DNA SEQUENCE TO A MILLION DOSES OF COVID-19 THERAPEUTIC ANTIBODY IN 9 MONTHS – MAKING THE SEEMINGLY IMPOSSIBLE, POSSIBLE

Matthew Osborne, Eli Lilly Kinsale, Ltd,
Osborne_matthew_d@lilly.com
Yao-Ming Huang, Eli Lilly and Co, Indianapolis
Robert O'Keeffe, Eli Lilly Kinsale, Ltd,
Jennifer Purdie, Eli Lilly and Co, Indianapolis

Keywords: COVID-19; Manufacturing; Technology Transfer; Charge Variants;

In March 2020, COVID-19 was declared a global pandemic with the novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) responsible for the infection. Since declaration, billions of people have been, and continue to be, impacted, with over 600 million cases reported world-wide and in excess of 6 million deaths (1).

In the early phases of the pandemic, it was recognized that neutralizing antibodies could represent an important class of therapeutics that could be rapidly developed and provide benefit, especially until vaccines were widely available. Lilly began working with partners in March 2020 and rapidly identified and developed two such neutralizing antibodies: bamlanivimab (2) and etesevimab (3). It was however recognized early in these efforts that manufacturing very large quantities of antibody would present a significant challenge and Lilly set a stretch goal of producing a million doses by the end of 2020 (4) and more beyond. This required significant at-risk manufacturing investments.

The focus of this presentation is to reflect on this challenge which involved rapid scaling and simultaneous technology transfer to multiple global manufacturing sites, concurrent with process development, whilst maintaining product comparability. This involved very early engagement of manufacturing sciences with development and discovery organizations and relied on leveraging the existing monoclonal antibody production platform, but also maximizing productivity (batch yield and throughput). To this end, a new iteration of the cell culture media platform was introduced for bamlanivimab and etesevimab, and this created some technology transfer challenges manifesting in product charge profile offsets that will be discussed in the form of a case study. In addition, the presentation will discuss other aspects encountered along the journey, including raw material shortages and mass transfer/scale-up considerations during technology transfer.

The presentation will conclude with considerations of the speed vs optimization conundrums of how to best supply medicine in the midst of a fast moving pandemic.

(1) WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int/
(2) Jones et al., The neutralizing antibody, LY-CoV555, protects against SARS-CoV-2 infection in nonhuman primates. Sci. Transl. Med.13, eabf1906 (2021).
(3) Shi, R., Shan, C., Duan, X. et al. A human neutralizing antibody targets the receptor-binding site of SARS-CoV-2. Nature 584, 120–124 (2020). https://doi.org/10.1038/s41586-020-2381-y
(4) https://investor.lilly.com/news-releases/news-release-details/lillys-neutralizing-antibody-bamlanivimab-ly-cov555-receives-fda