Delivering therapeutic mAbs for COVID-19: What can be done in just one year?

Speaker: **Dr. Brian Kelley, Senior VP, Process & Product Development, VIR Biotechnology**

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Questions and Answers from the Webcast on May 20, 2021

Question	Answer
How was cGMP DS run initiated without safety testing on the non-clonal cell pool (e.g., mycoplasma, sterility)? Was safety risk to the facility considered?	Yes, but the risk was judged very low based on lab policies and procedures that are in place to manage and mitigate potential risks . In addition, the facility used single-use bioreactors upstream.
Why do we use cGMP for a cell pool?	We used a cell pool to accelerate the production of clinical trial material.
How much stability data (DS and DP) was filed for the IND? Either from GMP or from non-GMP pilot runs?	Data from cGMP, pilot and development studies were all exhibited in the IND. The cGMP Drug Product data were very limited, but a relatively short expiry was requested; the expiry was subsequently extended based on real-time data.
Many activities can be run in parallel but that comes at a cost. Did you have any budget constrains?	The total investment was larger than a typical PhI program due to cGMP Gen1 batches, but otherwise the resourcing/staffing at Vir was normal; at our CDMO partner, there were times when there were parallel efforts requiring additional staff.
In the accelerated timeline, what was the timescale for process characterization work gating to PPQ?	PPQ runs were not gated to the completion of PC. The Drug Substance PC duration was approximately 4 months.
Was analytical product comparability between Gen 1 and Gen 2 material sufficient to not require additional / supplemental tox studies?	Yes. We selected the final clone to produce material similar to Gen1, and also tuned the production culture parameters slightly.
Thanks Brian- fantastic presentation and overview. Can you comment on pre-IND interaction(s) with FDA regarding timing before IND and FDA flexibility?	We had meetings with the FDA, EMA and MHRA. All supported the 'pool for cGMP' concept, and provided advice on how to proceed with the Gen2 process and emergency authoirization.
Thanks for demonstrating what is possible. Can you comment on where you believe the points of highest risk are and how to best mitigate?	The stability of Drug Product was a key risk for us, so we chose a relatively low product concentration to minimize the risk of aggregation.
Can the demand be fulfilled by multiple antibodies ?	A cocktail would require 2X or 3X the production capacity of a monotherapy.

What time savings did you achieve as a result of potentially modifying your viral clearance strategy or did you follow a traditional scope ?	The viral clearance strategy was the same as typical Ph I programs.
Some CMC processes are protected by trade secrets rather than patents, do you envision that to be a challenge for a manufacturing consortium?	Many upstream (e.g., fed-batch CHO) and downstream (e.g., ProA capture, 1-2 polishing steps, virus filtration, UF/DF) processes are known, standard techniques.
With this COVID speed being demonstrated, what's the expectation for future antibodies from development to BLA?	That's the million-dollar question! If your company is willing to take on the challenge, these timelines could be replicated. I would advise for a more measured pace (avoid 'Gen1 pool for clinic') unless fully warranted.
How can this accelerated production process of therapeutic mAbs be compared with vaccine production ?	That depends on many factors...
Will the cocktails of mAbs be able to provide protection against these different SARS-CoV-2 variants?	It depends on the breadth of the individual mAbs.