Biologics Manufacturing, An Opportunity To Partner With CRDMOs To Bring Speed, Mitigate Risks

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Over the past few years, biopharmaceuticals, also known as biologics or biological medicinal products, have become a popular class of drugs. As per industry reports, the global biologics market is expected to be worth around USD 719.84 billion by 2030 and will expand at a compound annual growth rate of 7.8 per cent from 2022 to 2030.

One reason for their rising popularity is that they are highly effective at treating a wide range of conditions and are typically associated with fewer side effects. This includes autoimmune disorders (rheumatoid arthritis and multiple sclerosis), cancers (breast cancer, leukemia, and lymphoma), inflammatory diseases (Crohn's disease or ulcerative colitis), infectious diseases (hepatitis), and even osteoporosis.

Biologics, however, are expensive to produce, limiting the access to these novel therapeutics. Given the benefits of biologics drugs, pharma companies today are looking at alternative and effective approaches to make them easily available and affordable for patients.

Biologics drugs or biopharmaceuticals are pharmaceuticals produced from biological systems. They are designed to interact with specific parts of the cell surface or intracellular components, allowing them to provide targeted and more effective treatments than traditional small-molecule drugs. The majority of biopharmaceuticals being developed today and available in the market are monoclonal antibodies (mAbs), which are proteins made in living cells to help patients fight various diseases.

The generic versions of these biologics drugs, referred to as biosimilars are biological products that are highly similar to an approved biopharmaceutical product (innovator biologic). As per a recent report from McKinsey, the biosimilars market is expected to grow to USD 30 billion by 2025 and to more than USD 60 billion by the end of the decade.

Biosimilars offer the same therapeutic benefit and treatment advantages as the innovator biologic and are also made from living biological systems like the approved biopharmaceutical product. The specific cells (seed) used are different; however, in both cases, the innovator biologic or its biosimilar seed material makes (encodes) the same protein.

In contrast, small molecules or conventional medications are most commonly made from chemicals and have the potential to possess a higher level of undesired off-target effects. Although several small molecules have been launched to rave reviews, there has been a remarkable surge in the number of biopharmaceutical products in recent years.

The complexity of biologics manufacturing

Unlike conventional medicines, biologics and biosimilars cannot be created by following a chemical 'recipe'. Biological drugs are produced by growing live cells in bioreactors and it is these cells that produce the required drug. Their structures are also more complex coming from the large size associated with biological molecules. Thus, developing biologics is a more difficult process than producing conventional chemical drugs.

Biologics manufacturing is very sensitive to the process used, starting material (seed), growth conditions and raw materials. Any change in one or more of these can impact product quality. This places a very high emphasis on not only the final product but also the in-process controls. Therefore, any change in the process or the manufacturing conditions and raw materials used could lead to a change in product quality and batch-to-batch variability that is unacceptable.

It is for this reason that biosimilar manufacturing is a lot more challenging and biologics are difficult to copy. Any change in the process or the inputs used to make them increases the possibility of dissimilarity from the innovator biologic. This is why the first step for biologics or biosimilar development is establishing the manufacturing process (including the starting materials – most importantly, a well-characterised cell bank or the seed used for cells to be grown).

The success of commercial manufacturing of biopharmaceuticals depends on several steps being designed well, characterised and supported by robust analytical tools to assess product quality and impurity profiles along the way. Also, large molecules are complex and therefore necessitate a battery of tests to establish potency, purity, safety and efficacy, adding to the cost of these drugs.

Many biologic molecules are also associated with post-translational modifications and glycosylation (adding sugar molecules to an otherwise long protein), to complete the process of generating the desired drug. This involves transformations that the cell performs on its own to modify the basic protein backbone structure.

Small molecule drug synthesis does not involve any such transformations. For biologics therefore, a well-developed cell bank and the right nutrients for the cells, the micro and macro environment in which the cells grow, the downstream steps (where the protein is purified from all other impurities) all play a key role in obtaining a consistent product, which requires detailed studies (product characterization) to establish the quality of the biologic.

Collaboration with CRDMOs as an approach to reduce CAPEX and speed to market

Following the development of a biologics product, launching it in the market comes with its own set of challenges. There is a need to use a qualified and validated biologics manufacturing facility, which is a capital-intensive proposition. The overall life cycle from the discovery of a biologic to its launch on the market is also a very long cycle involving preparing a scalable process and conducting extensive clinical trials.

The capital- investment is particularly acute for biotech firms in the clinical stage that are virtual or have limited infrastructure. For large biopharmaceutical manufacturers, investing in capacity for new products has its own challenges, mostly stemming from uncertainty of demand. Relying on Contract Research Development and Manufacturing Organizations (CRDMOs) offers flexibility while delivering speed to market and capex avoidance.

CRDMOs allow the integration of drug discovery services with development and manufacturing services, all under one roof. The biopharmaceutical development team at a CRDMO works with several clients to optimize their productivity and help them

reduce their eventual cost of goods, while maintaining high quality. CRDMOs such as Syngene are in a unique position to apply a wealth of experience at various stages of development and manufacturing.

According to the 19th Annual Report and Survey of 'Biopharmaceutical Manufacturing Capacity and Production,' published in 2022 by BioPlan Associates, 86.9 per cent of respondents outsourced some biopharmaceutical manufacturing in 2022, compared to 82.6 per cent in 2021.

Respondents also indicated higher spending on such activities over time. The most frequently outsourced activity reported was analytical testing/bioassays at 31.7 per cent, followed by toxicity testing at 31.6 per cent, fill/finish operations and testing of cell line stability at 26.7 per cent.

Presently, there are more than 132 approved biopharmaceutical products in the US and EU, of which 50 per cent are mAbs (monoclonal antibodies), and the remaining products are other biologics.

There is also a higher demand for drugs, vaccines and supplements for animal health, fueled by the growing number of companion animals present. To meet this market requirement, animal health companies are also increasingly collaborating with CRDMOs.

For example, one of the world's leading animal healthcare companies recently partnered with Syngene to manufacture drug substance for bedinvetmab, a first-in-class monoclonal antibody used for treating osteoarthritis in dogs.

This agreement initially centred on creating the drug substance, paves the way for the development and manufacturing of other molecules in the coming years, and is expected to be worth up to USD 500 Million over 10 years.

While biologics products are effective, with a potential for fewer side effects, developing such products requires strong technical expertise and a well-equipped facility. Also, manufacturing such products or their generic versions, referred as biosimilars, requires high CAPEX investments with significant lag time before seeing a return on investment. Furthermore, seeking necessary regulatory approvals for the facility and producing biopharmaceuticals in a cost-effective manner is complex and challenging.

To mitigate these stumbling blocks, partnering with a CRDMO with US-FDA (US Food and Drug Administration) or EMA (European Medicines Agency) approved facilities for biologics manufacturing, can help significantly.