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Continuous biomanufacturing provides many important strategic advantages for the production of protein therapeutics through process integration, simplification and intensification. To achieve upstream process intensification, Sanofi is currently developing robust cell culture processes that can achieve ultra-high cell densities and productivities ("push to high") while minimizing cell-specific perfusion rates ("push to low"). We have applied ATF perfusion technology and improved the cell culture environment to achieve high cell densities and volumetric productivities with minimal ATF filter fouling. Meanwhile, we have employed high-throughput screening strategies to increase medium depth and reduce medium requirements. We will describe results as well as ongoing efforts to further intensify this continuous cell culture platform and realize even more of its significant upward potential.

Continuous biomanufacturing also has the potential to deliver robust, steady-state product quality, resulting in enormous operational flexibility. Instead of traditionally defining batches by unit operation, product can be batched in time (first-in, first-out), removing downstream processing constraints and minimizing production cycle times. In this presentation, we use both theoretical models and experimental data to evaluate the effects of perfusion on product quality, considering the impact of perfusion-specific controllable parameters (e.g., perfusion rate, bleed rate, target viable cell density) on product quality. We also compare and contrast product quality attributes between perfusion and fed-batch processes and examine the feasibility of maintaining a process and product quality at steady state while presenting relevant, real-world case studies.