ABO-102 CLINICAL PROGRAM
MPS IIIA has no currently approved treatments and leads to early neurocognitive decline. In children, most start a rapid cognitive decline by 3 years of age, and 70% do not reach the age of 18.

ABO-102 is a novel gene therapy for MPS IIIA which introduces a functional hSGSH coding sequence. This particular AAV vector can cross the blood–brain barrier and then release the functional gene in cells, allowing them to process lysosomal material effectively.

ABEONA THERAPEUTICS CASE STUDY: SCALING UP AAV293 SUSPENSION CELLS
Pall collaborated with Abeona Therapeutics to evaluate the Allegro™ STR bioreactor family as a scalable vector production platform. The investigation assessed the scalability of a PEI-mediated transfection process between the 50- and 500-L scale for production of a recombinant AAV (rAAV) vector. The Allegro STR 50 and 500 were run in parallel during production, and bioreactor performance was evaluated based on cell growth, metabolic profile, and viral vector production.

The cell expansion process took 21 days from vial thaw to inoculation of the Allegro STR 50 and 500 bioreactors, followed by a further 15 days from inoculation to harvest.

EXPERIMENTAL RESULTS
Consistent cell growth and viability trends were observed across scales, and both bioreactors achieved a peak cell density of approximately $1.8 \times 10^6$ cells/mL (Figure 1). The STR 50 had a slightly lower viability in the second half of the culture resulting in a lower viable cell density at the time of harvest, and also consumed more glucose compared to the STR 500. The root cause of these differences was not identified, but could be attributed to slight differences in transfection efficiency between the two vessels. Lactate trends were similar across scales throughout the course of the culture. Oxygen demand was shown to effectively scale between the STR 50 and STR 500 bioreactors by maintaining a constant power per unit volume input across vessel sizes (Figure 2).

Samples were saved for rAAV titer measurement starting on day 7 of the culture, and titer trends were similar across scales. The STR 50 and STR 500 bioreactor achieved final AAV9 titers of $4.8 \times 10^{10}$ and $4.3 \times 10^{10}$ genome copies (gc)/mL, respectively (Figure 3).

CONCLUSIONS
Scalable upstream technologies are critical to enable the manufacturing capacity needed to bring gene therapy treatments with large target populations to market. These results demonstrate a scalable rAAV production process between the Allegro STR 50 and 500 bioreactors. rAAV titer production was similar between scales, with both bioreactors achieving over $4 \times 10^{10}$ gc/mL upon harvest. Growth parameters and metabolic profiles compared well between scales.