OPEN LABEL EXTENSION OF A PHASE 1B CLINICAL STUDY TO EVALUATE THE EFFECT OF REXACERACT (GT-02287) IN PARKINSON'S DISEASE

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Objective

Open-label study to evaluate the long-term safety, tolerability, and exploratory clinical outcomes of the oral, brain-penetrant glucocerebrosidase (GCase) modulator rexaceract (GT-02287) in people with Parkinson's disease (PD).

Background

- Pathogenic variants in *GBA1*, a gene encoding for the lysosomal enzyme GCase, constitute the most common genetic risk factor for PD and are associated with more rapid motor and nonmotor progression.
- *GBA1* variants (GBA-PD) impact endolysosomal trafficking of GCase, which leads to endoplasmic reticulum (ER) stress, lysosomal and mitochondrial dysfunction, reduced GCase activity, alpha-synuclein aggregation, and neuroinflammation[1].
- Beyond GBA-PD, GCase deficits have also been observed in patients with idiopathic PD (iPD) and may be related to the accumulation of aggregated α-synuclein.
- Preclinical evidence has demonstrated that rexaceract corrects molecular pathway abnormalities contributing to the pathogenesis and progression of PD, indicating its potential to slow disease progression.
- This Phase 1b open-label study in people with PD followed a Phase 1a study in healthy volunteers[2]. This study consists of two parts: Part 1 with daily dosing for 90 days and Part 2, a 9-month optional treatment extension after completion of Part 1. The treatment phase of Part 2 has recently been completed.

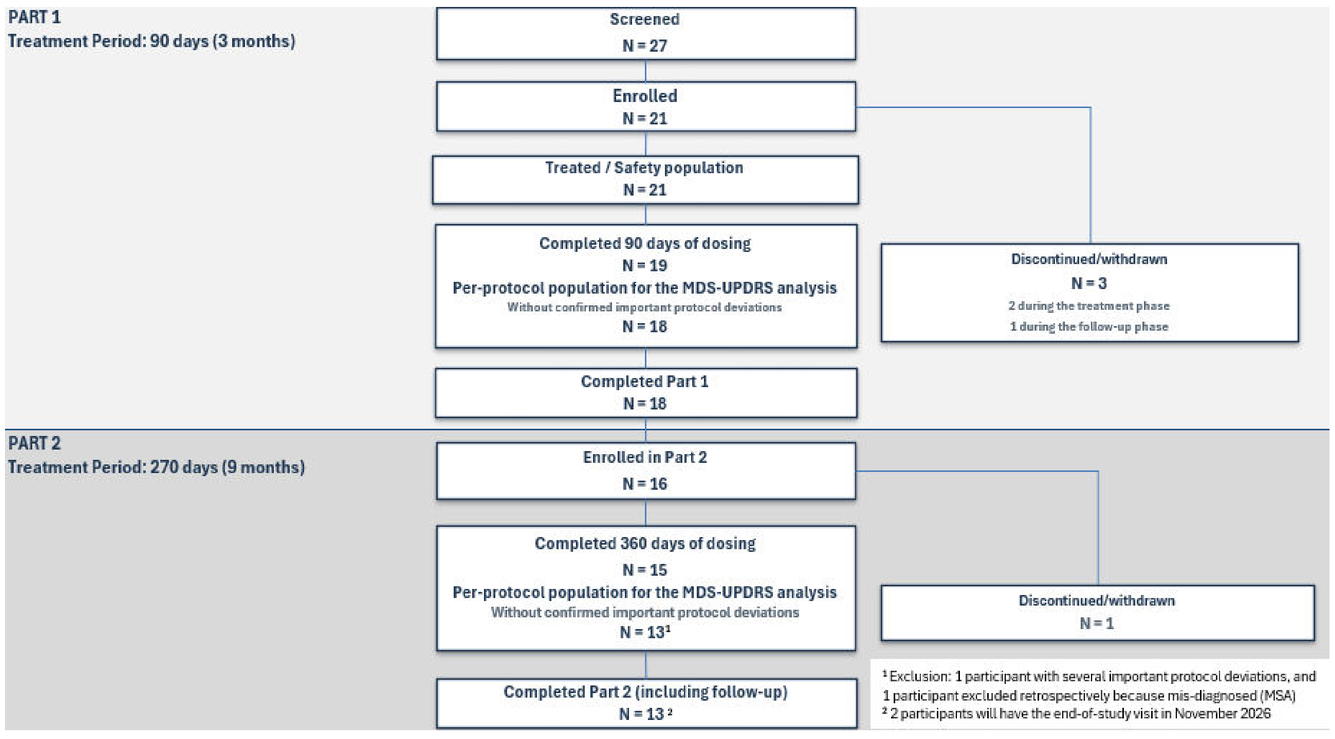
Methods

- Individuals aged 30-85 years who had been diagnosed with PD within the last 7 years and who were either treatment-naïve or on a stable dose of dopaminergic therapy were eligible.
- All participants received oral rexaceract 13.5 mg/kg/day and could reduce the dose to 11 mg/kg/day for inadequate tolerability.
- Treatment–emergent adverse events (TEAEs), vital signs, laboratory tests, physical examinations, body weight, 12-lead ECGs, and Columbia-Suicide Severity Rating Scale were used to evaluate safety and tolerability.
- Secondary and exploratory endpoints included pharmacokinetics, clinical scales (MDS-UPDRS, etc.), and plasma/ dried blood spots/ cerebrospinal fluid (CSF) biomarkers.

Overall Enrollment and Demographics

- 21 participants were recruited at 7 sites in Australia: 16 participants from 6 sites continued into Part 2, and 15 completed 360 days of dosing.
- Main baseline characteristics were: mean age 63.5 years; mean disease duration 3 years; 1 treatment-naïve participant, 19 on levodopa +/- other PD drugs, 2 on deep brain stimulation, 3 *GBA1* carriers (2 with severe and 1 with mild variants), 1 with a *PRKN* variant, 5 with other variants of unknown significance.

CONSORT DIAGRAM

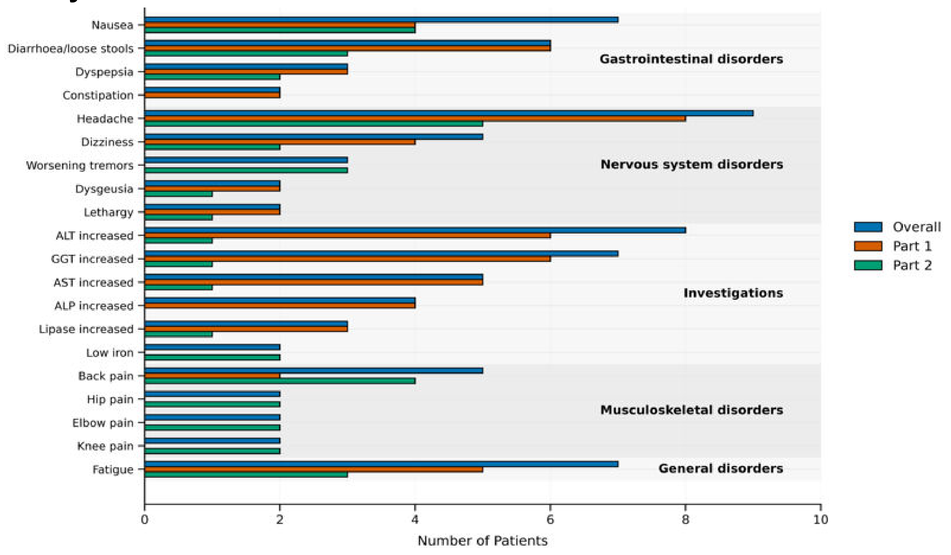


Results

Favorable long-term safety and tolerability

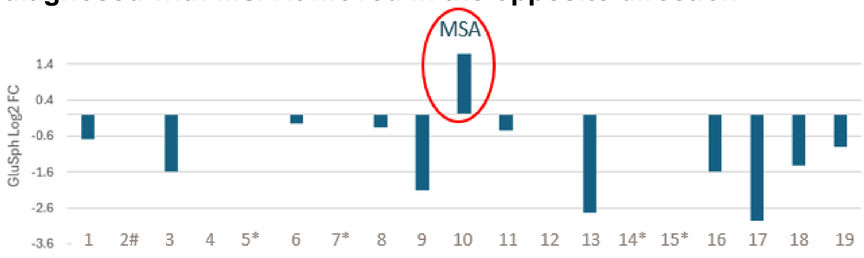
- No new safety concerns were identified during Part 2 Data Monitoring Committee reviews.
- The overall incidence of TEAEs was lower in Part 2 than in Part 1; the majority of events were mild (83%).
- Most frequent TEAEs: headache was the most common event. In 4 of 9 participants, headaches were assessed as related to rexaceract, while most unrelated headaches were secondary to lumbar puncture.
- No new clinically relevant liver enzyme elevations were observed with continued dosing for up to 1 year.

Most Frequently Reported (in >2 participants) TEAEs by System Organ Class and Study Part



CSF glucosylsphingosine (GluSph) is reduced in most participants with PD after 90 days of dosing

Individual CSF GluSph log2 fold changes from baseline after 90 days of dosing showed a reduction or no change in participants with PD, while in the patient later diagnosed with MSA it moved in the opposite direction

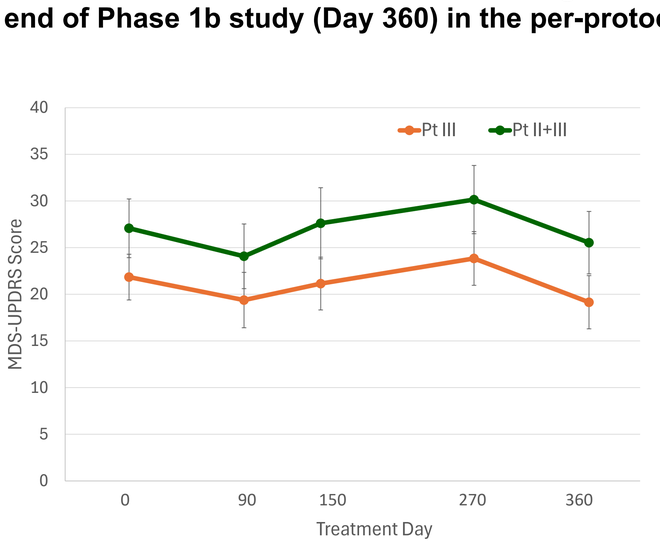


N=12; 6 participants with D90 CSF samples not available or not analysed: # CSF hemolytic at D90; * No or insufficient CSF sample

MSA: Multiple System Atrophy

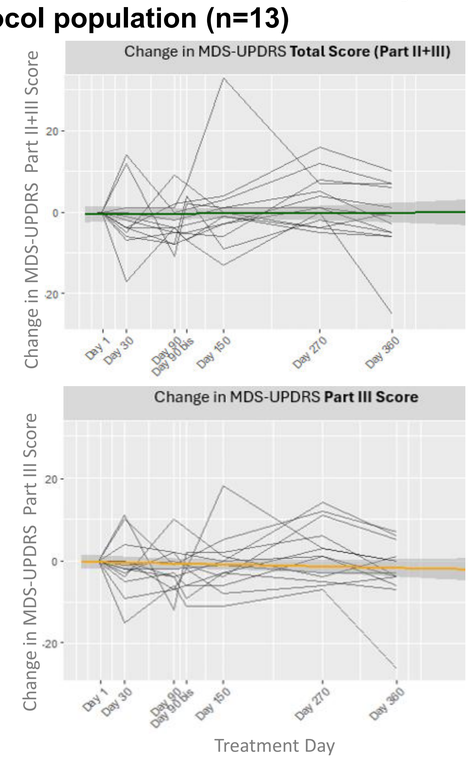
MDS-UPDRS motor scores are stable over 360 days of dosing

Mean MDS-UPDRS motor score and change in the MDS-UPDRS motor score by end of Phase 1b study (Day 360) in the per-protocol population (n=13)



Data are mean ± s.e.m.

Source: MDS-UPDRS Part II and Part III data listing dated 23-Oct-2026 (data are not cleaned and final)



Conclusions

The extension part of this Phase 1b study evaluating the safety, tolerability, exploratory clinical outcomes, and biomarkers of rexaceract showed that:

- Daily oral administration of rexacerat at 13.5 mg/kg (weight-corrected dose range: 10.4-15.1 mg/kg) for 12 months was well tolerated
- Overall, stabilization of MDS-UPDRS motor scores was maintained over 12 months
- Following 90 days of dosing, CSF GluSph was stable or reduced in PD participants. Long-term biomarker and pharmacokinetic analyses are ongoing.

The safety and clinical results support the continued development and evaluation of rexaceract for the treatment of people with PD in a randomized, placebo-controlled double-blind Phase 2a study.

Acknowledgements

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[1] Fregno I. et al. Int J Mol Sci 2025; 26(9):4392. [2] Pozzi R. et al. Mov Disord 2026;41(2):522-527.