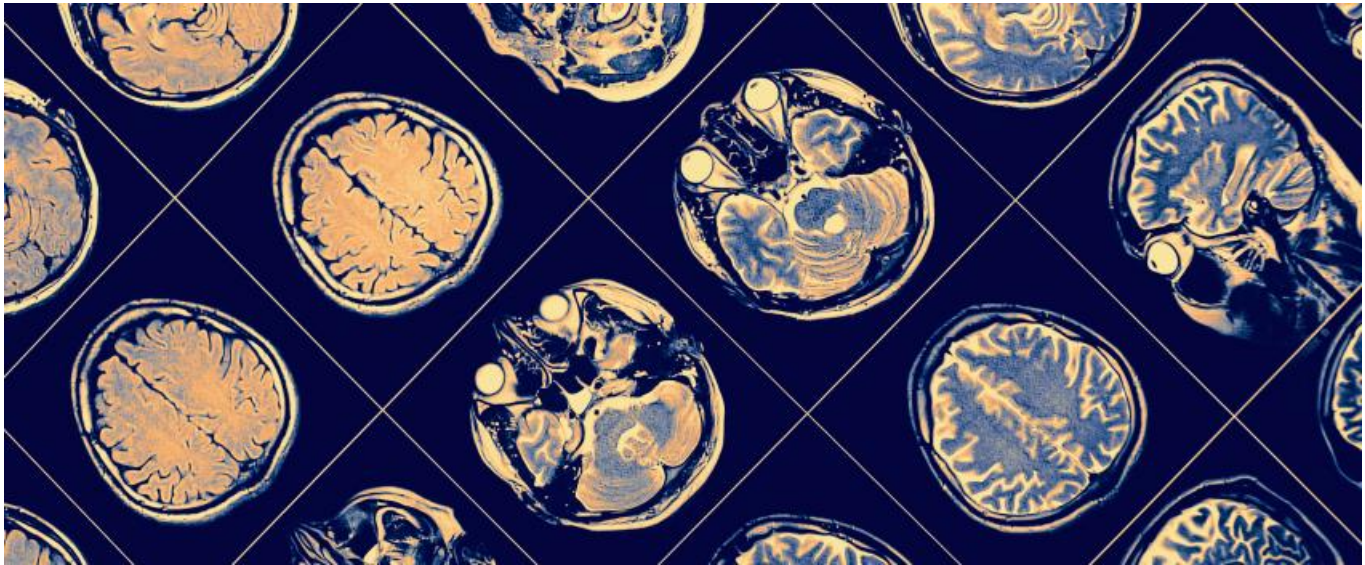


A busy year ahead for Parkinson's disease



[Joanne Fagg](#)



As several big pharma companies drop Parkinson's projects, attention turns to gene therapies and repurposing diabetes drugs.

Parkinson's disease research has ended in numerous dead ends despite substantial efforts over many years. Recently, Biogen and Sanofi scrapped their Parkinson's candidates, cipanemab and venglustat respectively, owing to lack of efficacy, and a disease-modifying therapy has yet to materialise.

But the push to find drugs that help beyond reducing symptoms continues, and *Evaluate Vantage* has delved into the pipeline of projects in active late-stage clinical trials. This year is shaping up to be crucial for the field, with 10 studies expected to yield data or to complete in 2021.

One target that crops up multiple times is GLP-1; this approach, traditionally employed in type 2 diabetes, [is also being tested in Alzheimer's](#). Among other avenues of research, it is hoped that gene therapy could offer a one-time cure for Parkinson's.

Repurposing

[Research has suggested that GLP-1 agonists](#) have neuroprotective benefits, and several trials of marketed diabetes drugs, as well as new GLP-1-targeting projects, are under way in Parkinson's. Some of these studies are investigator sponsored, including the most advanced, a UCL-run phase III trial of AstraZeneca's Bydureon called Exenatide-PD3.

This study aims to build on an [earlier trial](#) by the same research group that showed that, at 60 weeks, off-medication scores on the rating scale MDS-UPDRS had improved by [1.0 points in the exenatide group and worsened by 2.1 points](#) in the placebo cohort. Results are some way off, with the clinicaltrials.gov primary completion date of Exenatide-PD3 in 2023.

In the meantime, data are expected from several phase II studies of GLP-1 agonists, including a trial of Novo Nordisk's Victoza, being run by Cedars-Sinai Medical in collaboration with the Danish company and The Cure Parkinson's Trust. That study is set to complete in September.

September will also see the completion of a mid-stage trial of Pepton's sustained-release exenatide formulation PT320.

Neuraly is also evaluating a new formulation of exenatide, this time a pegylated version; pegylation is said to increase permeability through the blood-brain barrier. That project is further behind Pepton's, with its phase II trial set to complete next year.

Gene therapies

While gene therapies could offer a longer-term solution, this approach has suffered its fair share of setbacks recently, and Parkinson's disease has been no exception: [Voyager's VY-AADC was put on clinical hold in December](#) after abnormalities were seen on patients' MRI scans. Voyager's partner Neurocrine subsequently dropped the project.

Other groups hoping for a better outcome include Sio Gene Therapies with AXO-Lenti-PD, a lentiviral vector project designed to restore levels of dopamine via the delivery of three genes needed for dopamine synthesis. The hope is that this will stabilise disease and reduce L-dopa medication; still, the asset is an updated version of Oxford Biomedica's Prosavin, which [generated weak efficacy](#) and was ultimately abandoned.

In the first two cohorts of the [phase II Sunrise-PD study](#), AXO-Lenti-PD led to [promising](#) improvements in the UPDRS Part III "off" score, albeit in a very small number of patients.

The project has been hit by manufacturing delays, however, and the processes to provide clinical trial material for larger studies have yet to be finalised.

Big pharma groups are also getting involved in gene therapy, most recently Lilly, which [bought Prevail last December for \\$880m up front](#), gaining the Parkinson's candidate PR001. The AAV-based project aims to transfer the *GBA1* gene that encodes the enzyme beta-glucocerebrosidase, which is required for the disposal and recycling of glycolipids. It is estimated that as many as 7-10% percent of Parkinson's patients worldwide carry at least one *GBA1* mutation.

The phase I/II Propel trial of PR001 is ongoing, and before Prevail's acquisition the company said it would provide biomarker and safety analysis on a subset of patients by mid-2021.

Other early-stage deals, such as [Abbvie's move to corner the preclinical researcher Mitokinin yesterday](#), show that big companies are also interested in exploring other novel technologies.

With a respectable roll call of late-stage trials gearing up to read out, the coming years will hopefully yield bigger steps forward in this disease.

Selected active disease-modifying projects in Parkinson's disease (Ph2 and 3)

Project	Description	Company	Trial, primary completion
Bydureon (exenatide)	GLP-1 receptor agonist	Astrazeneca	Ph3 Exenatide-PD3 , Jun 2023, sponsored by UCL
PRX002 (prasinezumab)	Anti- α -synuclein MAb	Roche/Prothena	Ph2b due to start Q2 2021 (ph2 Pasadena failed)
AAV-GAD	AAV GAD gene therapy	Meiragtx	Completed ph1 and ph2 , IND expected H1 to start new trial
ANVS401 (phenserine)	Amyloid precursor protein, alpha-synuclein & tau inhibitor	Annovis Bio/Horizon Therapeutics	Ph2 , initial data due early 2021, dose-response data due late summer
AKST4290 (lazucirnon)	C-C chemokine receptor type 3 antagonist	Alkahest	Ph2 Teal , Mar 2021
CNM-Au8	Gold nanoparticles	Clene Nanomedicine	Ph2 Repair-PD , Apr 2021
SAGE-718	NMDA modulator	Sage Therapeutics	Ph2 open-label Paradigm , Jun 2021, topline early 2021
NYX-458	NMDA modulator	Aptinyx	Ph2 , Jun 2021
SR-Exenatide (PT320)	GLP-1 receptor agonist	Peptron	Ph2 , Sep 2021
Liraglutide (Victoza/Saxenda)	GLP-1 receptor agonist	Novo Nordisk	Ph2 , Sep 2021, sponsored by Cedars-Sinai Medical Center
Adlyxin (lixisenatide)	GLP-1 receptor agonist	Sanofi	Ph2 Lixipark , Sept 2021, sponsored by University Hospital, Toulouse
ANAVEX 2-73 (blarcamesine)	Muscarinic & sigma-1 receptor agonist	Anavex Life Sciences	Improvements in cognitive tests in ph2 , OLE ongoing,

Selected active disease-modifying projects in Parkinson's disease (Ph2 and 3)			Oct 2021
AXO-Lenti-PD	Dopamine gene therapy	Sio Gene Therapies/Oxford Biomedica	Promising results from first two cohorts in ph2 Sunrise-PD ; ph2 Explore-PD to start 2021
NLY01 (pegylated exenatide)	GLP-1 receptor agonist	D&D Pharmatech/Neuraly	Ph2 , Jul 2022
CDNF Parkinson's Project	Cerebral dopaminergic neurotrophic factor	Herantis Pharma	Ph1/2 showed serious adverse events related to the surgery and drug administration process; ph1/2 long-term safety study, Sep 2022
Bydureon (exenatide)	GLP-1 receptor agonist	Astrazeneca	Ph2 , Oct 2022, sponsored by Center for Neurology Stockholm and Karolinska Institutet
SUN-K706 (K0706, SCC-138, vobobatinib)	BCR-ABL tyrosine kinase inhibitor	Sun Pharma Advanced Research	Ph2 Proseek , Mar 2023
UCB0599	Alpha-synuclein aggregation inhibitor	UCB	Ph2 , Oct 2023
PR001	AAV GBA1 gene therapy	Lilly/Prevail Therapeutics	Ph2 Propel , biomarker data mid 2021, completes Jun 2027

Sources: EvaluatePharma, clinicaltrials.gov & company releases.

[More from Evaluate Vantage](#)

Evaluate HQ
[44-\(0\)20-7377-0800](tel:44-020-7377-0800)

Evaluate Americas
[+1-617-573-9450](tel:+1-617-573-9450)

Evaluate APAC
[+81-\(0\)80-1164-4754](tel:+81-080-1164-4754)

© Copyright 2023 Evaluate Ltd.