CO-CULTURING CELL LINES FOR EFFICIENT MANUFACTURE OF MULTISPECIFICS

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Key Words: electrostatic-steering, co-culture, multispecifics, clinical manufacture

Pfizer's electrostatic-steering technology for the production of multispecific antibodies has proven to be robust for fast development timelines, with high productivity and consistent product quality. Electrostatic-steering involves the production of parent homodimers that have been engineered to recombine as a more stable molecule in the multispecific form, after a reduction and oxidation reaction. Typically, these parent homodimers are produced from two different cell lines in monocultures, purified separately through the Protein A step, then mixed in a redox reaction for multispecific production prior to final purification and formulation. While this strategy has attractive characteristics, such as high and consistent product quality of two platform-like monoclonal antibodies (mAbs), the benefits are countered by a long, resource consuming manufacturing campaign, caused by the requirement of two separate bioreactors producing the parent homodimers from different cell lines. Additionally, multiple independent manufacturing batches increases the risk of manufacturing deviations and failures that would impact the ability to deliver the heterodimer product. Given that manufacturing infrastructure is a key limiting factor in industrial portfolio pipelines, the reduction of time, resource requirement, and batch numbers in the manufacturing campaign is highly desirable.

Coculture of the two cell lines expressing the parental homodimers enables the concurrent production of the parents in a single reactor. Both parents can then be purified together, followed by a redox reaction which produces the multispecific antibodies. The coculture strategy will reduce hold times and batch records, lower release assay requirements, and could result in a 34 % reduction in campaign timelines.

This presentation will show data which demonstrate the successful development of a coculturing manufacturing strategy that is reproducible. The potential of this strategy for clinical manufacturing will be illustrated via robust data from bench and pilot-scale studies. Additionally, the presentation will review our findings on product quality and manufacturability, as well as providing insight into further reproducibility.

Coculturing parent homodimers displays an inherent advantage over monocultures when utilizing electrosteeering for multispecific antibody production. Through co-culturing, the electrosteering strategy, with robust product quality characteristics, high productivity, and fast development timelines, can be delivered in shorter manufacturing campaigns. This case study demonstrates the feasibility of a novel approach for the large-scale clinical manufacturing of multispecific antibodies which promises faster clinical development.