Roundtable Session 2 – Table 5 - Facility Expansion - Scale-out (as opposed to scale up) is much more common in the CGTP space. What CMC considerations should be taken into account when scaling out for commercial approval?

Facilitator: Jasmine Gupta, *Synthekine*

Scribe: Bingwu Yu, *Ultragenyx*

Abstract:

Cell and gene therapy is emerging to be a highly promising field in modern medicine. Bringing such therapies quickly to the clinic and to the market relies on an efficient manufacturing process that is rapidly scalable and is capable of handling growing demand. Historically, scale-up strategy has been the industry norm for commercial manufacturing. However, due to the interest in personalized medicines, the scale-out concept has gained traction in the way biologics are manufactured. A scale-out process entails using multiple bioreactors in parallel at a given facility. The process seems straightforward but poses some unique challenges. We will discuss these along with CMC considerations that should be taken into account for developing a scale out manufacturing process for commercialization.

Discussion Questions:

1. What is your organization's approach towards strategizing scale out vs scale up process for manufacturing CGT products? Is scaling out or a combination of scale out/scale up approach preferred for commercialization of CGT products? What are the key drivers that help facilitate this decision?

2. At what stage of the program development, do you initiate scale out planning? What are some of the advantages and disadvantages of the scale out process?

3. What are key CMC considerations for developing a successful scale out process for commercialization?

4. What is your experience with planning validation studies for scale out process? Are these studies performed in-house or externally? How many batches are needed to demonstrate successful validation? What are some of the challenges that you have encountered during validation?

5. Have you sought Agency's feedback for scale out process?

Notes:

In general, the driver for scale-out approach is business need, especially for cell therapy that has a maximum scale limitation when the operation time limited while still keeping the cells viable. Scale out is to have identical manufacturing process in parallel. Therefore CMC consideration should focus on the risk factors that could cause non-identical manufacturing process. Inherit variability of starting material cells, equipment used, operator training can direct impact the scale out results. Different testing site (CRO) could contribute to plausible non-comparable scale out products. Lacking of understanding CQA and CPP is a challenge on good process control. In addition, process change is inevitable so it can be a burden when implement to scale out processes. It is proposed that automation can be very helpful to reduce the process variability.

The timing to develop scale out approach in early phase is limited due to resource constrain.