TT-P34: a novel first-in-class peptide drug for treatment of Parkinson's Disease

TEITUR TROPHICS

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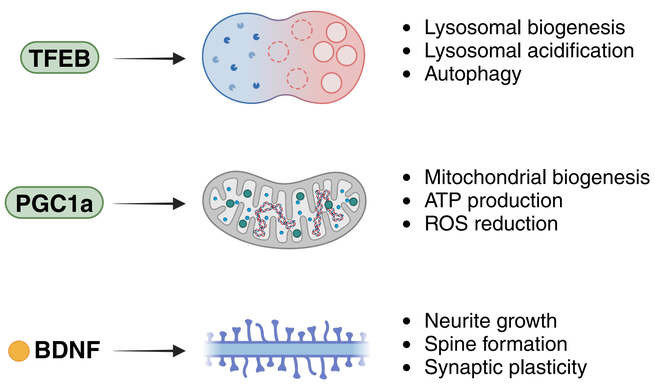
INTRODUCTION

TT-P34 is a novel cyclic peptide drug which has been developed by Teitur Trophics, a biotech company based in Aarhus, Denmark.

Mechanism
The peptide induces a brain-specific activation of transcription factor CREB to increase both mitochondrial and lysosomal biogenesis and neurotrophic support through upregulation of master regulators PGC1a and TFEB and neurotrophin BDNF.

Administration
The peptide is designed for once weekly subcutanous administration in patients. Through this route, current data supports delivery to the brain at sufficient levels in mice, rats and non-human primates.

Teitur aims to bring TT-P34 into clinical Phase 1 in Q2 2025.



METHODS

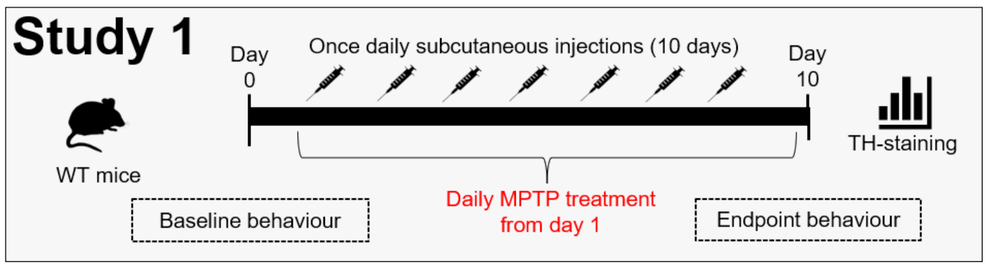
Aim of study: To investigate the potential of TT-P34 to rescue motor phenotype and neuropathology in two in vivo models of Parkinson's.

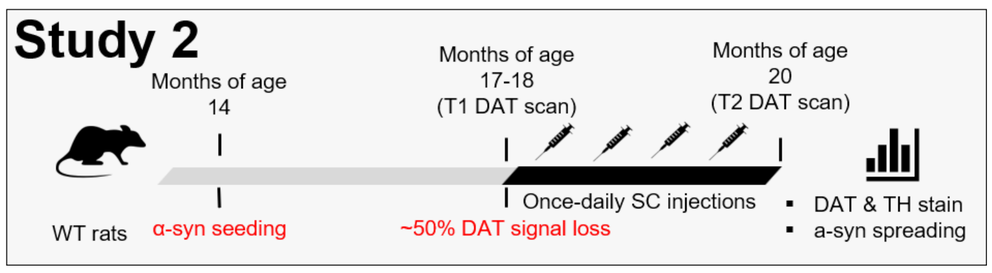
Study 1) Chronic MPTP-mouse parkinsonian model

- Treatment was started one day prior to MPTP treatment and continued once-daily at 5 different doses.
- Motor behavior measured included open-field test (distance, rearing) nad grip strength
- Postmortem analysis included TH-staining and quantification

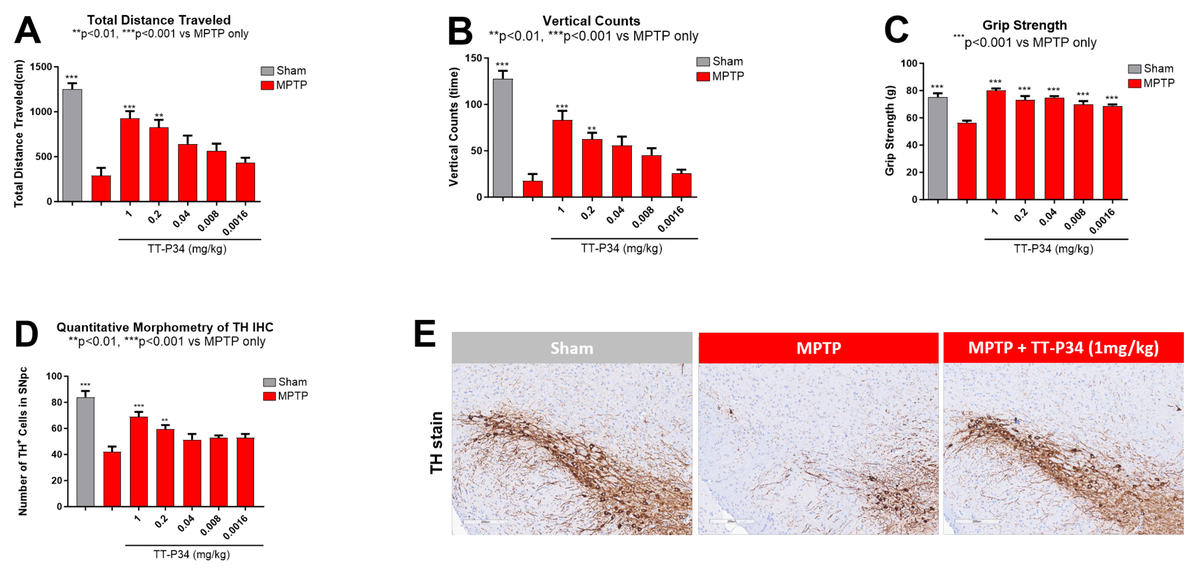
Study 2) Aged rats (14 months) injected with α-syn PFFs in amygdala

- Treatment was started 3 months after PFF injection, when DAT scan (^{18}F-FE-PE2I radiotracer) was decined to 50%. Treatment was continued once-daily for 3 months.
- DAT scans were taken in beginning (T1) and end (T2) of treatment.
- Postmortem analysis included TH, DAT and pSer129-stainings of striatum and amygdala.



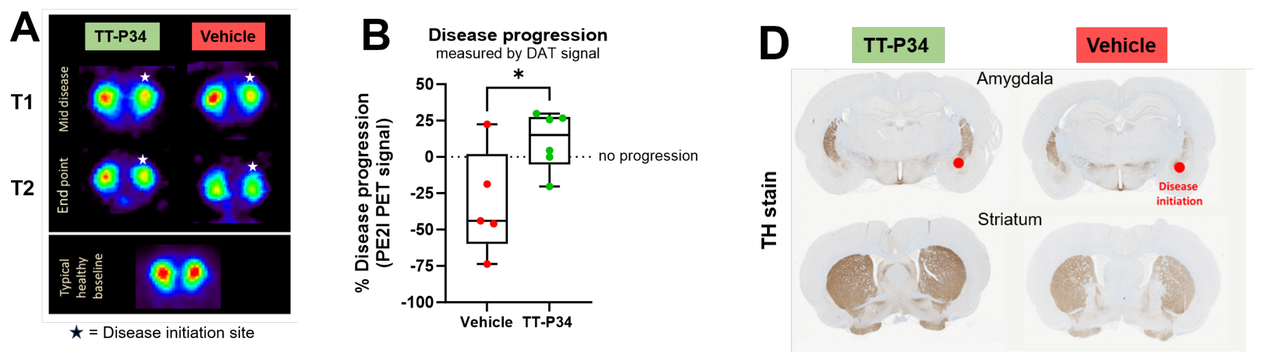


STUDY 1: MPTP MODEL



A) TT-P34 rescues motor function in dose-response manner measured in open-field test by distance traveled and **B**) vertical counts. **C**) Grip-strength was rescued at all doses. **D**) Quantification of TH+-neurons shows protection of dopaminergic loss with TT-P34 treatment. **E**) Representative TH+-images of Sham, MPTP and MPTP + 1mg/kg dose group.

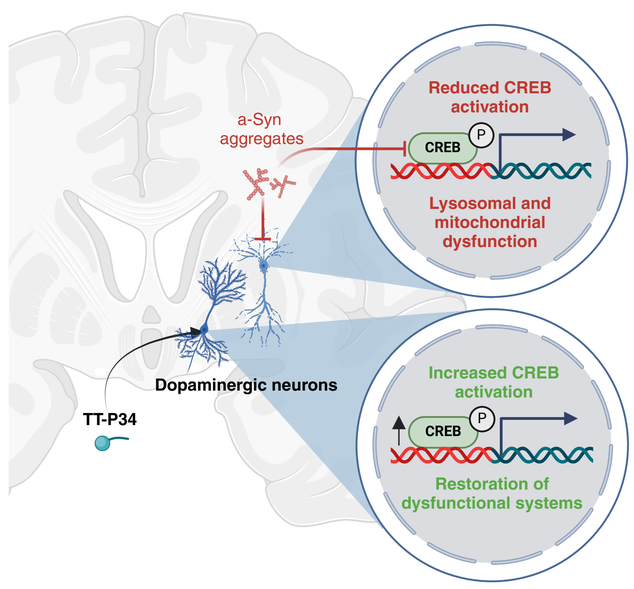
STUDY 2: α-SYN PFF MODEL



A) Representative images of ^{18}F-FE-PE2I radiotracer scans of PFF-injected rats at different disease-stages. **B**) Quantification shows TT-P34 completely halts Parkinson's disease progression. **C**) TT-P34 treatment lead to marked increase and protection of DAT signal, **D**) TH signal and reduced **E**) α-syn pSer129 levels as a measure of inclusion bodies.

CONCLUSION

TT-P34 activates CREB to drive key cellular pathways affected in PD including lysosomal and mitochondrial dysfunction. This protects against loss of dopaminergic neurons and reduces spreading and formation of aggregated α-syn. The preservation of dopaminergic neurons directly translates into a rescue of motor functions. Taken together, this validates the therapeutic efficacy of TT-P34 as a novel drug for PD and potentially other neurodegenerative diseases with mitochondrial and lysosomal deficits.



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- [1]Teitur Trophics (Aarhus, Denmark)
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DISCLAIMER

TT-P34 is an investigational new drug developed by Teitur Trophics and has not been approved by the FDA or EMA for any use.