

Long-Term Open-Label Data on the GCase Modulator GT-02287 (Rexaceract) in People with Parkinson's Disease

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Objective

- 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

Background

- Pathogenic variants in GBA1, which encodes for the lysosomal enzyme glucocerebrosidase (GCase), constitute the most common genetic risk factor for Parkinson's disease (PD) and are associated with more rapid motor and nonmotor progression
- GBA1 variants impact folding and trafficking of GCase, which leads to endoplasmic reticulum (ER) stress, lysosomal and mitochondrial dysfunction, reduced GCase activity, alpha-synuclein aggregation, and neuroinflammation
- Preclinical evidence has demonstrated that rexaceract corrects molecular pathway abnormalities that contribute to the pathogenesis and progression of PD, indicating that it has the potential to slow disease progression
- After a Phase 1 study in healthy volunteers, an open-label Phase 1b study in people with PD was initiated. The Phase 1b study consists of two parts: Part 1 with dosing for 90 days (data presented previously), and Part 2, a 9-month optional extension available to participants who completed Part 1 (preliminary data presented here)

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 and cerebrospinal fluid (CSF) biomarkers (sphingolipids, neurofilament, inflammatory markers, LAMP-2, and α-synuclein)
- Participants were recruited at 7 sites in Australia and participants from 6 sites continued into Part 2
- A protocol amendment was approved in 2025 to extend the study for an additional 9 months (Part 2) after completing Part 1 (the first 90 days) to further evaluate safety, tolerability, clinical scales and biomarkers

Results

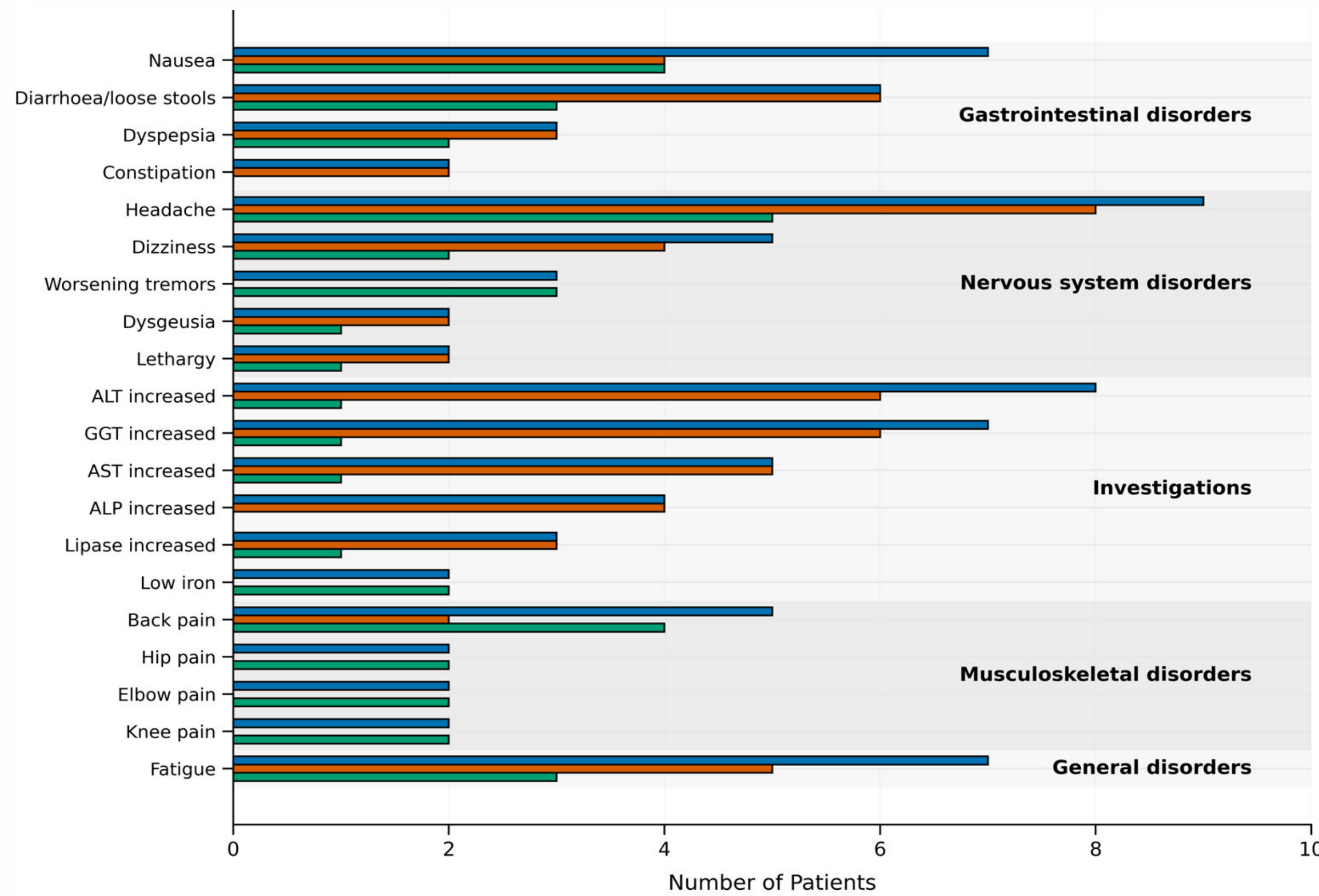
- 21 participants enrolled in the study
- Dosing in Part 1 was complete in November of 2025
- Of the 19 participants who completed dosing in Part 1, 16 chose to continue dosing in Part 2
- In Part 2, as of September 2026, 13 participants have completed 360 days of dosing (3 months in Part 1 and 9 months in Part 2). One was excluded from analysis due to a major protocol deviation, leaving a total of 12 evaluable participants at this timepoint
- No new safety signals in Part 2 are apparent at this time, and the transient elevations in liver enzymes that occurred in some participants in Part 1 did not recur in Part 2. Overall, most TEAEs were mild. 3 participants discontinued -1 due to poor tolerability (mild nausea, headache and panic; in Part 1) and 2 due to treatment-emergent SAEs, unlikely related to rexaceract (cerebrovascular accident; in Part 1 and muscle strain with mild posterior broad-based disc herniation; in Part 2, both requiring hospitalization)
- MDS-UPDRS motor scores in evaluable participants who completed Part 2 were stable over 360 days of dosing
- Whilst there was a marked difference in MDS-UPDRS motor scores at Day 90 between participants with high and low baseline CSF GluSph (reported previously), MDS-UPDRS motor scores were stable at Day 360 regardless of the baseline CSF GluSph levels

Conclusions

- Preliminary long-term data from the ongoing Phase 1b study in people with PD suggest that the novel GCase-targeting small molecule rexaceract is safe and generally well tolerated over 360 days of dosing
- The newly collected 9 month Part 2 data (up to Day 360) show no new safety signals
- Preliminary Day 360 results from 12 (of 16) patients participating to Part 2 show no meaningful progression of motor symptoms
- Participants with both high and low CSF GluSph at baseline show stabilization of MDS-UPDRS motor scores by Day 360
- These preliminary results support continued development of rexaceract as a potential disease-slowng treatment for PD
- A Phase 2 study in people with PD is planned

No New Safety Signals Apparent In Part 2 of the Phase 1b study of Rexaceract

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



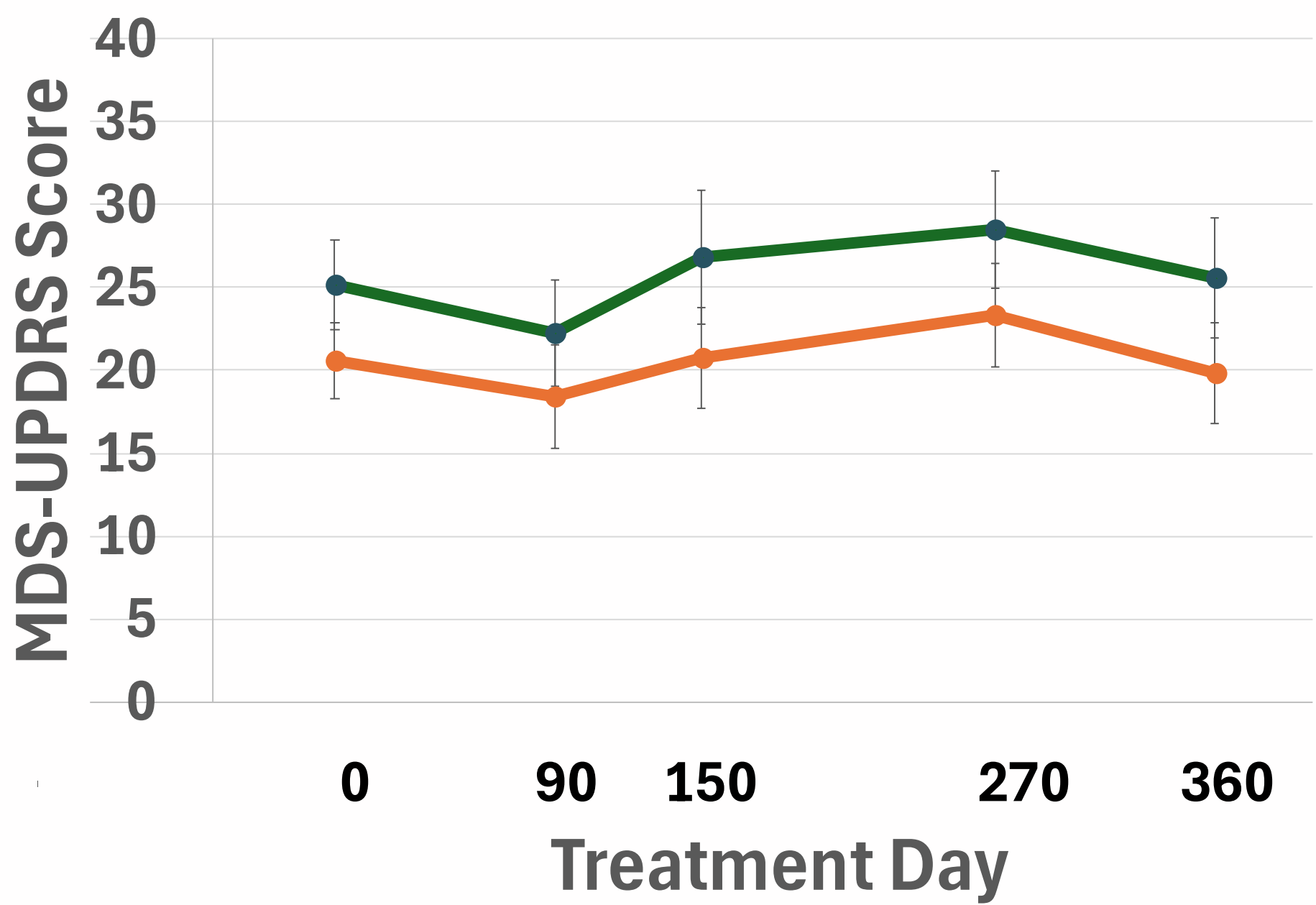
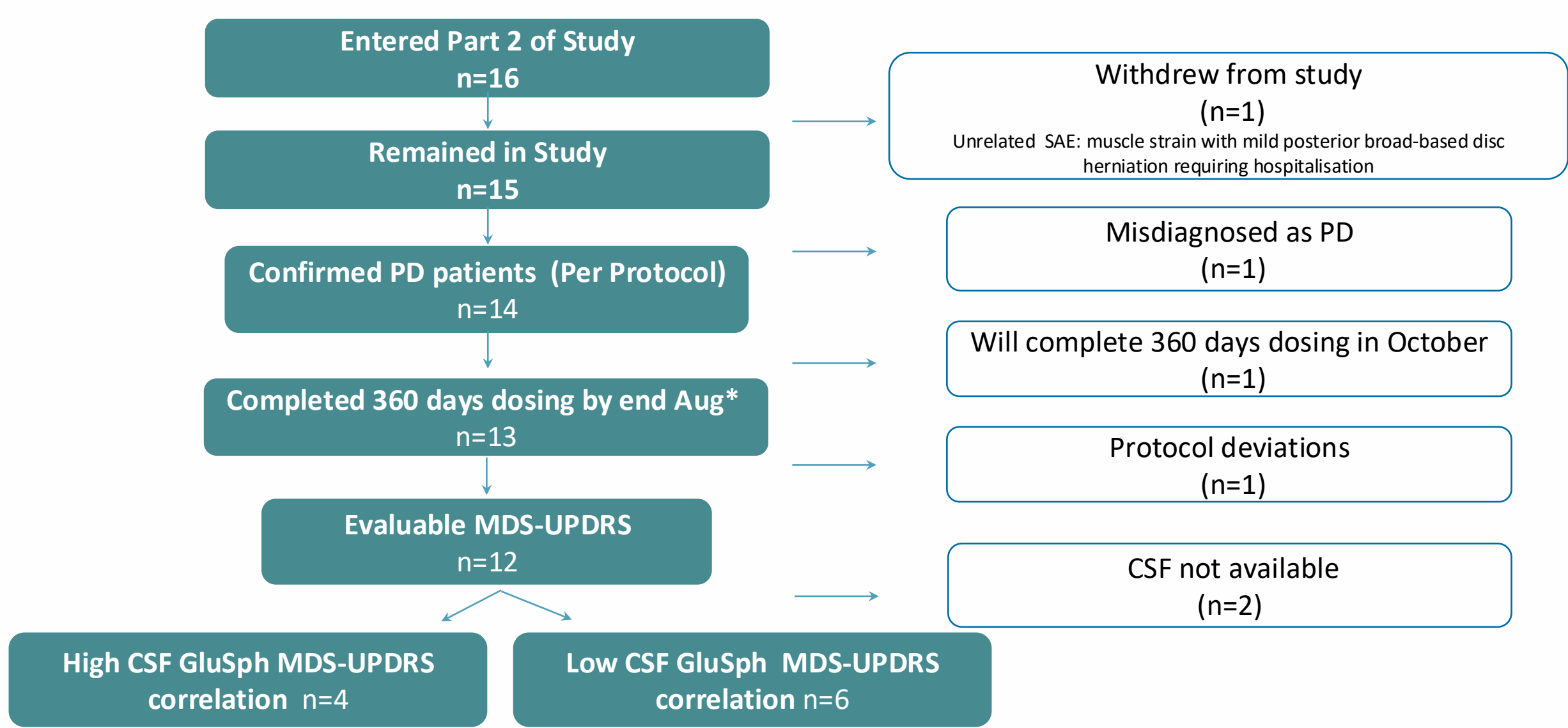
Notes:

- Overall, a lower incidence of TEAEs occurred in Part 2 compared with Part 1
- Headache was assessed as a TEAE related to rexaceract in 4 of 9 participants
- Only 1 musculoskeletal event was assessed as possibly related to rexaceract

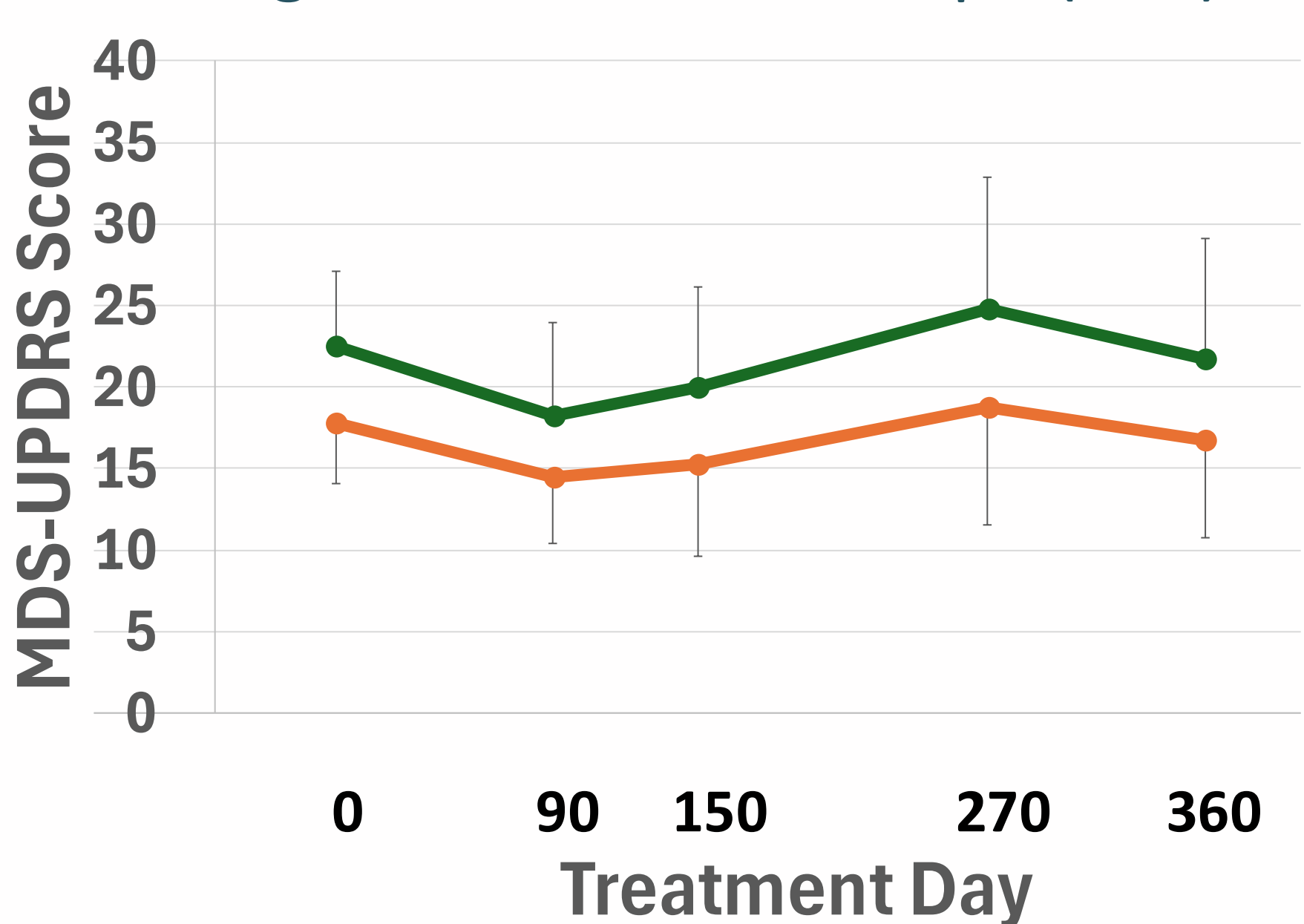
Source: AEs listing dated 4-Sep-2026 (data are not cleaned and final)

MDS-UPDRS Motor Scores are Stable over 360 Days of Dosing with Rexaceract

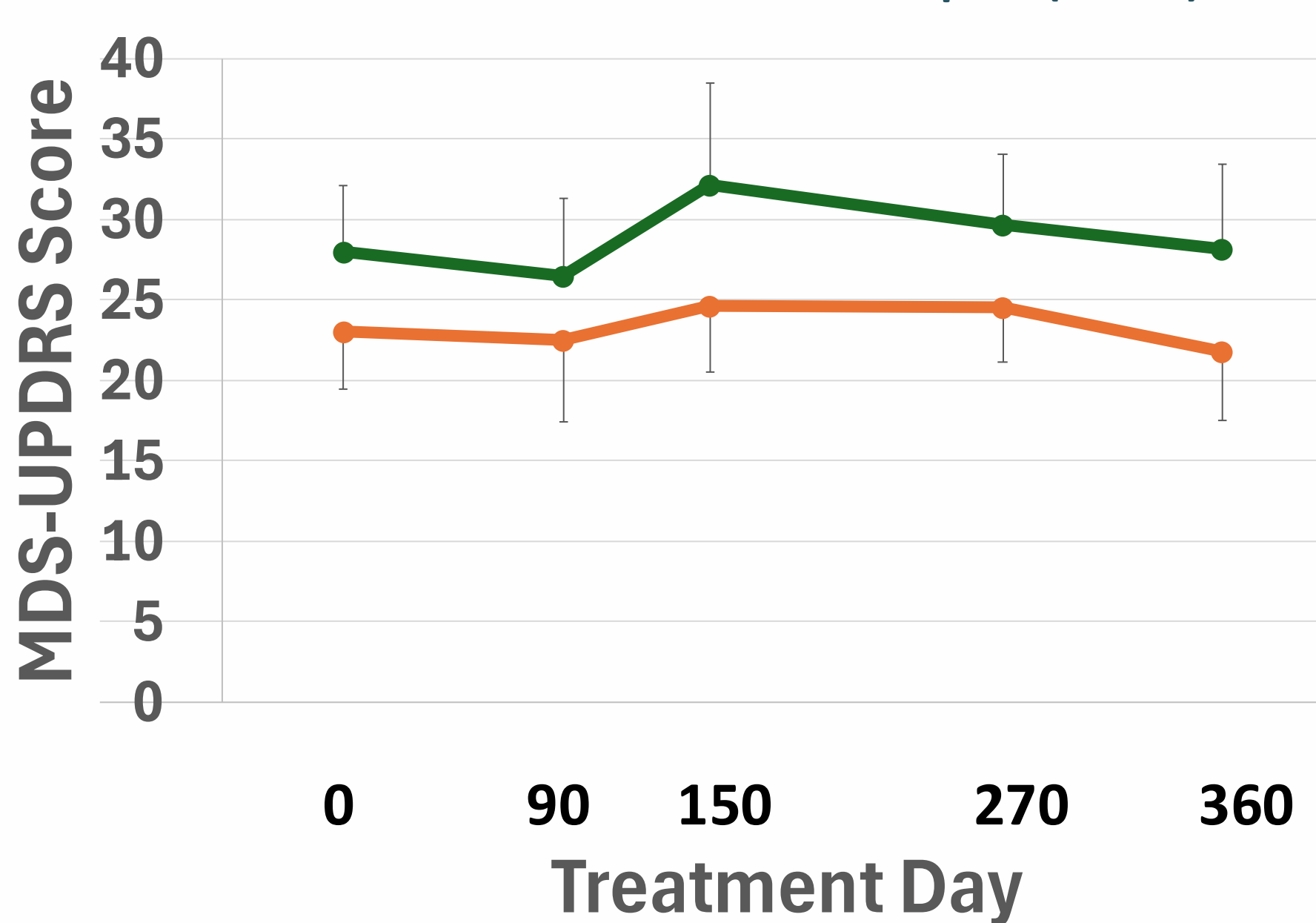
All Evaluable Patients (n=12)



'High' Baseline CSF GluSph (n=4)



'Low' Baseline CSF GluSph (n=6)



Pt III Pt II+III
Data are mean + S.E.M.