

# Parkinson's Gene Therapy Now in Phase 2 Trial, VY-AADC, Continues to Show Motor Benefits, Voyager Says

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[Voyager Therapeutics](#) announced likely plans to request approval of [VY-AADC](#) as a Parkinson's gene therapy, based on feedback it received from the U.S. Food and Drug Administration (FDA) and eventual outcomes of a newly opened Phase 2 trial.

The company also reported that its Phase 1 trial of VY-AADC showed improvements in patients' motor function and reduced



use of medications, among other benefits, further supporting a future [biologics license application](#) (BLA).

Progressive loss of dopamine-producing neurons in the substantia nigra – a brain area controlling movement – is a hallmark of Parkinson's. Normally, the neurotransmitter dopamine is released into a brain region called the putamen, which contains dopamine receptors.

But in Parkinson's, this process is impaired. And while levodopa – a precursor of dopamine – is effective in treating Parkinson's, patients require the enzyme AADC to make this conversion. This enzyme, however, is markedly reduced in the putamen.

Voyager's VY-AADC, which consists of a modified and harmless [adeno-associated virus](#), is designed to deliver the *DDC* gene – which contains the instructions for making AADC – directly into the putamen.

As a result of a requested [type C meeting](#), the FDA indicated that successful completion of the ongoing Phase 2 trial ([NCT03562494](#)) may be sufficient to accept the BLA's submission for review.

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This single-site study is assessing the distribution, efficacy, and safety of VY-AADC02 in Parkinson's patients with [motor fluctuations](#). Its primary goal is to analyze whether one-time administration of the gene therapy candidate reduces patient-rated motor fluctuations compared to placebo one year after surgical infusion into the brain.

Patient enrollment – an estimated 42 participants – is currently ongoing at the [University of Pittsburgh Medical Center](#). For information on contacts, click [here](#).

The FDA, in a written response, also said that if Phase 2 trial results failed to show significant benefit in easing motor fluctuations but still supported the use of VY-AADC02, Voyager may use results from a Phase 3 study in approximately 120 patients, depending on its efficacy and safety data. The Phase 2 trial, which opened in June, is expected to conclude in December 2020.

Voyager also [announced in a press release](#) early findings from a Phase 1 trial evaluating a one-time infusion of VY-AADC into the back of the head. Besides a positive tolerability profile, results showed increased coverage of the putamen in all eight patients, reduced surgical times by two to three hours, and improvements in patients' motor function at six months.

Investigators also reported that VY-AADC increased the activity of AADC in the putamen, suggestive of an increased capacity to convert levodopa to dopamine.

Motor improvements were observed in the four patients who completed assessments at six months, and matched those seen at the same time point in Voyager's Phase 1b trial ([NCT03065192](#)). This study enrolled 15 patients and assessed VY-AADC infusion through the top of the head.

Participants in both studies were, on average, 57 years old and diagnosed with Parkinson's for an average of nine years. Both trials showed marked reductions in daily use of oral levodopa and other Parkinson's medications upon [treatment](#) with VY-AADC. Voyager plans to present full data from the Phase 1 trial at future conferences.

Given these findings, the company determined that infusions through the back of the head will continue to be preferred and that, moving forward, the VY-AADC dose will be between the two higher doses in the Phase 1b trial,  $1.5 \times 10^{12}$  and  $4.7 \times 10^{12}$ .

"We are very pleased with feedback from the FDA regarding our pivotal program for VY-AADC that includes the potential to file a BLA based on the safety and efficacy results from the Phase 2 trial, or if needed, from the Phase 3 trial," Robert Pietrusko, senior vice president of regulatory affairs and quality assurance at Voyager, said in the release. "We look forward to continuing to work closely with the agency to expedite the development of this potentially important treatment for patients with Parkinson's," he added.

Based on results from the Phase 1b trial, the FDA recently designated VY-AADC a [regenerative medicine advanced therapy](#) as a potential treatment of therapy-resistant motor fluctuations in Parkinson's patients.

TAGGED FDA, MOTOR FUNCTION, PARKINSON'S, PHASE 1 TRIAL, PUTAMEN, VOYAGER THERAPEUTICS, VY-AADC.



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