

## CMC STRATEGY FOR AAV GENE THERAPIES IN THE AGE OF RMAT DESIGNATION

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The Regenerative Medicine and Advanced Therapy (RMAT) designation by the FDA allows for faster, and more streamlined approvals of cell and gene therapies for unmet medicinal needs. Advantages of RMAT designation include all of the benefits of the fast-track and breakthrough designation programs, including early interactions with the FDA. Voyager's VY-AADC program, an Adeno Associated Virus (AAV) gene therapy approach for advanced Parkinson's Disease (PD), was one of the therapies granted RMAT designation in 2018.

Owing to the durable nature of gene therapy, clinical development may entail just two trials before approval, a Phase 1 Safety/Dose escalation in patients, followed by a Phase 2/3 Efficacy trial. While this strategy is expected to greatly accelerate the path to licensure, it also requires a much earlier (and in some cases, heavier) investment on CMC Development and Manufacturing as compared to regular biopharmaceutical development. Also, an RMAT designation by the FDA does not reduce quality and CMC expectations for a BLA submission, further underscoring the need for robust CMC strategies.

This presentation discusses Voyager's overall development strategy for AAV-gene therapy, focusing on a two-stage CMC approach: one encompassing development activities leading to drug product manufacture for Phase 1/IND filing studies, and the other directed to late-stage/commercial manufacture for approval/launch-enabling pivotal studies. Ways to balance early CMC investment and optimize resources, while still enabling an aggressive fast-to-licensure timeline to bring urgent therapies to patients, are also covered.