Intensified continuous bioprocessing supports industry trends

New times bring new challenges.
First, a need for agile responses to changing market needs and global health threats, such as COVID-19 and bioterrorism. Second, the development of potent, targeted therapies for small patient populations required by precision medicine. Both have increased the demand for more flexible, manufacturing platforms and facilities with wider dynamic operating ranges.

In contrast to traditional, large-scale biomanufacturing facilities housing stainless steel bioreactors, or single-use facilities housing mid-scale bioreactors operated in fed-batch mode, Just –Evotec Biologics' cGMP biomanufacturing approach is based on a well-proven, continuous bioprocessing platform located in a facility consisting of Grade B and Grade C cleanroom modules (PODs) within a Grade D "ballroom" environment.

The optimized design of this "next-generation" facility reduces the overall plant footprint, environmental impact, and construction time and cost. In combination with J.Design, the continuous bioprocessing platform, this facilitates relatively low-cost, flexible and fully scalable manufacturing strategies, representing a paradigm shift in how to provide effective responses to current and future market needs.

Intensified, perfusion cell culture for increased productivity
Just - Evotec Biologics' new J.POD® cGMP manufacturing facility, located in Redmond, WA, houses 500 L and 1000 L single-use bioreactors. The continuous bioprocessing platform integrates intensified, high-performance, perfusion cell culture with a series of fully connected downstream processing unit operations. Scientists at Just – Evotec Biologics have optimized the compositions of the media and feeds used in the perfusion cell culture process to achieve outstanding performance of several commercial CHO lines as well as the company's proprietary cell lines, resulting in industry-leading product titers and overall process productivity.

Intensified, perfusion processes typically outperform traditional fed-batch process yields by 5 to 15-fold, due to higher cell densities and the possibility of extending culture duration from 15 to 30 days or even longer. For instance, Just – Evotec Biologics' cGMP perfusion cell cultures typically generate 2–4 g of product/L/day for monoclonal antibodies. This translates into drug substance batches of 4–8 kg for a 15 day 500 L bioreactor scale process or 25–45 kg for a 25 day 1000 L scale process.

Our proven continuous processing platform can be operated in hybrid or fully continuous mode. Hybrid processes are perfectly suited to the manufacturing of clinical products that may initially require a few kilograms of material but where the mass demand may substantially increase during clinical development as well as low volume commercial products, which may require tens to hundreds of kilograms of material. In contrast, fully end-to-end continuous bioprocessing is capable of very high mass outputs (metric tons) which can support a large market commercial supply at a relatively low cost of goods.

Continuous bioprocessing supports a flexible manufacturing strategy
One of the key advantages of a strategy based on continuous bioprocessing is that if larger quantities of product are needed, for example as the product progresses to late phase clinical development or if the market demand for the commercial product increases, the manufacturing process can be very easily scaled up. The continuous process can be adapted to provide the required amount of drug substance by simply adjusting the process duration, without needing to increase the size of the bioreactor or the purification columns. As noted previously, the amounts of drug substance generated from a single process are very substantial; however, if necessary, the process can also be 'scaled out' by multiplexing the entire process at the same scale. This avoids the significant technical risks associated with traditional scale up strategies and potential logistical risks associated with having to move to a different, larger facility. In addition, the process can be replicated at other J.POD facilities, providing a flexible manufacturing strategy based on location.

In summary, the intensified, continuous manufacturing approach developed by Just – Evotec Biologics is at the forefront of the paradigm shift towards continuous bioprocessing. It isn't only advantageous in terms of cost efficiency but can also reduce the risks associated with traditional process scale up. This flexible and highly efficient manufacturing strategy can support drug substance supply at all stages of clinical development through to commercial launch of biologic drugs.

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