CDNF in the First-in-Human Clinical Trial

12 months clinical data on the monthly infusions of CDNF directly into a targeted area of the brain of people living with Parkinson's

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And

Professor Per Svenningsson, Principal Investigator, Karolinska University Hospital

TreatER Webcast

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CDNF in the First-in-Human clinical trial
12 Months Secondary Endpoint – Efficacy

Professor Per Svenningsson, Principal Investigator

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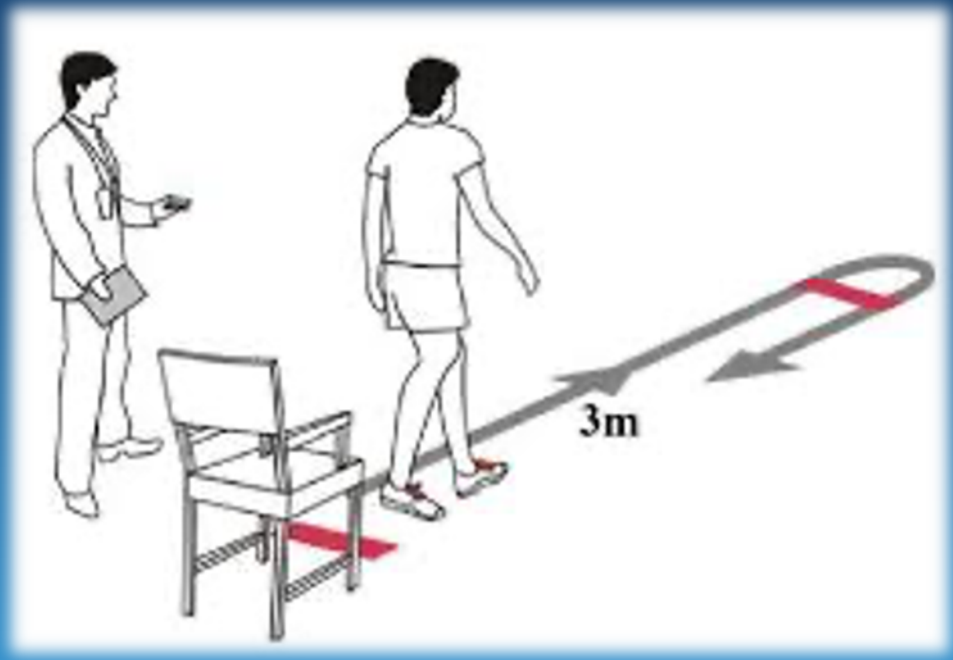
Efficacy Assessment During the Clinical Trial

Efficacy Was **Assessed At Screening**, **Prior To Treatment Start** And **During The Treatment Period**:

- **Patient home diary**: every half hour for three days before every infusion visit
  - ”ON” without dyskinesias, “ON” with non-troublesome dyskinesias, “ON” with troublesome dyskinesias, “OFF”, Asleep

Every 3 Months:

- **Unified Parkinson’s Disease Rating Scale (UPDRS)**
  - With medication for mental state, activities of daily living and complications of therapy
  - Without medication for 10 hours or more to examine the motor state of the patient
- **Timed-up-and-Go walking test without medication**
  - Persons with normal mobility can complete the test within 10 seconds
- **Parkinson’s disease questionnaire (PDQ-39)**
- **Clinical Global Impression (CGI)**



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Other Exploratory Efficacy Assessments

- **DAT-PET imaging** for density of dopaminergic neurons in different brain areas

- Analysis of **blood serum and cerebrospinal fluid** for
  - CDNF levels
  - Alpha-synuclein levels
  - Identification of new biomarkers in Parkinson's disease affected by CDNF

- Parkinson's **Kinetigraph** (PKG™) - wrist-worn movement measuring device worn for 6 days prior to each treatment infusion visit.

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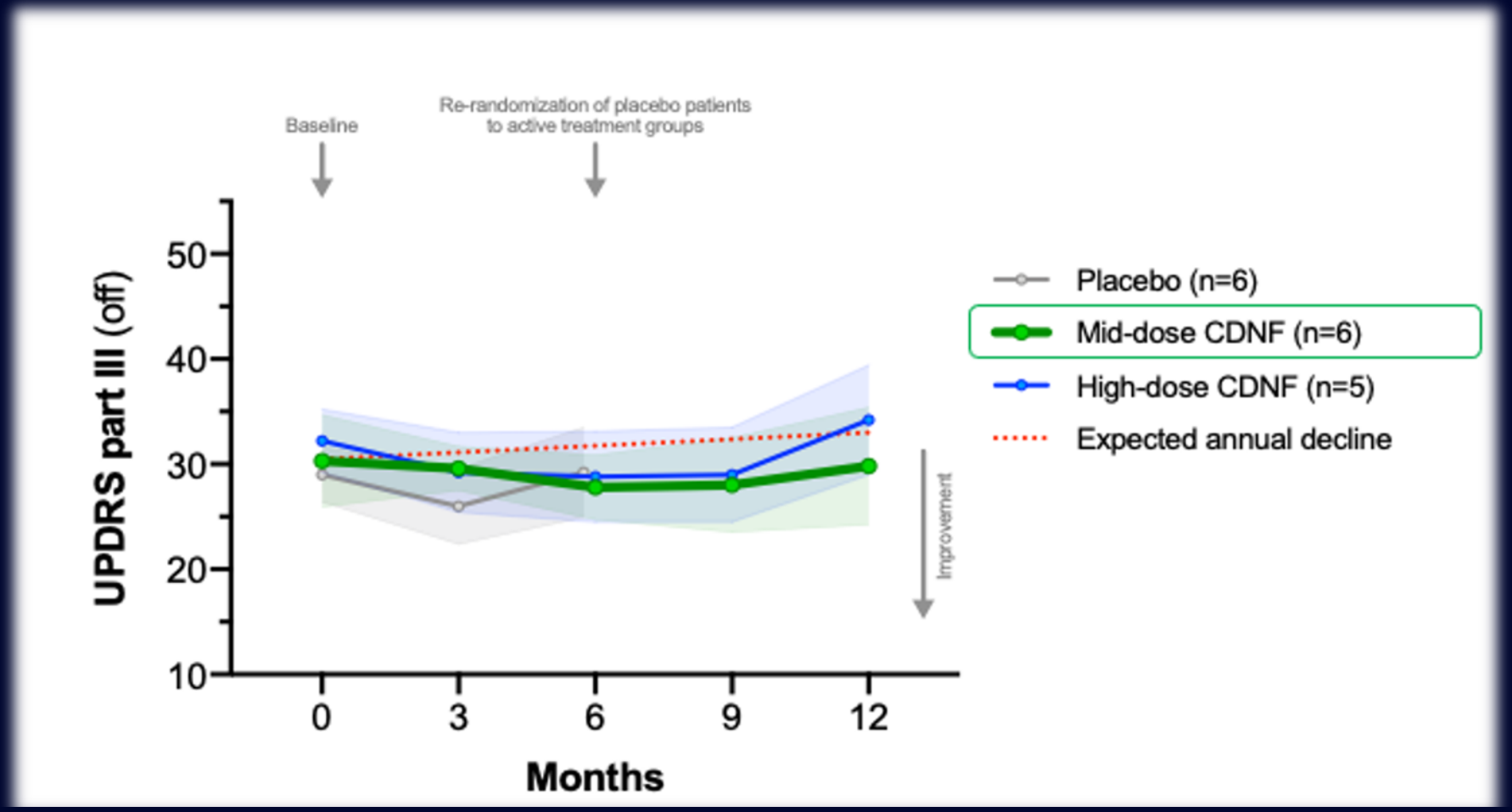
UPDRS Part III (Off) Absolute Scores



<u>All CDNF-Treated Patients:</u> achieved definition of 'minimal clinically important difference' in UPDRS part 3 (motor score); 1.4-2.6 point improvement (pooled data)

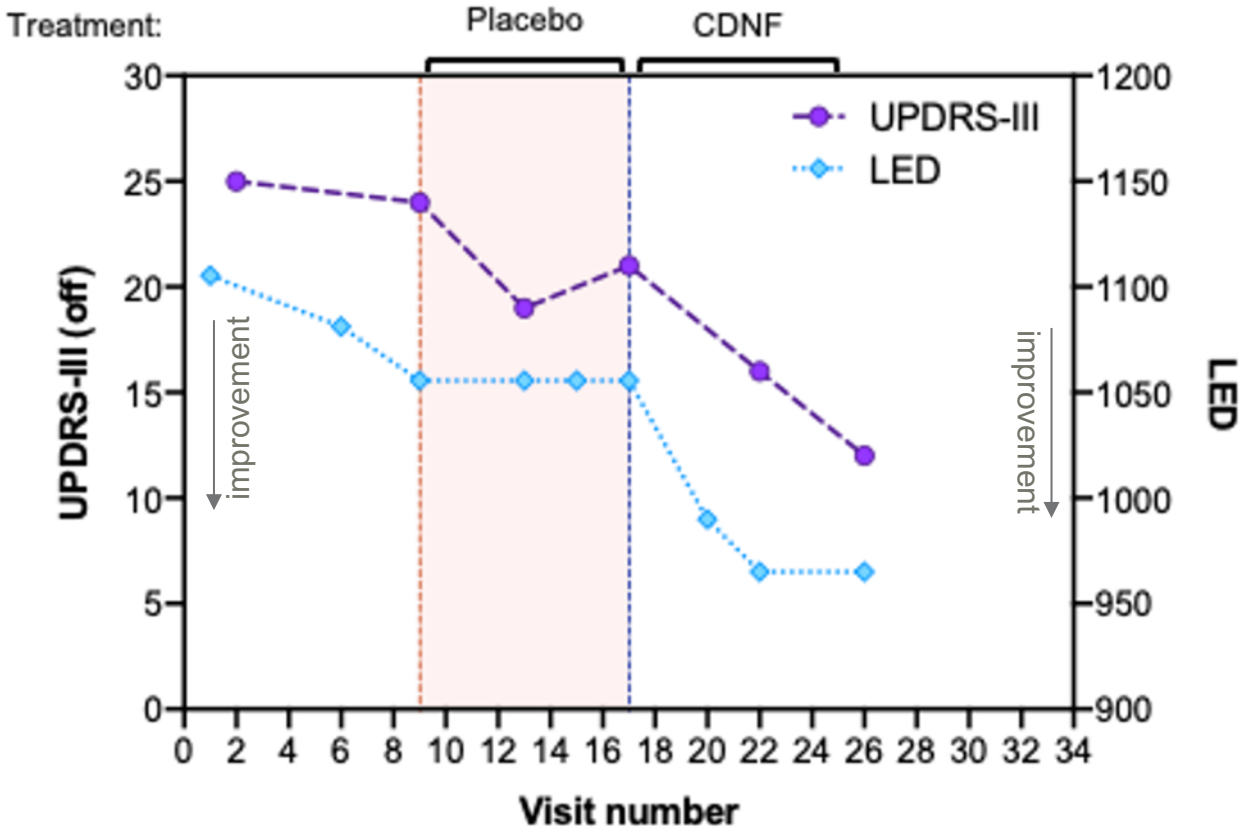
Example of A Responder

Patient Data:

- **Hoehn & Yahr stage: 2**
- **Disease duration: 10 years** (from first motor symptoms)
- **UPDRS part III at screening**
  - → OFF: 25
  - → ON: 11
- Levodopa response: 74%
- **OFF time per day: 5.8 hours**

Received **6 placebo infusions followed by 2 low and 4 mid doses of CDNF**

- Recorded AEs: dyskinesia starting at visit 17 (end of Main study)



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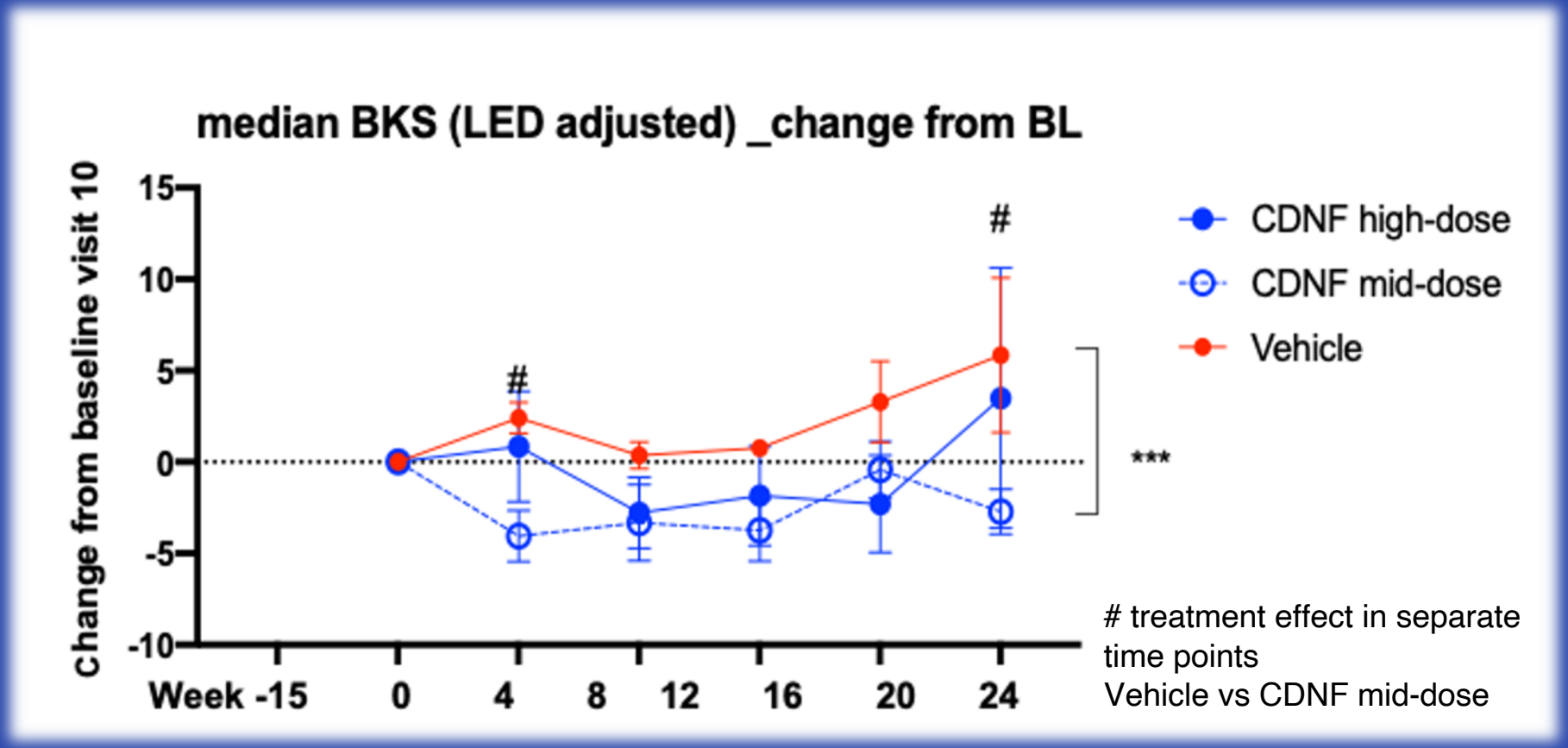
Parkinson's Kinetigraph™ (PKG™): preliminary analysis

BKS is the Bradykinesia Score, Adjusted for the Levodopa Equivalent Dose (LED)



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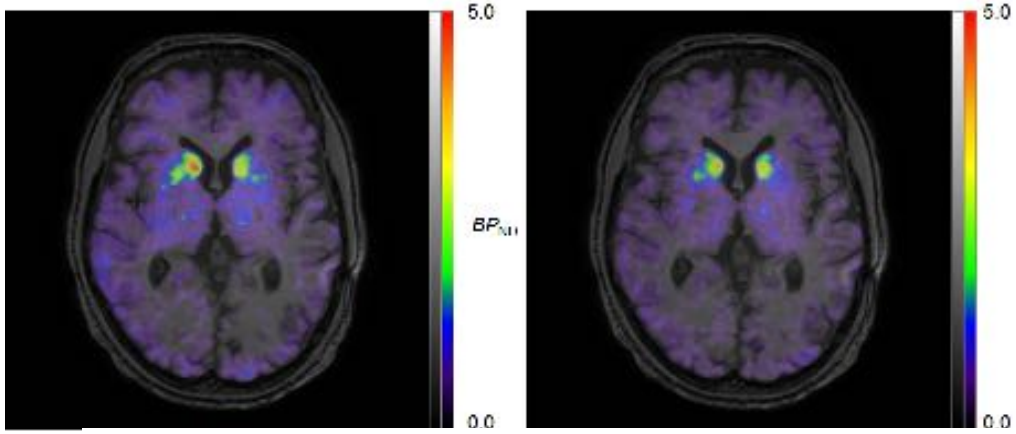
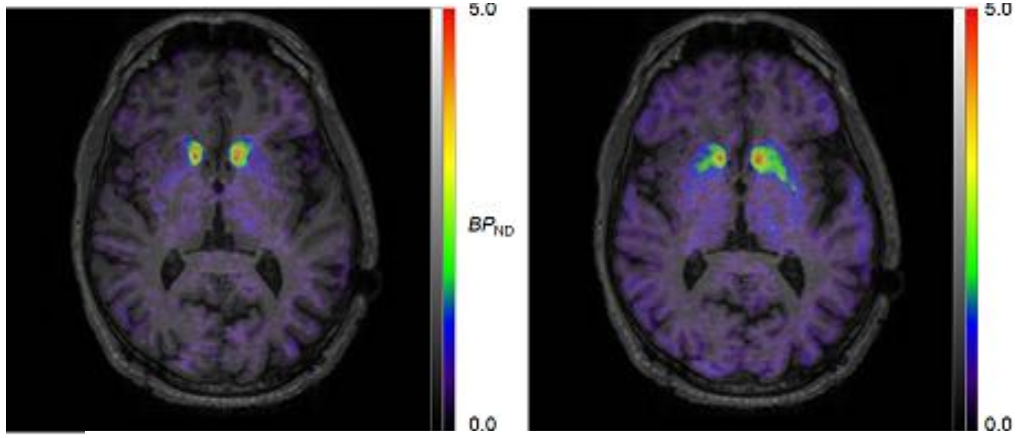
DAT-PET Scanning Examples

Example of decreased signal: patient on placebo



Baseline 6 months

Example of increased signal: patient on mid-dose CDNF



Baseline 6 months

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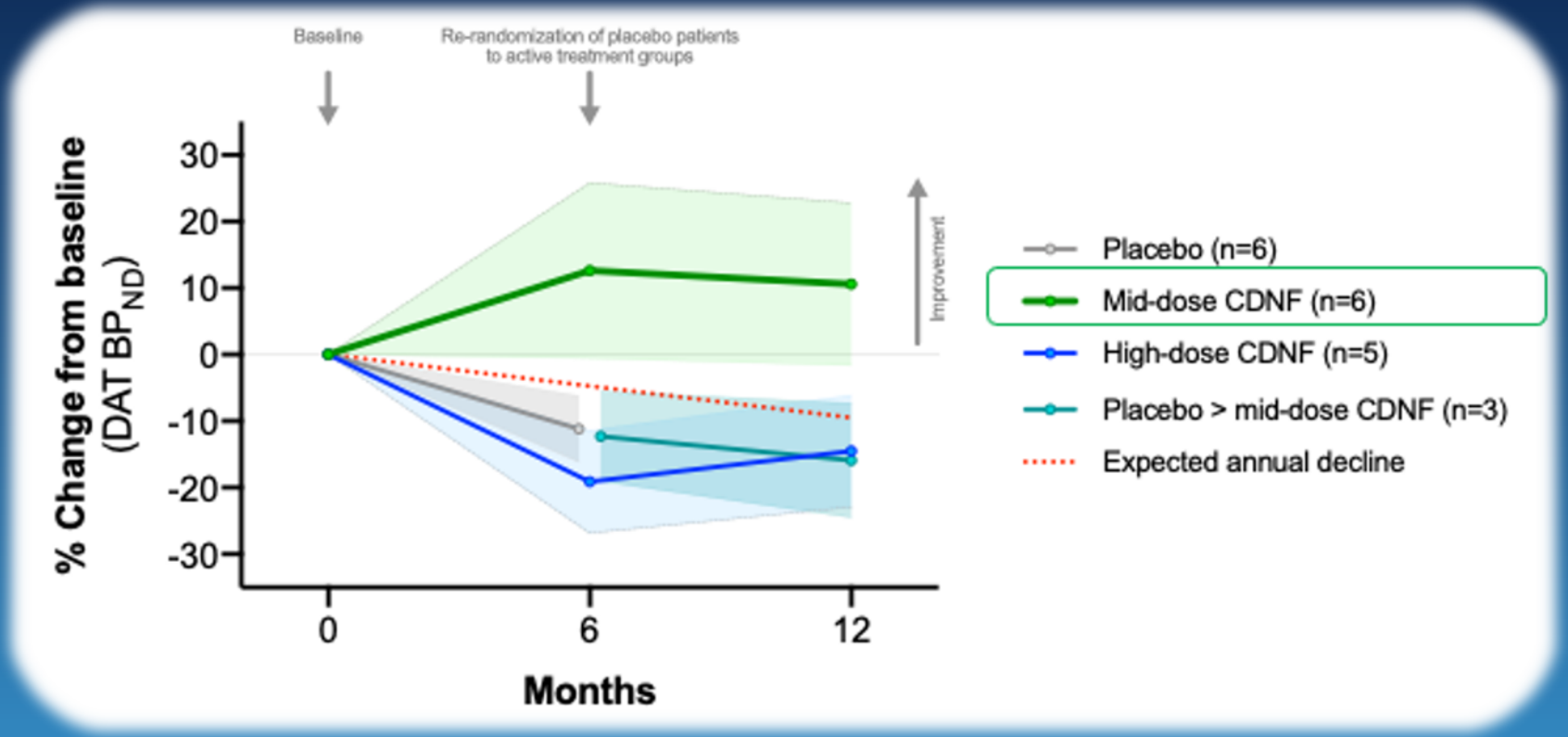
Exploratory Endpoint: Dopamine transporter (DAT) PET in putamen (the infusion target area)

- Mid-dose group (with placebo crossovers) % change average reduces -3.2% from Extension study start, high-dose increases +7.4% (for high-dose placebo crossovers PET data is not available)

- The original mid-dose group (without placebo crossovers) is 15% above Main study baseline at 12 months, while high-dose is 15% below



Note! For the two Placebo > High-dose CDNF patients, PET is not available for the 12-month datapoint.

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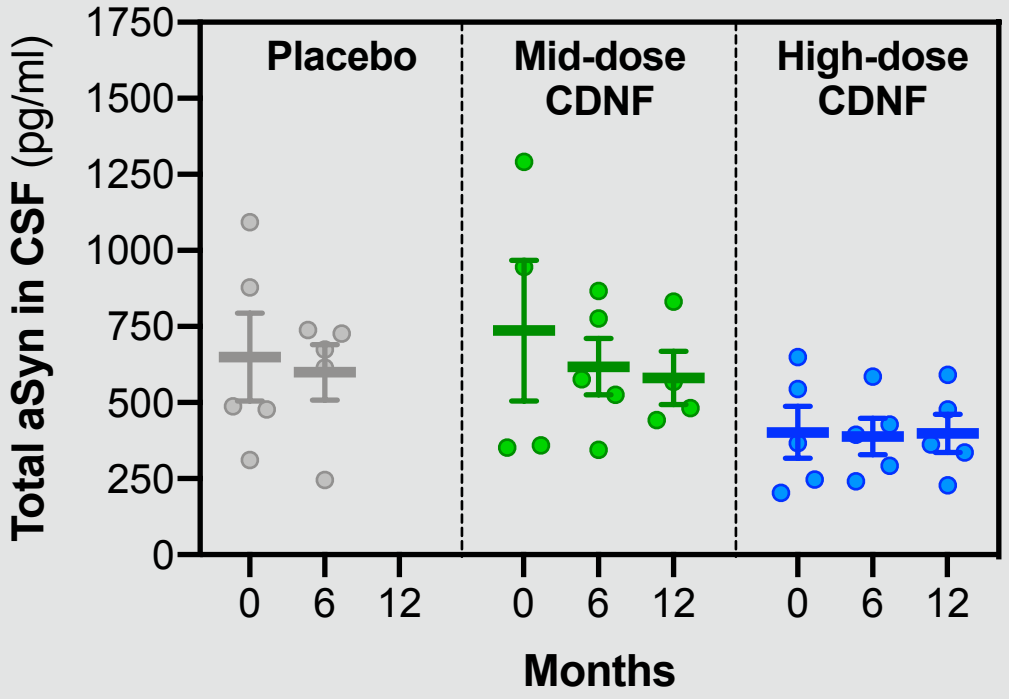
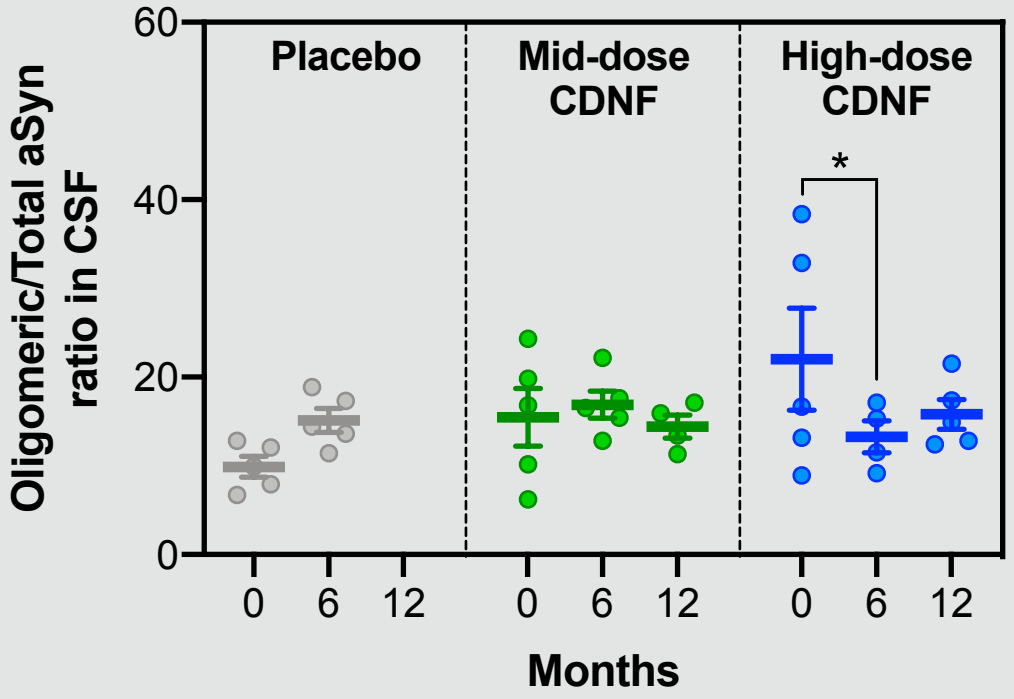
Exploratory Endpoint: levels of cerebrospinal fluid alpha-synuclein at baseline, 6 months and 12 months

TOTAL ALPHA-SYNUCLEIN



RATIO OF OLIGOMERIC/TOTAL ALPHA-SYNUCLEIN



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Conclusions

The **Study Was Designed to Show Safety and Tolerability** => Primary **endpoint met**!

The Study Was Not Designed to Show Efficacy:

- Too small patient numbers => a lot of noise from single patients and outliers
- The advanced PD patient population was not suitable to show effects of neuroprotective drugs

The Study Aimed to See Effects In Some Patients:

- **Several patients show significant improvement** on **UPDRS-III** (off)
- At least **2 patients** show significant **signal increase in DAT-PET imaging**
- Some other interesting cases on different clinical outcome measures

The Efficacy Endpoints Also Had A Safety Role **=> patients' PD did not get worse**

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