Roundtable Session 2 – Table 7 – Cost drivers (in CMC)

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Abstract:

With the continued pressure on healthcare costs, and the access to innovative drugs for unmet needs, this roundtable will discuss challenges and opportunities to drive value (e.g. reduce development CMC costs) in cell and gene therapy products.

Discussion Questions:

1. What CMC development costs are the main drivers?

2. Can manufacturing cost drivers be designed into the process and what are the risks?

3. Engineer and validation runs come with a significant cost. What examples are there to 'lean' these out without compromise to cGMP, IND/BLA enabling requirements?

Notes:

1. What CMC development costs are the main drivers?

- Cell culture media, including components such as growth factors
  - Costly, especially for uncommon growth factors.
  - GMP reagents for CAR-T: more competitive options available these days from vendors in regard to reagent quality and price, as there are quite a few CAR-T programs out there. Not there yet with pricing of growth factors for other therapeutics such as islet cells and HSCs.
- Plasmids: costly, especially since there is just one major player
  - Synthetic DNA could be a viable alternative, although some developers may be reluctant to switch from plasmid DNA to synthetic DNA.
  - Some companies want to be self-sufficient and make their own plasmid DNA.
  - One way to require a smaller amount of plasmid needed is to use producer cell lines, although will take time to develop.
  - Viral production at higher scale will provide cost savings in the long run.
- Besides materials, there are costly CMC activities such as:
  - GMP manufacturing in general
  - PPQ runs and the analytical testing required
  - Stability studies (expense and duration) – be smart about how you use each vial
  - Setting retains aside – a big upfront cost but necessary, especially if need to perform comparability studies down the line.

2. Can manufacturing cost drivers be designed into the process and what are the risks?

- Scaling up vs. scaling out:
    - Scaling up has less QC/QA (which are major cost drivers), so will provide cost savings in the long run. But failed batches will be very expensive.
- Platform processes:
    - Can provide enormous time savings. No tech transfer needed, no engineering runs if have a lot of experience from different programs.
    - One roundtable participant from a viral vector CDMO mentioned cost savings passed on to clients with Module 3 authoring. This CDMO provides information for clients to include in their regulatory submissions, and can also participate in sponsors' meetings with health authorities. Considerable savings compared to hiring consultants to write the same material.
    - Viral production will likely become more efficient with time, and as a result, more cost effective. Technological evolution. Monoclonal antibodies used to be much more expensive, but production from CHO cells and purification processes improved.
- Licensing/royalties:
    - Paying into IP for a CDMO's process can get very expensive.
    - Some CDMOs do not replace failed batches free-of-charge
    - Points to be aware of when evaluating CDMOs and negotiating.
- Regulatory feedback:
    - Don't be afraid to be critical and push back/negotiate with the agency, especially if FDA requesting much costlier items and you can make a case for why not.
    - Example from Grace Science's presentation this morning: FDA may potentially be flexible with the number of PPQ runs (disease/population dependent).

3. Engineer and validation runs come with a significant cost. What examples are there to 'lean' these out without compromise to cGMP, IND/BLA enabling requirements?

- Leveraging PD data without having to do three full validation runs – possible? Regulators may have flexibility, but it depends on product volume, patient population etc.
- Product shelf-life extension: may be able to obtain this if can prove to the agency that the product is still acceptable. But perhaps more feasible to do this in clinical stage than in commercial.