Neuro-regenerative therapeutics for Parkinson’s disease

October 9th, 2024

Herantis Pharma Oyj (HEL: HRTIS)

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Forward-looking statements

This company presentation includes forward-looking statements which are not historical facts but statements regarding future expectations instead. These forward-looking statements include without limitation, those regarding Herantis' future financial position and results of operations, the company's strategy, objectives, future developments in the markets in which the company participates or is seeking to participate or anticipated regulatory changes in the markets in which the company operates or intends to operate. In some cases, forward-looking statements can be identified by terminology such as "aim," "anticipate," "believe," "continue," "could," "estimate," "expect," "forecast," "guidance," "intend," "may," "plan," "potential," "predict," "projected," "should" or "will" or the negative of such terms or other comparable terminology. By their nature, forward-looking statements involve known and unknown risks, uncertainties and other factors because they relate to events and depend on circumstances that may or may not occurin the future.

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Executive Summary

- Clinical-stage public company developing therapeutics for Parkinson's disease (PD) and other CNS disorders
- HER-096: a disease-modifying peptide mimic of CDNF protein, shown to reverse damage and break the cycle of PD pathogenesis
- Phase 1a with subcutaneous administration:
  - Efficient brain penetration
  - Good safety profile
- Efficacy data:
  - Phase 1 trial of CDNF, which HER-096 mimics, showed signs of biological response in advanced PD patients
  - Strong preclinical data of HER-096
- Significant unmet need:
  - 328,000+ patients diagnosed yearly in target geographies
  - $10B+ global market in 2030
  - No existing disease-modifying or neurorestorative therapeutics

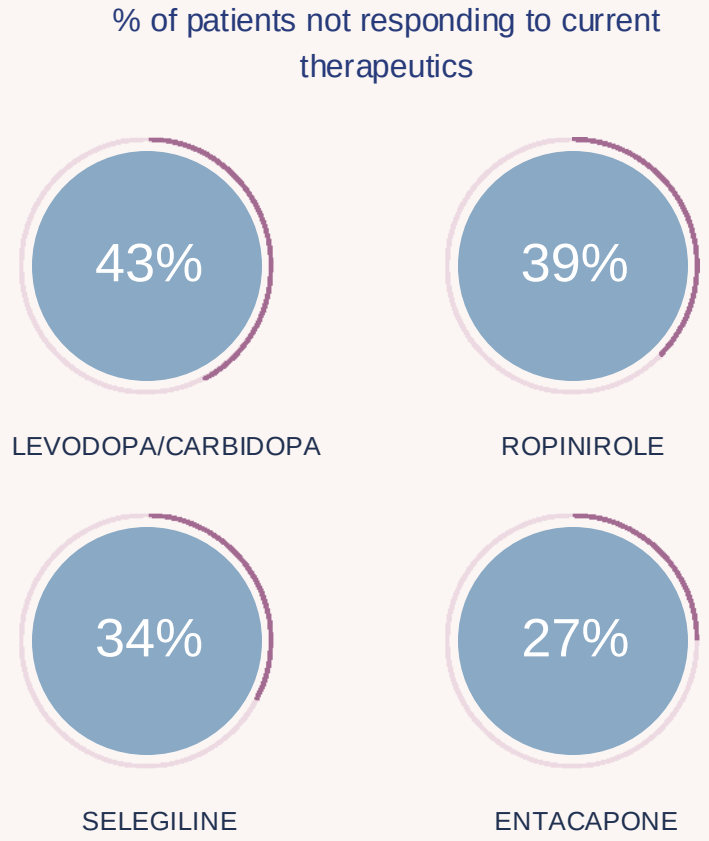
- Phase 1b trial ongoing
- Preparing for Phase 2 trials of HER-096 for Parkinson's disease

Innovation is urgently needed for PD treatment

Current therapies only treat symptoms and have significant side effects

Many patients have no symptomatic benefit, and none improve

No disease-modifying or regenerative therapeutics are available

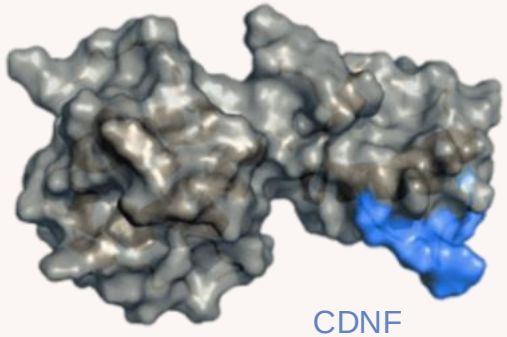


1. Levodopa/carbidopa: 100% minus response rate (patients attaining 25% improvement at 30 weeks); Ropinirole: patients not significantly improved at week 48 in clinical trial;
2. Selegiline: patients with significant wearing off effect + patients removed from trial due to insufficient response; Entacapone: 100% minus patients reporting clinical improvement

ref: Pahwa et al 2013 Parkinsonism and Related Disorders, Sethi et al 1998 JAMA Neurology, Pålhagen et al 2006 Neurology, Brooks et al 2005 European Neurology

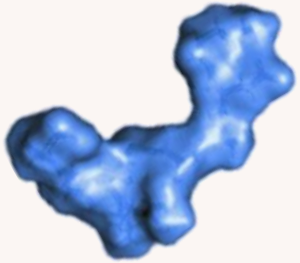
Herantis' HER-096 is an enhanced Phase 1–stage therapeutic based on clinically validated protein CDNF

CDNF



CDNF
active site

HER-096



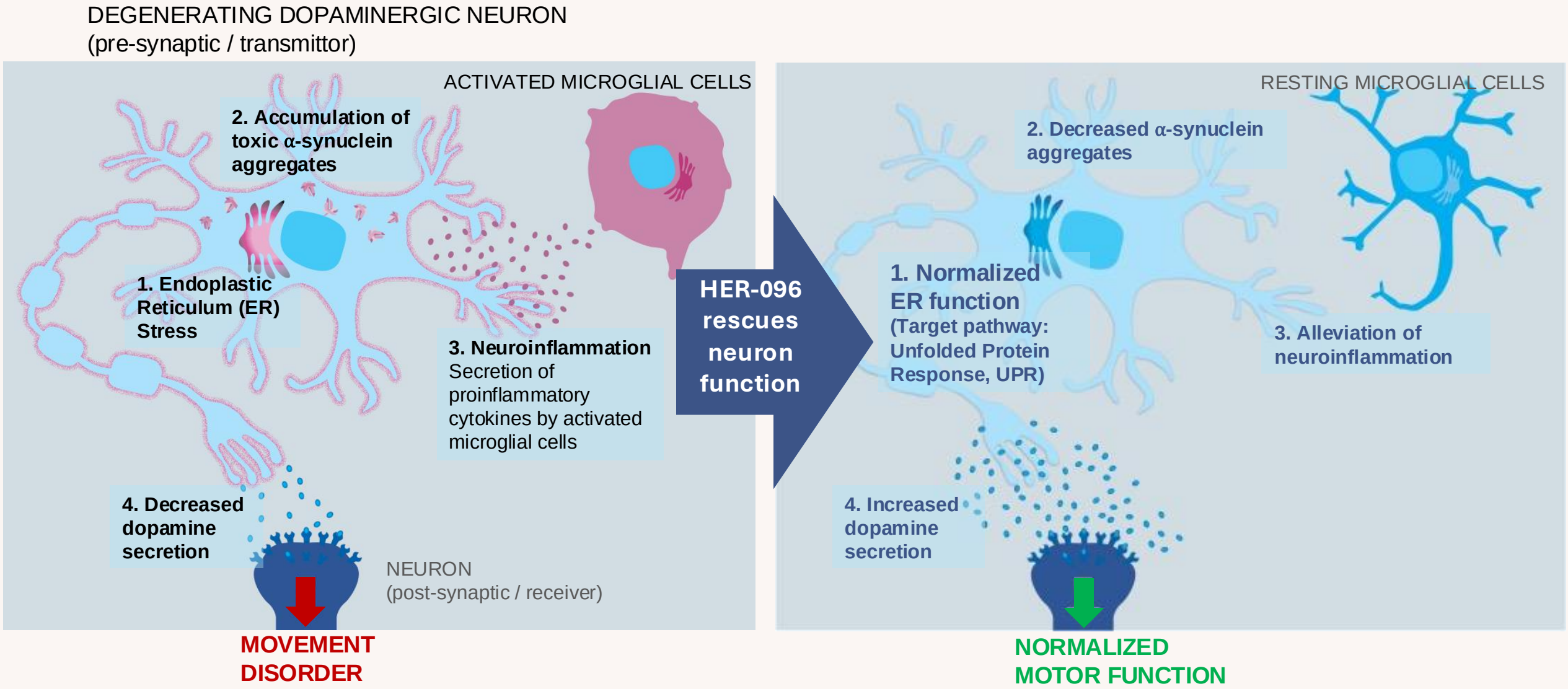
Phase 1 clinical trials of CDNF show unprecedented signs of neuroprotection and neuro-regeneration in the most advanced patients

Cannot cross the blood-brain-barrier

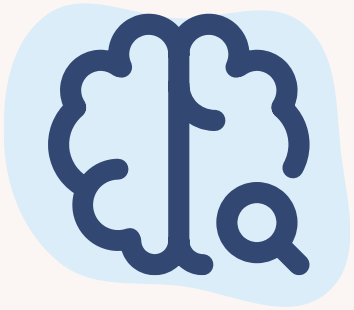
HER-096 mimics the CDNF active site and is optimized to cross the blood-brain-barrier for subcutaneous administration

Demonstrated safety and desired PK/PD in Phase 1a clinical trials

HER-096 has a neuro-restorative, disease-modifying mechanism of action



Key Advantages of HER-096



Neuro-restorative

Disease-modifying MOA shows evidence of not just slowing but reversing striatal damage for symptomatic improvement

Subcutaneous

Patient-friendly administration 1-3 times weekly, while effectively crossing the blood-brain-barrier for therapeutic effect

Safe

No systemic toxicity or serious adverse events noted, including those common with other PD treatments (dyskinesias, neuropsychiatric issues, hypo/hypertension)

BEYOND PD:

HER-096 has potential utility in several neurodegenerative and ischemic diseases

ALS

CDNF has demonstrated therapeutic effect in multiple preclinical models of amyotrophic lateral sclerosis, including protection of motor neurons and improvement of motor function

Stroke

CDNF has improved functional recovery in preclinical models of ischemic and hemmorhagic stroke owing to its role in neurogenesis previously ischemic neurons

HER-096

Potential applications based on demonstrated role of CDNF (mimicked protein)

Alzheimer's disease

CDNF has been shown to improve long-term memory in a preclinical model of Alzheimer's disease

Neuro-regeneration

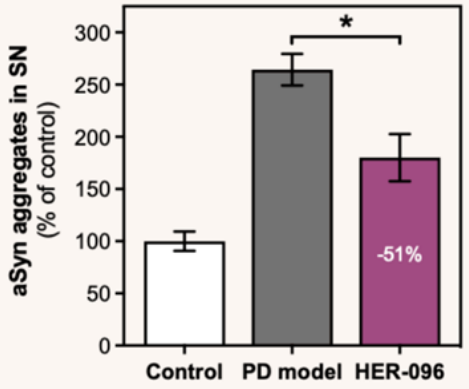
CDNF is broadly involved in neuronal regeneration and has many theoretical implications across diverse modes of injury, ischemia, aging, and neurodegeneration

Data & Clinical Trial Design

Preclinical, Phase 1a and Phase 1b

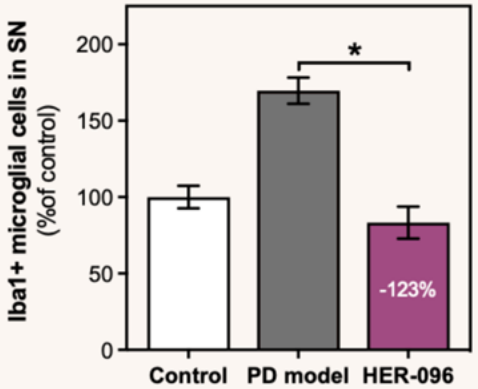
In vivo preclinical studies show the unique disease-modifying mechanism-of-action of HER-096

Reduced α-Syn aggregates



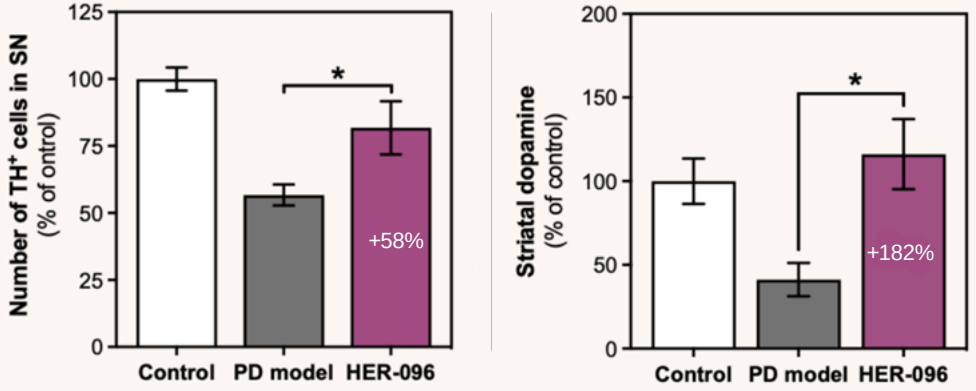
HER-096 reduces α-Syn aggregates - key component of neuronal damage

Reduced neuroinflammation



HER-096 reduces microglial cell activation in the substantia nigra in vivo

Increased dopaminergic neurons and dopamine



Increased striatal dopamine and nigral TH+ dopamine-producing neurons - essential neurotransmitter for symptom control

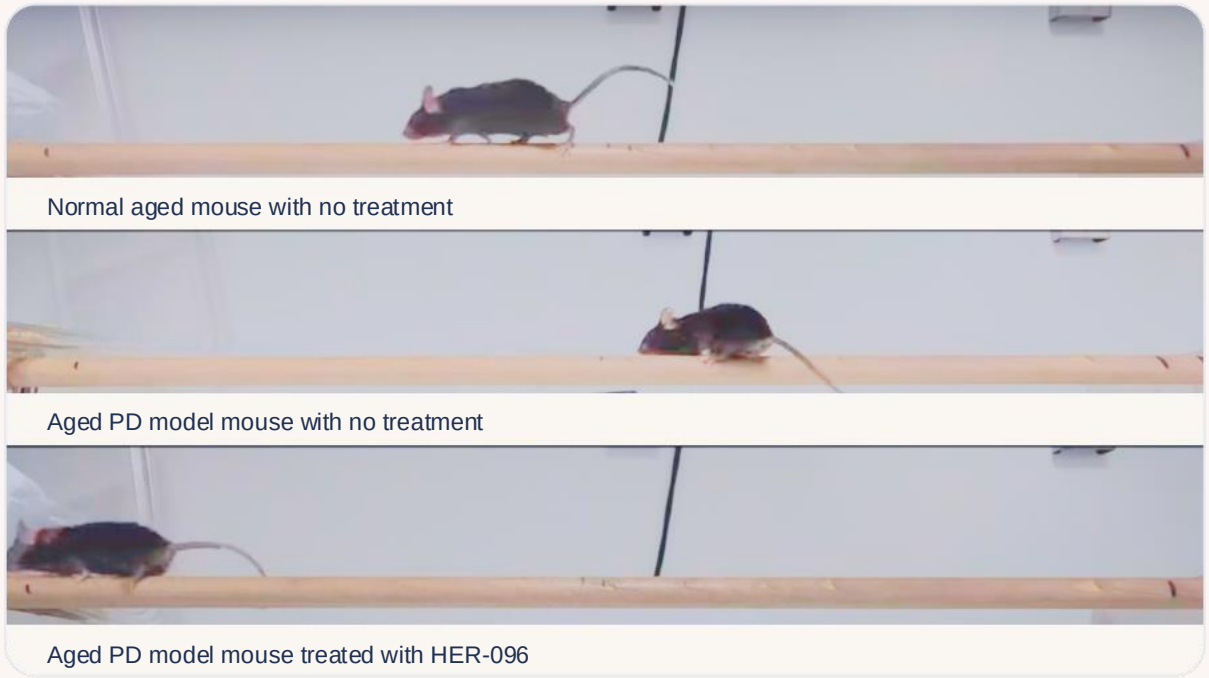
Mice were administered IP a human-equivalent dose of 200 mg HER-096 3 times per week for 4 weeks. Control = normal aged mouse without drug (vehicle only). PD model = PD model aged mouse without drug (vehicle only). HER-096 = PD model aged mouse with HER-096 drug. For substantia nigra (SN; graphs 1, 2, 4): Whole brains were prepared for immunohistochemistry of TH, Iba1, and α-Syn and the SN analyzed. For striata (graph 3): Striata were dissected from whole brain and lysed. Dopamine levels were determined by HPLC. Kulesskaya et al 2024, Cell Chem. Biol., doi: 10.1016/j.chembiol.2023.11.005

PRECLINICAL EFFICACY

Preclinical studies of HER-096 demonstrate potent neuroprotection

PD mouse model administered HER-096 has superior beam walking speed to both untreated PD mouse and normal aged mouse

Beam-walking test



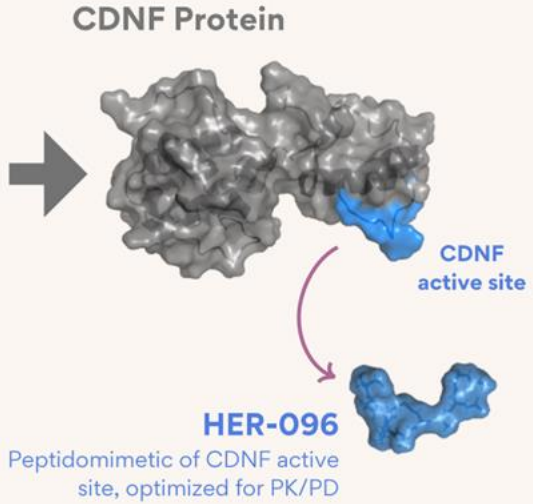
Normal aged mouse with no treatment

Aged PD model mouse with no treatment

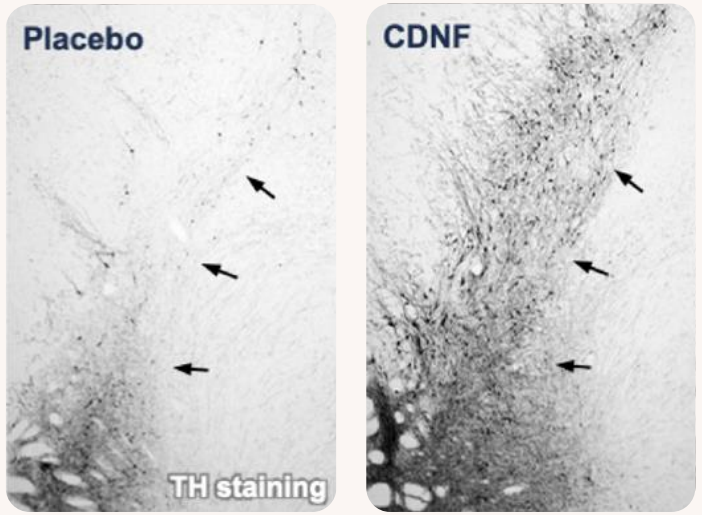
Aged PD model mouse treated with HER-096

Video snapshot at same timepoint shown. Video is available at: https://youtu.be/L3WmkhP2Opw
PD model = aged mouse with nigral α-Syn pathology

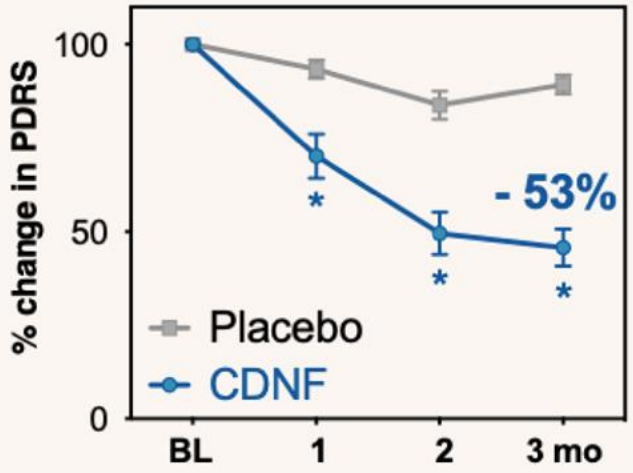
Neurorestoration by intraputamenal CDNF protein in a Rhesus model of PD



CDNF protein used as proof-of-concept for optimized therapeutic HER-096



2x increase in nigrostriatal dopamine neuron numbers with significantly enhanced axonal sprouting

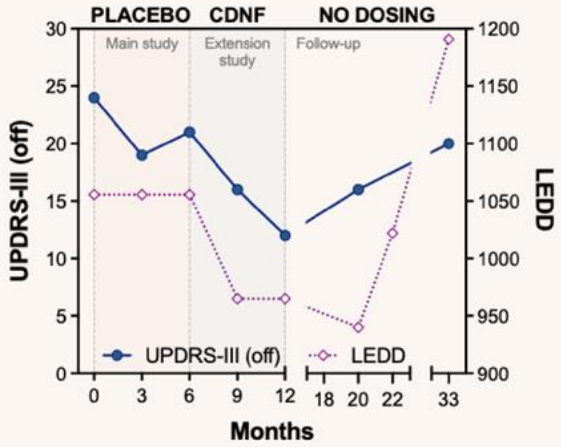


>50% improvement in gross motor function on Rhesus PD rating scale (PDRS)

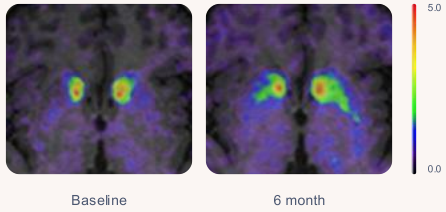
Three monthly doses of intraputamenal CDNF* were administered in an aged Rhesus monkey MPTP model starting six weeks after MPTP lesion. Clinical improvement was measured by PDRS and histological improvement was measured by TH staining at study endpoint.

*Intraputamenal CDNF was the proof of concept compound for HER-096. CDNF does not cross the blood-brain-barrier while HER-096 does. PK = pharmacokinetics; PD = pharmacodynamics.

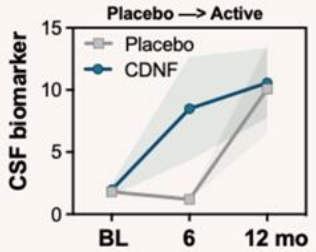
Phase 1 proof-of-concept study of intraputamenal CDNF shows signs of biological response in advanced PD patients



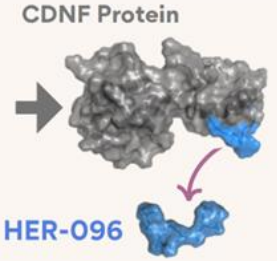
Although primarily a safety study with advanced patients, clinical improvement was observed in several patients



Evidence of striatal recovery by PET demonstrates disease-modifying mechanism



Exploratory CSF biomarker study identified three treatment response biomarker candidates



Unlike HER-096, requires delivery via brain implant

Safe and well-tolerated

Only safety concerns were related to the intraputamenal delivery device, which limited patient cohort to only advanced patients and led to our development of subcutaneous HER-096

An intraputamenal device was implanted for administration of CDNF. Patients were at least 10 years post-diagnosis and all showed advanced symptoms.

*Intraputamenal CDNF was the proof of concept compound for HER-096. CDNF does not cross the blood-brain-barrier while HER-096 does. Huttunen et al 2023, Movement Disorders, doi: 10.1002/mds.29426

Completed Phase 1a clinical trial of subcutaneous HER-096: design and objectives

Study design:

- Double-blind, placebo-controlled clinical trial
- Subcutaneously administered single ascending dose of HER-096 to healthy subjects
- Total of 60 healthy subjects participated in the trial; 48 in Part 1 and 12 in Part 2

Objectives:

- Safety and tolerability (of single dose) in healthy subjects
- Pharmacokinetics in young and elderly healthy subjects, including blood-brain-barrier (BBB) penetration in elderly [HER-096 concentration in cerebrospinal fluid (CSF)]
- Identification of exploratory biomarkers

ClinicalTrials.gov ID: NCT05915247

Part 1:

Male, age 20-45 years
Single escalating dose

- Single dose, 300 mg
  2 placebo + 6 HER-096
- Single dose, 200 mg
  2 placebo + 6 HER-096
- Single dose, 120 mg
  2 placebo + 6 HER-096
- Single dose, 60 mg
  2 placebo + 6 HER-096
- Single dose, 30 mg
  2 placebo + 6 HER-096
- Single dose, 10 mg
  2 placebo + 6 HER-096

Part 2:

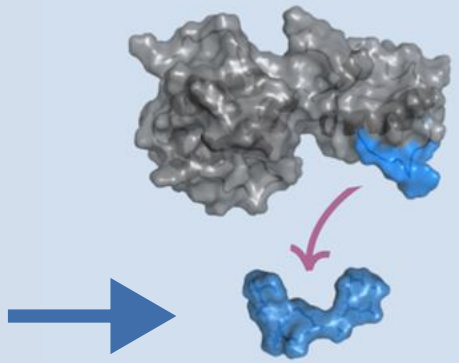
Male & female, age >50 years
Single dose

Single dose (200 mg)
CSF collection
12 men and women

Summary of demographic data

	Part 1	Part 2
Age (y)	32.4 ± 7.5	63.2 ± 6.3
Sex (males, %)	100%	50%
BMI (kg/m2)	24.7 ± 2.6	26.2 ± 2.7

CDNF Protein

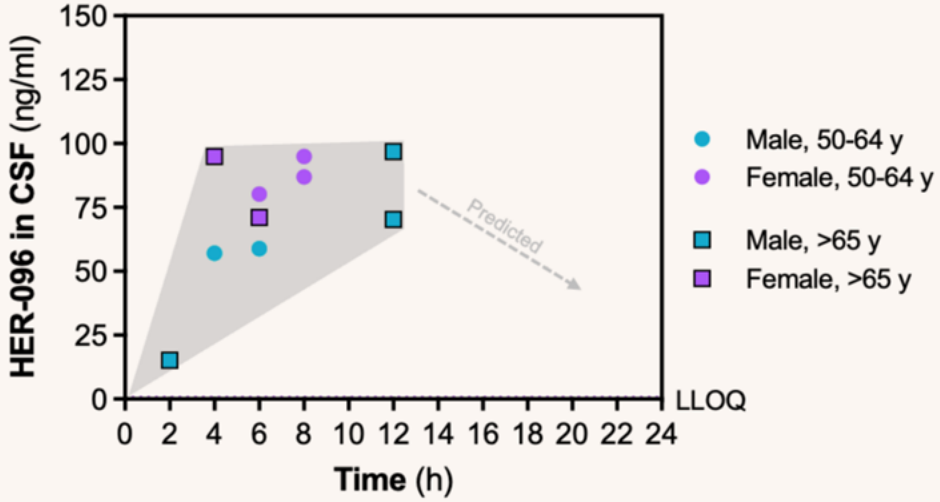


HER-096
Mimics CDNF active site

HER-096 was optimized for subcutaneous delivery, while maintaining clinical effect of CDNF

HER-096 effectively penetrates blood-brain-barrier and shows expected pharmacokinetics in healthy elderly individuals

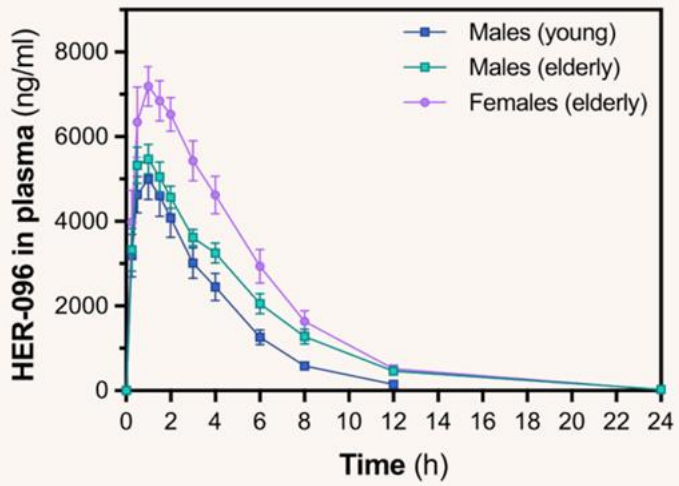
Levels of HER-096 in CSF after subcutaneous administration



MEAN CONCENTRATION = 72.6 NG/ML (RANGE 15.2-96.9)

HER-096 (200 mg dose) effectively penetrates BBB to reach CSF concentration predicted to be within therapeutic range

Plasma HER-096 in elderly individuals (single s.q. 200 mg dose)



Quick absorption rate with similar pharmacokinetics in elderly and young volunteers, with slightly longer elimination half-life in elderly

Normalization by weight eliminates sex difference in elderly

Phase 1b Clinical Trial Design

Study started Sep 2024 / expected topline data Q3/2025

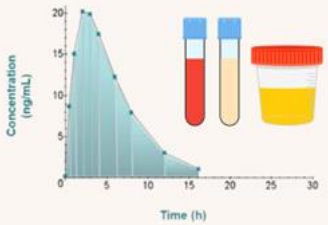
Objectives

1. Demonstrate safety of repeated subcutaneous dosing in PD patients
2. Study biological responses to HER-096 using surrogate biomarkers
3. Study pharmacokinetics for planning dosing for Phase 2

Endpoints

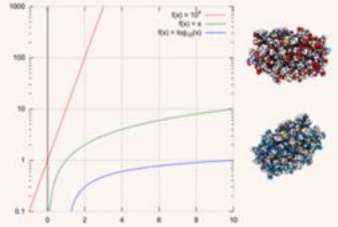
Primary

Safety and tolerability of multiple repeated doses



Secondary

PK in plasma, CSF, and urine



Exploratory

Biomarkers in plasma and CSF

Study subjects

PART 1

Up to 12 healthy individuals

50-78 years old, male and female

PART 2

Up to 24 PD patients (mild-to-moderate symptoms)

50-78 years old, male and female

Dosing

1 S.Q. injection

×

2 times weekly

×

4

4 weeks

Business & Funding

The unmet medical need in PD is matched by a large global market for PD therapeutics

$9B

Addressable market in US and EU5 by 2030

1.1M

Total PD patients in US and EU

3.2%

Estimated CAGR of PD therapeutics market through 2030

20%

Conservative estimate for market capture based on competitive landscape

$10B

Projected market in target geographies (number of patients x[1] projected cost)

1) Based on estimated drug costs at 20% premium to Duodopa price from bioscience valuation for Herantis (up to $45K/patient), variability across geographies and with different payees (e.g., Medicare), and number of patients across target geographies (US and EU)

Secured research funding for Phase 1b clinical trial of HER-096 for PD

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

PARKINSON'S UK
CHANGE ATTITUDES.
FIND A CURE.
JOIN US.

€3.6M cash

In 3 tranches over 2 years, contingent on milestone completion

Repayment triggered by out-licensing or sales revenue

Projects supported

1. Fund Phase 1b Clinical Trial of HER-096 for PD
(repeated subcutaneous dosing safety in PD patients)

2. Support ongoing biomarker identification project
(exploratory biomarker data collection during Phase 1b trial, and ongoing research on predictive outcomes)

Herantis has secured €6.1M non-dilutive research funding since April 2023

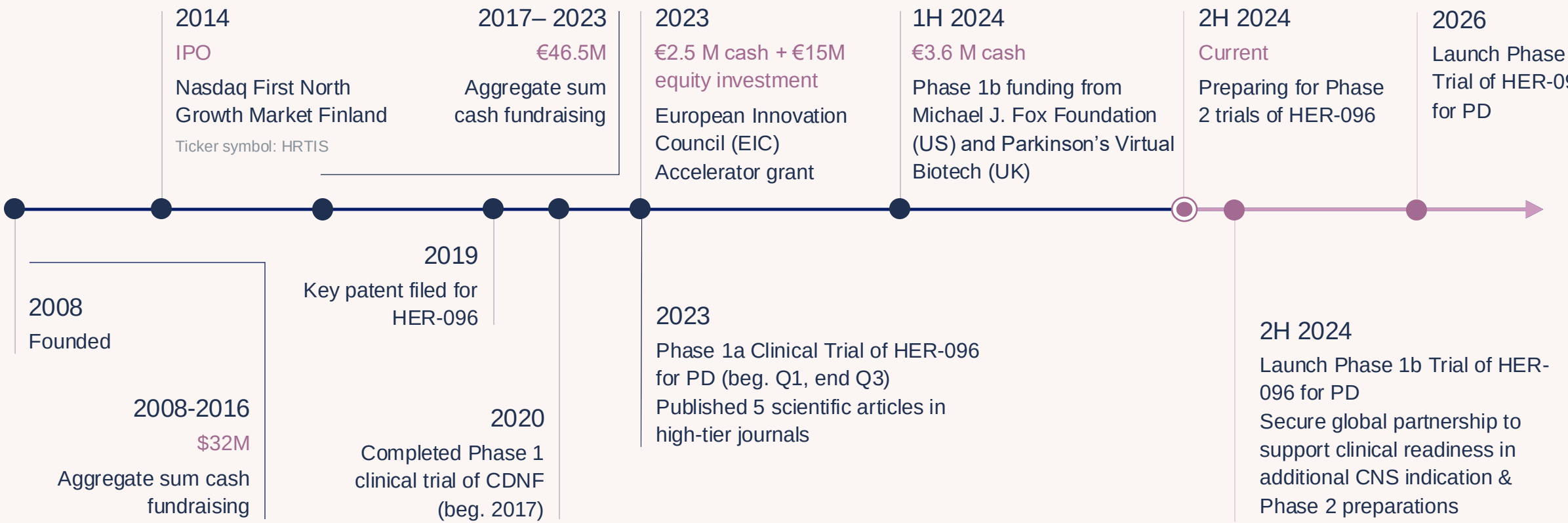
European Innovation Council (EIC) Accelerator grant of €2.5M in April 2023 for advancing Phase 2 preparation

Co-funded by the European Union

Herantis has secured €15M investment commitment from EIB

EIB committed direct equity investments through EIC Fund. First tranche of €1.5M raised in December 2023.

Strong clinical progress matched by consistent investor interest



Executive Team

Antti Vuolanto, DSc

CEO

20+ years experience in financing, partnering, R&D, and biologics manufacturing; D.Sc. in Bioprocess Engineering

Tone Kvåle

CFO

25+ years experience in biotech, medtech, and life science, including multiple prior roles as CFO of public biotech companies

Henri Huttunen, PhD

CSO, Co-Founder

25+ years experience in neuroscience and therapeutics development; served as CEO prior to transitioning to CSO

BOARD OF DIRECTORS

Timo Veromaa, MD, PhD, EMBA

Chairman of the Board

Current: Professor of Practice of Drug Development, University of Turku, Finland; Chairman of Teneboron Ltd.
Former: Exec. Chairman DomainEx Ltd; CEO & Pres. of BioTie Therapies (acq. Accord Tx); Chairman Finnish Bio Banks; Chairman Finnish Bioindustries

Frans Wuite, MD, MBA

Vice Chairman of the Board

Current: Board Director Healthcap VII GPSA; co-founder Rigi Tpx AG
Former: CEO Acesion Pharm ApS; CEO & President Oncos Tpx; COO Warren Pharma; Co-founder & Board Director Araim Pharma; Amgen senior management

Aki Prihti

Board Member

Current: CEO Aplagon Oy; Board member Rokote Lab Finland; Founding partner Inveni Capital
Former: Board member & CFO HVR Cardio; Corporate Finance at Salomon Brothers

Mats Thorén

Board Member

Current: CEO Vixco Capital; Board member Arcoma AB, Xbrane Biopharma, and FluoGuide
Former: Founding parter Catella Healthcare

Hilde Furberg, MSc

Board Member

Current: Industrial advisor Investinor; Board member Pluvia Biotech, Bio-Me, PCI Biotech, Sedana Medical
Former: European Head of Rare Disease Europe/General Manager Diseases EMEA at Genzyme/Sanofi

SCIENTIFIC ADVISORS

Anders Gersel Pedersen, MD

Chairman of the Scientific Advisory Board

Current: Board Member and Scientific Committee Chair at Hansa Biopharma; Board Member at Genmab; Deputy Chairman of the Board at Bavarian Nordic; Chairman of the Board at Aelis Farma
Former: 19 years at Lundbeck, including as EVP of R&D; Director of oncology clinical research at Eli Lilly; Board Member at TopoTarget and ALK-Abelio

Alberto Espay, MD, MSc

Scientific Advisory Board Member

Current: Director, Professor, and endowed chair of the University of Cincinnati Gardner Family Center for Parkinson's Disease and Movement Disorders (OH, USA)
Former: Chair of the Movement Disorders Section of the American Academy of Neurology; associate editor of Movement Disorders (journal); 300+ academic papers

David Dexter, PhD

Scientific Advisory Board Member

Current: Associate Research Director of Parkinson's UK; Visiting Professor of Neuro-pharmacology at Imperial College London; biology lead for Parkinson's virtual biotech
Former: Deputy Head of the Division of Brain Sciences at Imperial College London; founder of Parkinson's UK Brain Bank; identified 3 of the 6 mechanisms linked to PD

Daniele Bravi, MD

Scientific Advisory Board Member

Current: Associate Prof. at the Movement Disorder research center, S. Raffaele Inst.
Former: Vice President of PD Strategy at Lundbeck R&D, CMO and VP of Drug Development at Lundbeck USA; EFPIA clinical development group member; Speaker of the European School for Scientific and Regulatory Affairs

Preparing for Phase 2 trial of HER-096 for PD

Milestone	Led by	Program	2H 2024	1H 2025	2H 2025	1H 2026	2H 2026+
Phase 1b Trial	Herantis	HER-096 for PD	●	●	●		
Phase 2 Trial	Potential Partner	HER-096 for PD				●	●
Seek Out-lic./Collab.	-	HER-096 for PD	●	●	●	●	●

Highlights

- First-in-class disease-modifying, neuro-regenerative therapeutic for Parkinson's Disease
- Phase 1 trial of key compound CDNF demonstrated clinical response in several patients, even with advanced-stage disease
- Successfully completed Phase 1a clinical trial of lead candidate HER-096
- Phase 1b trial ongoing - readout in Q3/2025
- Preparing for Phase 2 trials of HER-096 for PD

Antti Vuolanto, D.Sc. CEO antti.vuolanto@herantis.com