LIFE SCIENCE CONNECT

Accelerating mAb Development to Meet mAb Market Demand

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As the number of monoclonal antibody (mAb) drugs entering the market continues to rise, accelerating development to meet demand will require solutions that maximize efficiencies while minimizing risk.

The common challenges that manufacturers face include optimizing development processes, reducing time to market, and selecting the right partner to shepherd their scale-up activities.

mAb manufacturing has made significant strides in the last three decades. Approximately 35 years ago, monoclonal antibody biotherapeutics gained their first FDA approval; eight years later, a second mAb was approved. In the subsequent 20 years, a relatively small number – roughly 50 – mAb treatments had received FDA approval. That paradigm began to shift in 2015, and the number of mAb treatments that have received regulatory approval has doubled in the last six years. In addition to the marked increase in approvals is an influx of mAbs in clinical development; currently, there are more than 870 mAbs in the clinical pipeline.

Monoclonal antibody biotherapeutics now account for roughly a fifth of the FDA's new drug approvals every year, with cancer treatments accounting for the majority of new drugs. The influx of cancer therapeutics is driven in part by the Chinese market. Another key driver for mAb proliferation has been in the manufacturing of antibodies to combat the current pandemic, which has resulted in more than 20 infectious disease agents currently in the clinical pipeline.

In addition to full-length monoclonal antibodies, researchers are also looking at next-generation antibody products, including antibody drug conjugates (ADCs), antibody fragments, antibody-like proteins, engineered antibodies, and others. Moreover, there is also a marked focus on the biosimilar market, which is currently worth roughly $4.3B, and is expected to nearly double by 2026. As new targets are identified and the market grows, it will be essential for manufacturers to increase their efficiency to meet this increase in demand for new biotherapeutics; ultimately, becoming more efficient will help accelerate the delivery of these therapies into the market.

Early-Stage mAb Optimization

Achieving market acceptance for new mAbs can be limited by inefficiencies in their development and manufacturing processes. Common challenges that manufacturers face include insufficient titer, raw material issues, and problematic protein quality. To overcome these challenges, it is important to partner with a global supplier that has commercially available products to support high titer, can ensure supply assurance, and offers customer service to support custom media development and analytical analyses.

Whether custom formulations are developed in-house or off-the-shelf advanced catalog formulations, media development and optimization are critical to improving productivity and simplifying workflows by increasing titers and improving protein quality. There are a number of advanced media choices available to optimize processes, including animal origin-free (AOF) and chemically defined (CD) media, available in multiple formats and optimized for different cell lines.

These include the Gibco™ Dynamis™ Medium, which is designed to offer the highest batch and fed-batch performance; the Gibco High Intensity Perfusion CHO Medium, designed to enable high titers in a wide range of CHO cells, regardless of the perfusion platform; and the newly launched Gibco Efficient-Pro™ Medium, an innovative CHO medium that enables high levels of specific and volumetric productivity.

Innovative feeds, reagents, and additives can help optimize processes, reduce variability, and improve overall workflows; determining the optimal additives for a process can be a critical early step for ensuring later success.

Some innovative Gibco feeds and reagents are also available to support optimization; these include the Gibco Efficient-Pro Feeds, Gibco EfficientFeed™ C+, Gibco Efficient Feed B+, Gibco Peptones, and Gibco GylcanTune Supplements.

Small-scale, rapid prototyping services can also help provide quick turnaround for products, enabling manufacturers to troubleshoot and scale up faster. Typical rapid prototyping services offered by Thermo Fisher include a fast, pilot-scale media manufacturing service, with turnaround times of approximately 10 to 20 working days in either 200 liter or 10kg batches, which can aid in early-stage mAb development. Some of the benefits of rapid prototyping include testing the manufacturability and scalability of a formulation prior to cGMP scale-up; modifying formulations by adding or removing a raw material and testing how it will impact a process; testing new and unique raw materials; and converting media to a new format, such as from a liquid to a powder formulation.

Maintaining consistency during scale-up is crucial; utilizing analytical platforms that can help developers troubleshoot issues and model optimal processes can serve to ameliorate costs and improve efficiencies. Gibco PD Express™ Services incorporates advanced analytics to support process development, improve yields, and improve process understanding. The platform features several core capabilities, such as its spent media analysis, which allows users to evaluate utilized media and identify potential improvements by analyzing the nutrient needs of a specific cell culture system. Its key driver identification analysis, which supports a deep dive into a medium's performance drivers, can help developers pinpoint raw material issues, perform complex media characterization, and troubleshoot emergent problems.

The application of proteomics and metabolomics to identify how media components are being used by cells is a revolutionary new way to optimize media.

This nascent technology, called multi-omics, is opening new doors in biomanufacturing and pharmaceutical process development through the application of proteomics and metabolomics in identifying intracellular pathways. Multi-omics is a revolutionary new way to optimize media, and Gibco PD Express Services offers developers a range of multi-omics capabilities to support process development. Furthermore, Thermo Fisher is well equipped to support a company's unique early-stage cGMP sourcing needs and provide access to a broad portfolio of cGMP chemicals from reputable suppliers, mitigating risks, increasing productivity, and reducing a biopharma's total cost of ownership.

Liquid, Dry, and Advanced Granulation Technologies

It is important during scale-up to choose a medium format that will suit an application's unique process and bioprocessing goals.

Some of the factors impacting this decision are a company's in-house capacity, the time available for media preparation, in-house storage space, shipping costs, the amount of media required, and other extraneous expenses.

An ideal supplier offers more than high-quality projects – ideally, their offerings would encompass suitable batch sizes, flexible packaging, cell culture media expertise, and custom services.

Thermo Fisher offers multiple media formats, including liquid and dry powdered medium, or DPM, as well as its Advanced Granulation Technology™ (AGT™). The liquid and DPM formats each possess pros and cons – while the dry format is more economical for shipping and storage due to its longer shelf life, its reconstitution can be labor-intensive and costly. Conversely, the liquid format, which is easy to use and has a reduced risk of cross-contamination, can be expensive to ship and has a comparatively shorter shelf life.

Thermo Fisher's AGT format leverages the pros of both the liquid and the DPM in an easy-to-use, pre-adjusted granular form that delivers all the benefits of the liquid media without the cost, storage, and transportation issues. In-house experts can help develop a custom formulation, tailored to a company's specific platform. Thermo Fisher is able to manufacture a client's proprietary formulation in their desired format, all while achieving rapid turnaround targets, supporting manufacturing redundancy, harmonizing facilities, and minimizing supply interruptions.

Late-Stage Production of mAb Products

Investing in state-of-the-art, single-use, scalable bioreactors with innovative, next-generation features can simplify scale-up and optimize mAb manufacturing. While a traditional bioreactor can support most mAb scale-up, advanced bioreactors can facilitate improved efficiency and performance, resulting in increased return on investment through improved productivity and decreased downtime. The Thermo Scientific™ HyPerforma™ DynaDrive™ Single-Use Bioreactor's improved seed train process allows users to transfer any process from 50 L to 5,000 L with a turndown ration of 20:1 at higher scales.

Many of the challenges associated with mAb scale-up can be overcome by solutions rooted in digitalization. By reducing the complexity involved in scale-up, tech transfer, and data management, companies can reap compounding benefits for their manufacturing processes. Incorporating an integrated solution that records data and maintains the fidelity of information end-to-end, and enabling streamlined data transfer through a fully integrated open architecture system is key to this approach. Thermo Scientific TruBio™ software facilitates easy, reliable, and repeatable process development and commercial cell culture processes. Powered by the DeltaV™ control systems from Emerson, this easy-to-use platform enables the consistent flow of data from research and process development to clinical scale and production.

Users are able to integrate the platform with most existing vessels to simplify their tech transfer and data management, enabling multi-unit functionality and enhancing speed to market.

Finally, it is essential for biopharma companies to choose a partner with expertise and experience that applies holistically across the commercialization process.

Thermo Fisher specializes across the therapeutic development, scale-up, and commercialization paradigm. This includes process characterization, advanced analytics, product development, process optimization, tech transfer, biotech, business modeling, life science, investment evaluation, project risk mitigation strategies, timeline management, and media manufacturing. Thermo Fisher also possesses a truly global manufacturing footprint, complemented by world-class logistics and distribution solutions.

Optimizing Commercialization for mAbs With Support and Experience

A partner with scale-up expertise and experience is a critical part of the commercialization process for any therapeutic. When selecting an ideal scale-up partner that can help successfully shepherd a biologic to the commercial market, it is important to evaluate their expertise and experience across a range of metrics. This includes process characterization, advanced analytics, product development, process optimization, tech transfer, biotech business modeling, risk mitigation strategies, timeline management, media manufacturing support, cGMP sourcing strategies, and process simplification.

With innovative products and services, advanced analytics, experienced teams, and worldwide redundancy, Thermo Fisher can serve as an ideal collaborator throughout the mAb manufacturing process.

With its large manufacturing footprint and strategically located facilities, Thermo Fisher has the flexibility to minimize delays and maximize the quality of clients' outcomes. This presence, coupled with its world-class logistics and distribution solutions, allow Thermo Fisher to streamline supply chains and help ensure just-in-time delivery.

Ultimately, the right supplier and scale-up partner can help biopharma companies greatly reduce costs, mitigate supply risks, and increase productivity for their mAb products. Thermo Fisher's comprehensive expertise, combined with its networked manufacturing locations and global supply assurance, make it an excellent choice for CDMOs, global biopharmas, and small start-ups alike.