This high level of understanding is essential before a manufacturing process can be developed, whether that work is conducted in-house or by an outsourcing partner. Only once the CQAs have been well defined can the important process parameters that impact those CQAs be identified – and, equally important, the parameters that are not critical.

Local Connections Becoming More Important

The COVID-19 pandemic has raised questions about the reliance of biopharmaceutical companies on extended supply chains. In addition to diminishing savings owing to the maturation of emerging economies, the logistics challenges can be quite daunting. Supply disruptions also have the potential be more severe, as was seen during the first months of the pandemic.

Sponsor firms are realizing the advantages of partnering with raw material suppliers and service providers in closer proximity. Sponsors cannot oversee the work being done at contract development and manufacturing organizations (CDMOs) on a day-to-day basis. Partnering with service providers in the same or close time zones facilitates more effective communication, which supports more valuable, collaborative relationships.

A CDMO with the Right Experience to Get Your Biosimilar Approved

Avid Bioservices brings an ideal combination of the expertise in protein science, analytics, process engineering, and CQAs and experience on the innovator side of contract development and manufacturing to support clients with their biosimilar programs. Avid began as a subsidiary of Peregrine Pharmaceuticals – an innovator company – while offering contract development and manufacturing services using the company's excess capacity. The company has been developing and manufacturing biologics for nearly three decades, providing customers with process development, manufacturing, regulatory, quality, and other support. Avid Bioservices became a standalone dedicated biopharmaceutical CDMO in 2018, and Avid's common stock is currently traded on NASDAQ as "CDMO."

At Avid, we have the extensive knowledge, expertise, and capabilities needed to develop highly efficient and robust processes for the production of biosimilars that have a high likelihood of receiving regulatory approval, even for the most complex and challenging biologic drugs. With our current manufacturing capacity, we can accommodate many different projects at any one time, supporting them through the clinic and commercial launch.

Expanding to Support Projects through Large-Scale Commercial Supply

Another exciting development at Avid is the expansion project currently underway. Begun in late 2020, Phase 1 of the project involves the addition of a second purification suite that will essentially double the output of our existing Myford North facility in Southern California. The suite should be online in early 2022. Earlier this year, Avid initiated the expansion for Phase 2 to further build out the company's Myford facility to include a second manufacturing train with both upstream and downstream processing suites, known as Myford South.

In addition to increasing capacity, we have also had significant success improving the efficiency of our internal processes by simplifying workflows and employing lean manufacturing principles. The overall goal is to continually streamline operations. This strategy is also being applied to the expansions; we are building out with techniques, methods, and equipment with which we are already familiar.

These expansions are driven by the requests we are receiving from existing and potential new customers. Historically, we have supported clinical development and commercial manufacturing for emerging biotechs, as well as large pharma. Our successes with these projects have brought us wider recognition within the industry and led to interest among additional large multinationals with larger capacity requirements.

Once the new capacity is installed, Avid will be able to take on a wider range of projects with larger commercial demands and continue to support clients from the early process development stage all the way through commercialization and post-launch production. As such, we will be able to not only meet the needs of more new clients, but also meet the growing needs of our current clients.

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