Table 30: Cell Therapy: Unique Challenges and Strategies to Meet Patient Needs

**Facilitator:** Wallace Kaserer, *Janssen Pharmaceutical R&D, LLC*

**Scribe:** Bob Kozak, *Bayer*

**SCOPE:**
Cell Therapies are increasingly becoming more relevant as a current as well as future therapy. To date results have demonstrated miraculous outcomes in key indications justifying the hope and potential for these therapies. There is a lot of excitement around these therapies and more of them are coming into early development phase 1 studies and potential commercialization. Cell therapies offer many unique challenges and it will be important for industry to find strategies to overcome these challenges that reduce risk to patient safety and improve outcomes.

**QUESTIONS FOR DISCUSSION:**
1. Early Phase:
   a. What is an appropriate control strategy during early phase studies?

2. Comparability:
   a. What are the key challenges that cell therapies present for comparability?
   b. What are the critical assays that offer the best data to support comparability?
   c. What strategies are utilized to mitigate comparability risk?

3. Critical Reagents and Raw Materials:
   a. What critical reagents present the biggest challenges and how best are these reagents controlled?
   b. What raw materials present the biggest challenges and how best are these materials controlled.

4. Lentivector:
   a. What are the challenges to control lentivector?
   b. What is an appropriate potency strategy for lentivector?
   c. What are acceptable specifications for the potency of the lentivector?

5. Other critical topics

**DISCUSSION NOTES:**
1. Early Phase Control Strategy
   a. In general cell specifications can be relaxed at this phase, note made of still expectations for >70% viability
   b. Vectors and DS may have higher specification expectations
   c. Detailed information needed for plasmids and vectors
      i. If using CMOs, need history of products made in facility and may need specific assays to prove no cross contamination
   d. Rapid micro at release and mycoplasma PCR expected
   e. Definition of potency may be broad, may use matrix approach of assays to cover
MOAs

2. Comparability Discussion
   a. Patient to patient variability is a challenge
   b. Reference to Novartis Kymirah experience suggested when a series of location comparability studies necessary they were successful in comparing A to B; B to C; then C to D

3. Raw Materials
   a. Discussion of media qualification included using normal cell experience to predict suitability
   b. Using better selection method for cells to achieve high purity may reduce problems with impurity profile
   c. Attempt to use consistent RM sources across all sites
   d. Need careful history of all RMs in contact with cells, plasmids, vectors etc, risk of pathogens and impurities

4. Lentivectors
   a. Some agencies asking for separate DS section for vectors
   b. Assays and issues thought to be well known and defined more like platform
   c. Examples were E. coli banks used and asked for extensive information and characterization

5. Regional Challenges
   a. Similar issues and questions was general experience from US/EU/Canada
   b. Some specific additional issues in EU are environmental assessment information timing and review variance. EU suppose to be improving and reducing variability