

## **CONTINUOUS IMPROVEMENT IN BISPECIFICS MANUFACTURING: ADVANTAGES AND DISADVANTAGES OF A 2-CELL VS. 1-CELL CULTURE PROCESS**

Jessica Wu, Genentech, Inc., USA  
wu.jessica@gene.com

Key Words: bispecific, knobs-into-holes, half-antibodies, cell line, facility fit

This presentation will summarize Roche's recent successes with bispecific molecules and trace the evolution of the manufacturing strategy for knobs-into-holes bispecifics at Genentech. Two strategies have been used to manufacture knobs-into-holes bispecifics: a 2-cell culture approach, in which two unique half-antibodies are produced in independent cell cultures and then assembled post-harvest, and a 1-cell culture approach, in which four polypeptide chains are expressed within a single cell line. This presentation will describe how the initial 2-cell approach enabled manufacturing of early knobs-into-holes bispecifics, the development and manufacturing challenges encountered with this approach, and the technology advances that have now enabled a more efficient 1-cell approach. General pros and cons for the 2-cell vs. 1-cell strategies - including considerations for cell line development, process development, and facility fit - will be discussed.