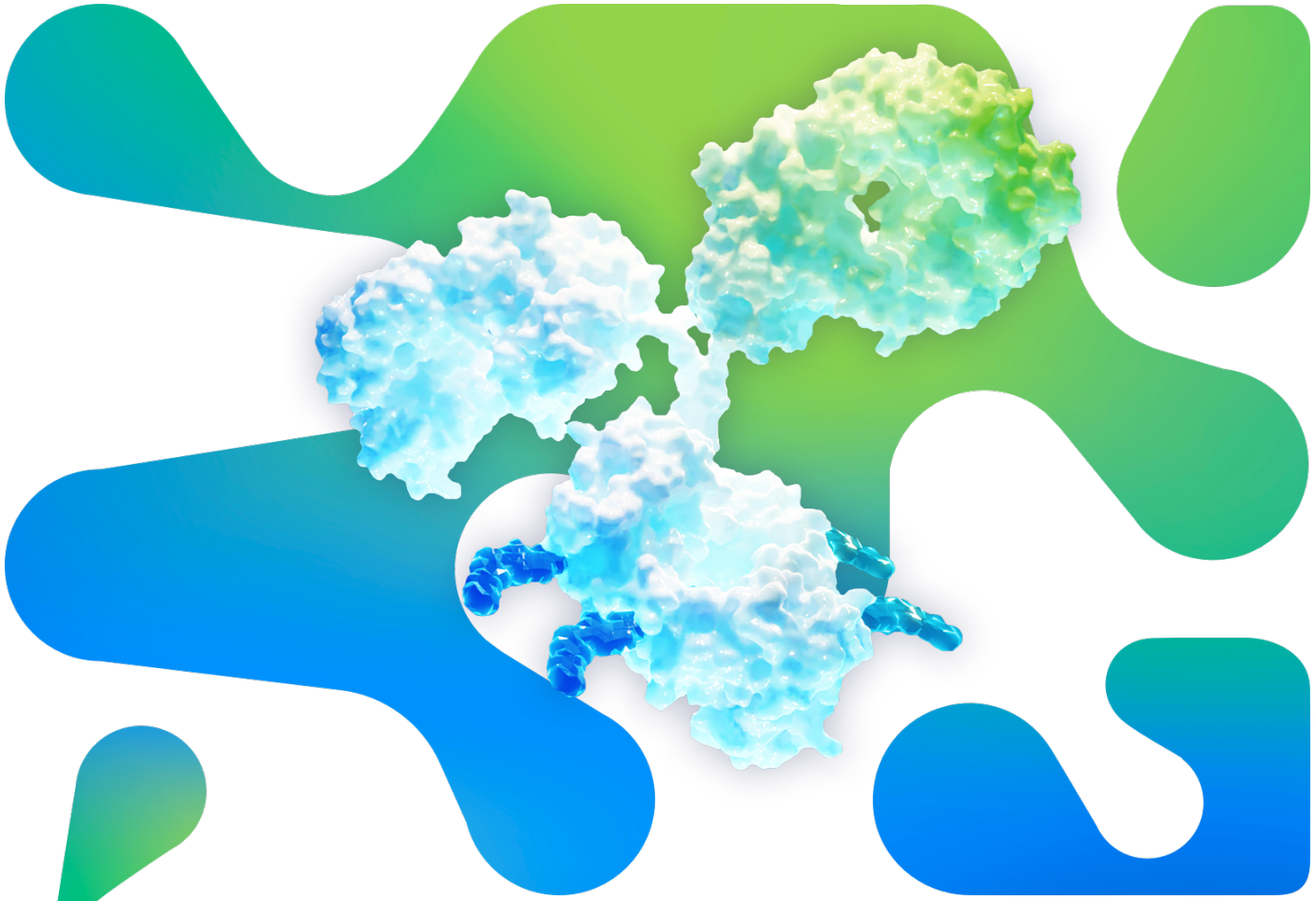
gbi BIOMANUFACTURING

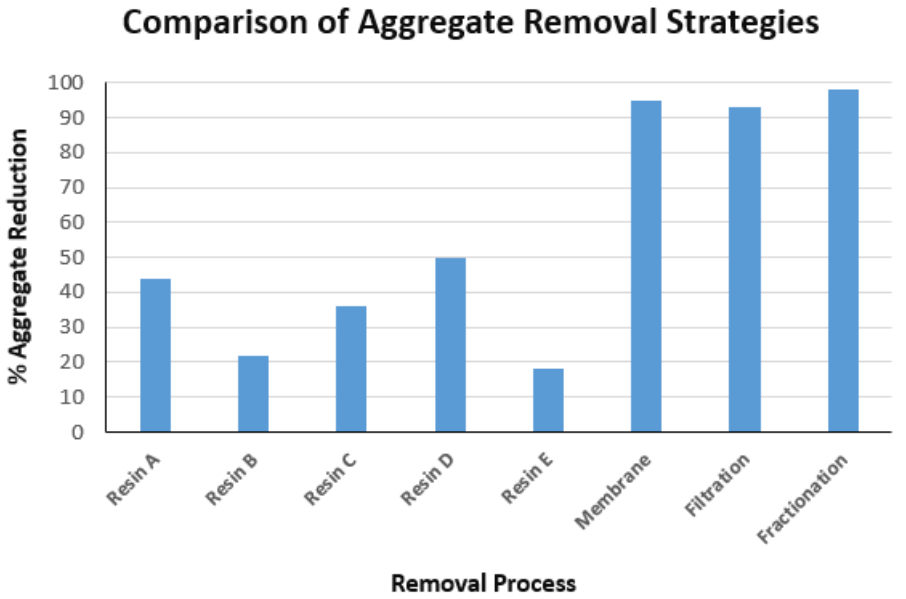
GOODWIN CASE:

Aggregate Removal Development and GMP Manufacturing for a Conjugated Theranostic Product



Aggregate Removal Development

- Product is a complex biologics molecule used for diagnostic imaging in oncology. It is in late-stage clinical trials.
- Process requires several operations:
  - pH adjustments
  - Heating
  - Time-sensitive operations
  - Transition metal removal
- Upon scale-up, with these operations lead to the formation of high molecular weight (HMW) aggregates exceeded levels outside product specification
- Several strategies were investigated to selectively remove undesired HMW aggregates:
  - Chromatographic resins
  - Filter materials
  - Chromatographic membranes
  - Salt fractionation
- Filtration provides excellent aggregate removal while adding minimal change and scalability to the current process compared to other methods
- A selective filtration process was developed upon scale-up to produce desired product in high monomeric purity



Aggregate Filtration Upon Scale Up

Scale	% HMW Aggregates	% Monomer	% HMW Aggregates	% Monomer
	Before Filtration		After Filtration	
Small	1.7	97.2	N/A	N/A
Intermediate	13.2	86.3	3.0	96.9
Large	14.6	84.7	2.0	97.9

Product Specification: *HMW Aggregates ≤ 5.0%* *Monomeric purity ≥ 90%*

Conclusion

- A robust and selective filtration process to remove HMW aggregates was developed to generate a complex biologic product in high monomeric and radiochemical purity
- Filtration was implemented in current manufacturing process, requiring minimal process change and can be scaled for larger cGMP manufacturing campaigns
- Several successfully cGMP batches have been carried out to supply materials for late-stage clinical trials.

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