HERANTIS PHARMA

Phase 1a Topline Results Webinar

October 25, 2023

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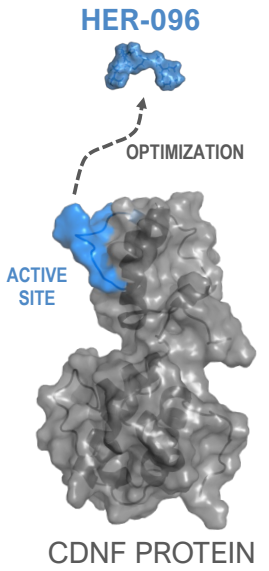
Herantis – At a Glance

- **Herantis Pharma plc** was **founded in Helsinki, Finland in 2008; Listed** at Nasdaq First North Helsinki
- **Developing disease-modifying treatment** to address the unmet clinical need in Parkinson's disease and other neurodegenerative diseases
- Lead asset **HER-096** is a small engineered peptide molecule with a **unique mechanism of action** and **subcutaneous injection** as an **easy route of administration**
- **Experienced board and management team;** Scientific advisory board with **globally leading experts in Parkinson's disease** from industry and academia
- Results from the **Phase 1a clinical trial readout** in October 2023: The trial **met primary** and **secondary endpoints**

HER-096 is a Perfect Drug Candidate for Parkinson's Disease

HER-096

- Synthetic peptidomimetic molecule
- Designed based on the active site of CDNF protein
- Unique and broad Mechanism of Action: Modulation of Unfolded Protein Response (UPR) pathway to reduce cell stress to slow down or stop the progression of Parkinson's disease
- Patient-friendly subcutaneous administration



HER-096 & Parkinson's disease treatment

- **Symptomatic improvement**
- **Long-term effect** with disease modification: slow down or stop the process of midbrain neuron degeneration at the early stage of the disease
- Subcutaneous administration 1 – 3 times per week

Multi-billion market opportunity

- 10 million patients globally
- Current Parkinson's disease pharmaceuticals market size $5B
- Market 2029: $11B, growth driven by disease-modifying treatments (source: GlobalData)

Brief Summary of the Positive Topline Phase 1a Data

- HER-096 Phase 1a clinical trial met primary and secondary endpoints
- Subcutaneous single dose injection of HER-096 had overall good safety and tolerability profile
- Pharmacokinetic data showed
  - Quick absorption of subcutaneously injected HER-096 to plasma
  - Linear pharmacokinetics across the dose groups
  - HER-096 can be delivered into the central nervous system in humans
- Next steps include:
  - Phase 1b clinical trial with the aim to demonstrate safety and tolerability for multiple (repeated) subcutaneous dosing of HER-096 in Parkinson's disease patients (planning to start the trial in 2024)
  - Preparations for Phase 2 readiness
  - Explore the potential of HER-096 in other indications

Phases of Drug Development Before Market Authorization

NON-CLINICAL DEVELOPMENT

Discovery

- Target molecule validation
- Screening of compounds

Preclinical

- Lead optimization
- Preclinical proof-of-concept
- Preclinical toxicology
- Route of administration, formulation etc

CLINICAL DEVELOPMENT

Phase 1

- Safety in healthy volunteers
- Understanding of pharmacokinetics, safe dosage
- Biomarkers, proof-of-mechanism

Phase 2

- Safety in patients
- Efficacy, clinical proof-of-concept

Phase 3

- Safety and efficacy in broader population
- Comparison to standard of care
- Quality-of-life measures

HER-096

Phase 1a

- ☑ Safety of single dose in healthy subjects
- ☑ Blood-brain barrier penetration in healthy subjects

Phase 1b

- ☐ Safety of multiple doses in Parkinson's (PD) patients
- ☐ Pharmacokinetics of multiple doses in patients
- ☐ Biomarkers in PD patients (evidence of biological response)

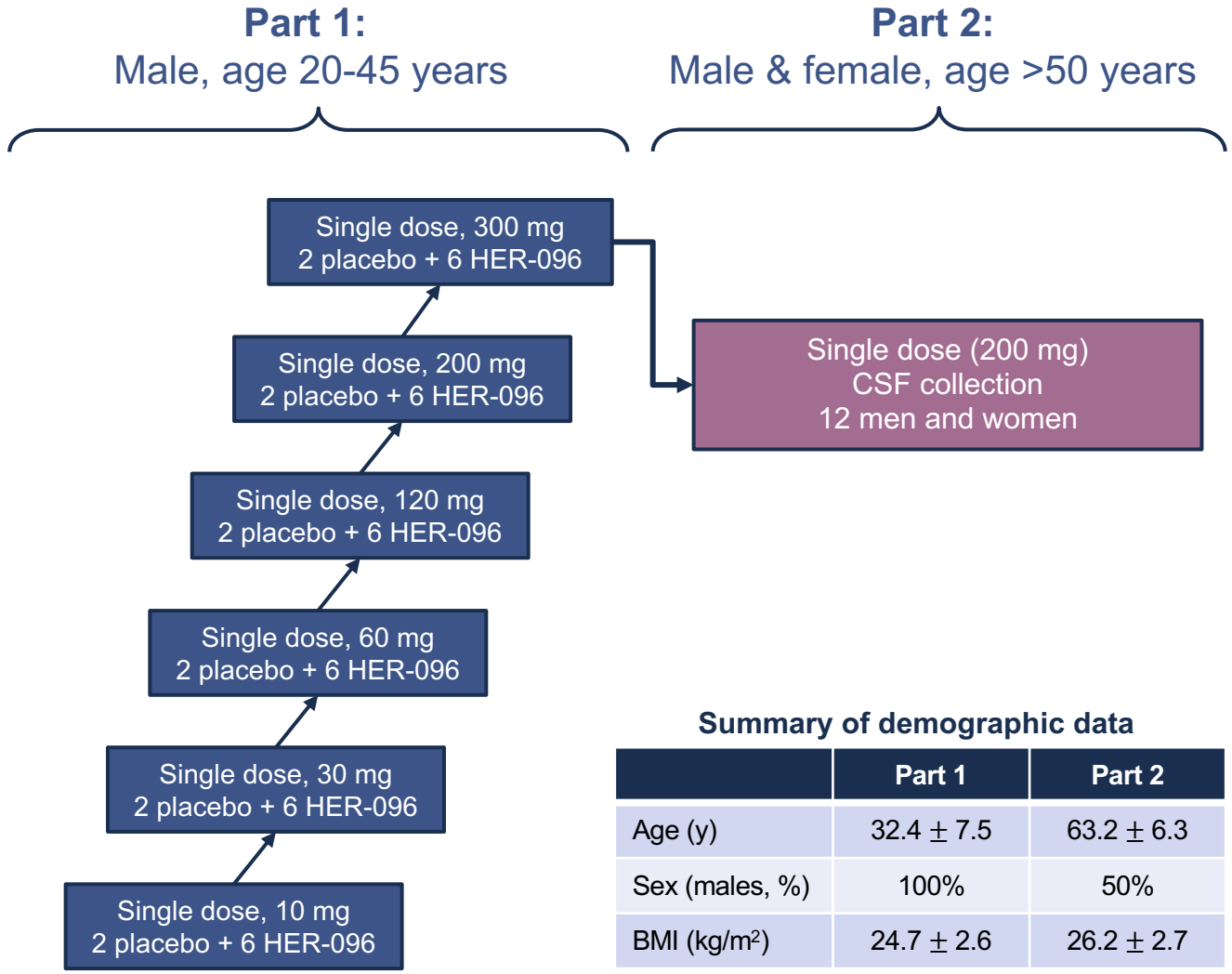
HER-096 Phase 1a First-in-Human Trial Design and Objectives

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)*]
- Exploratory biomarker analysis (on-going)



Summary of demographic data

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

Summary of Adverse Events

Part 1: Dose escalation cohort							
	10 mg (n=6)	**30 mg** (n=6)	**60 mg** (n=6)	**120 mg** (n=6)	**200 mg** (n=6)	**300 mg** (n=6)	**Placebo** (n=12)
AEs (number / subjects)	8 / 4 (67%)	11 / 6 (100%)	10 / 4 (67%)	14 / 5 (83%)	17 / 6 (100%)	25 / 6 (100%)	11 / 7 (58%)
TEAEs (number / subjects)	3 / 3 (50%)	11 / 6 (100%)	8 / 3 (50%)	12 / 4 (67%)	15 / 6 (100%)	25 / 6 (100%)	8 / 5 (42%)
Severe TEAEs (number / subjects)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)
Serious AEs (number / subjects)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)
Other significant AEs (number / subjects)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)	1 / 1 (17%)	0 / 0 (0%)	0 / 0 (0%)

Note: doses 10-60 mg were given as a single injection, doses 120-200 mg as two simultaneous injections, and dose 300 mg in three simultaneous injections.

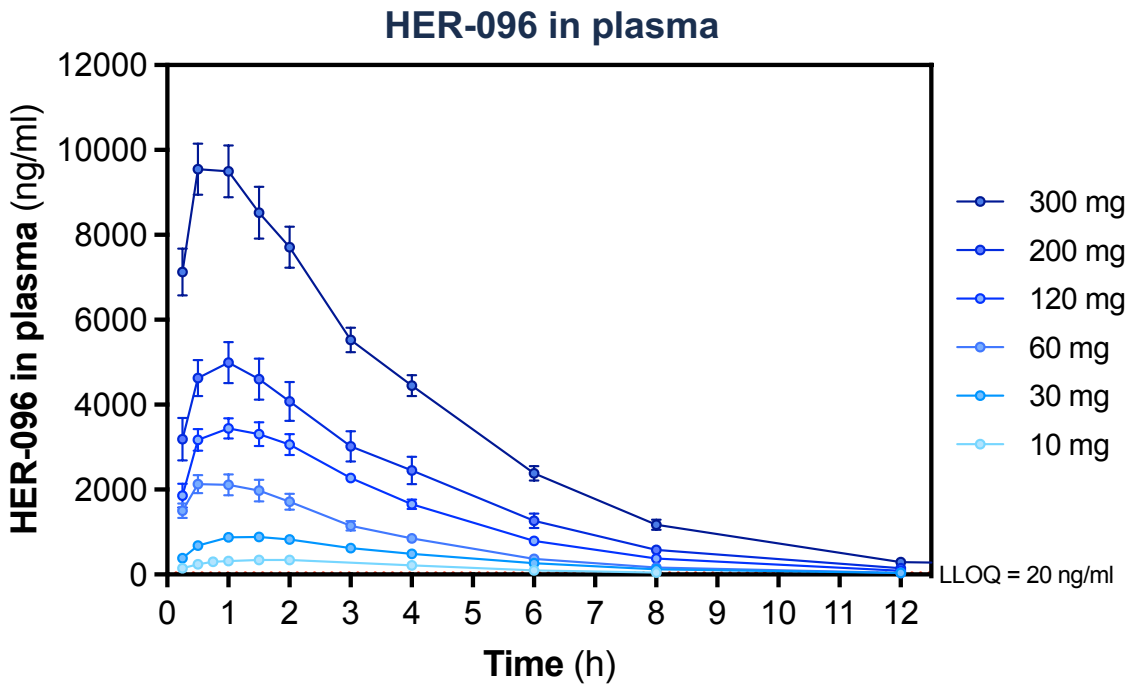
Part 2: Older/elderly cohort			
	Female (n=6)	**Male** (n=6)	**Total** (n=12)
AEs	35 / 6 (100%)	19 / 6 (100%)	54 / 12 (100%)
TEAEs	33 / 6 (100%)	17 / 6 (100%)	50 / 12 (100%)
Severe TEAEs	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)
Serious AEs	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)
Other significant AEs	0 / 0 (0%)	0 / 0 (0%)	0 / 0 (0%)

AE = adverse event
TEAE = treatment-emergent adverse event

Safety Data Allows Further Clinical Development

- Overall good safety and tolerability profile in young (20-45 y) healthy males, and older (50-64 y) and elderly (65-75 y) healthy females and males.
- No Serious Adverse Events (SAE).
- One significant AE was reported, where a subject experienced a vasovagal reaction (fainted) in relation to dosing and dosing was discontinued.
- Adverse events were mainly local reactions. Mild local injection site adverse events were reported both in the HER-096 and in the placebo groups, but number of local AEs in the HER-096 treated subjects increased with dose level and with number of injections.
- The good safety profile allows moving forward in clinical development with subcutaneous HER-096 injections.

Part 1 Pharmacokinetic Data Shows Expected Absorption and Elimination Profile in Plasma



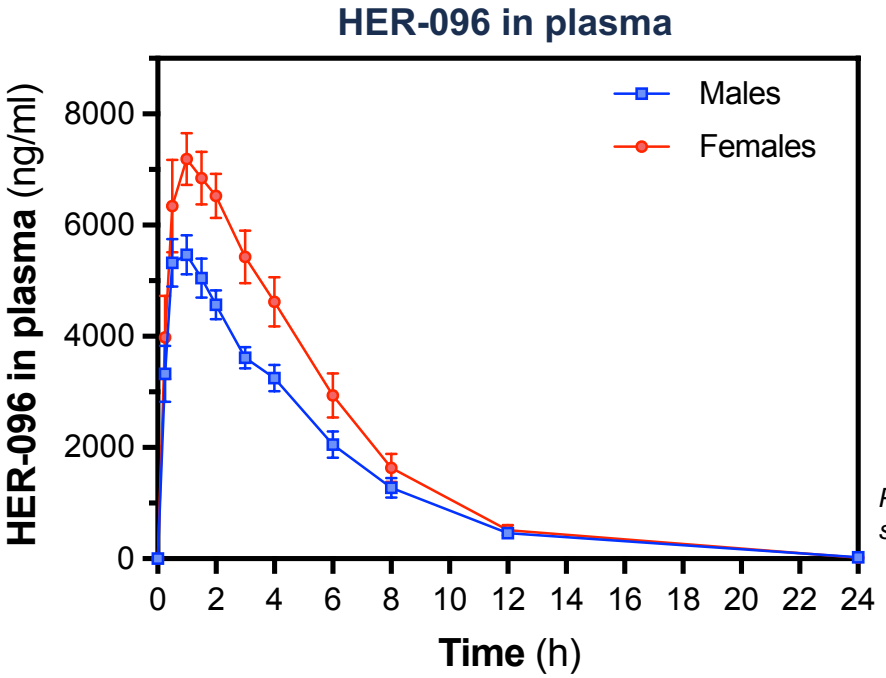
	10 mg	30 mg	60 mg	120 mg	200 mg	300 mg
C_{max} (ng/ml)	363	906	2235	3468	5406	9663
T_{max} (h)	2.01	1.34	0.71	1.14	1.06	0.81
$T_{1/2}$ (h)	1.78	1.91	1.9	1.91	1.97	2.18
AUC_{last} (h*ng/ml)	1655	4301	8453	15446	24530	42510
AUC_{inf} (h*ng/ml)	1687	4231	8462	15464	24552	42584
Lambda Z (1/h)	0.394	0.372	0.367	0.364	0.355	0.334

C_{max} = maximum concentration
T_{max} = time at which maximum concentration is reaced
$T_{1/2}$ = elimination half-life

AUC = area under the curve
Lambda Z = terminal elimination constant

- Quick absorption and expected plasma elimination half-life (appr. 2 h)
- Renal excretion is the main route of elimination as predicted by preclinical studies
- Linear pharmacokinetics between 10–300 mg helps determining safe and effective dose range

Part 2 Plasma Data Shows Similar Pharmacokinetics in Elderly Subjects

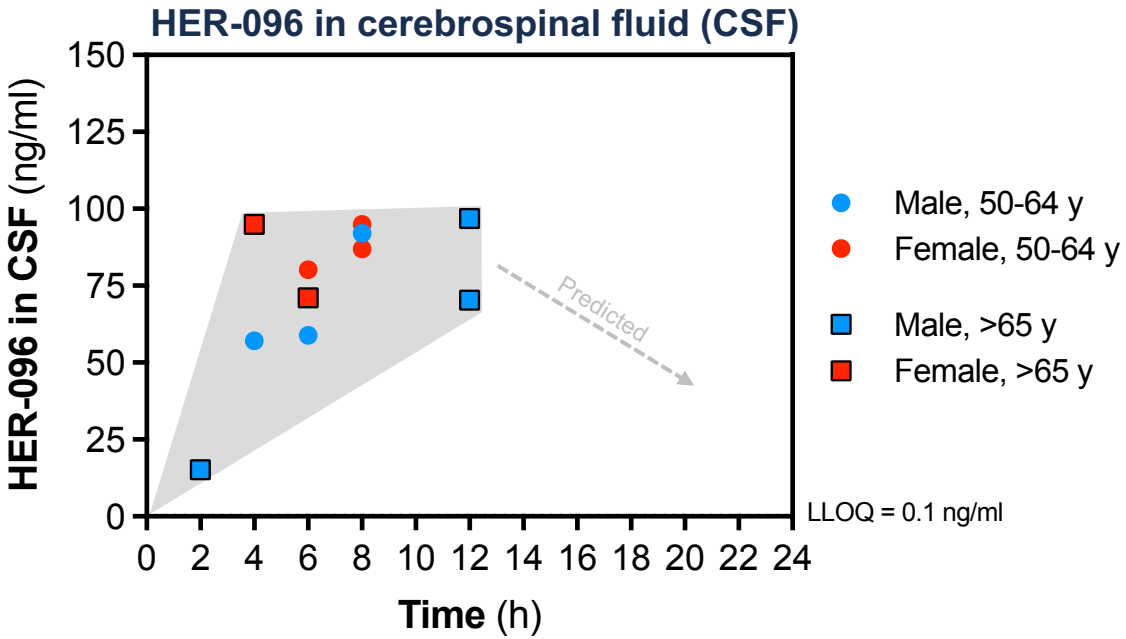


Part 2 subjects received a single 200 mg dose

	Males	Females
C_{max} (ng/ml)	5573	7333
T_{max} (h)	0.84	0.91
$T_{1/2}$ (h)	2.66	2.39
AUC_{last} (h*ng/ml)	31354	42202
AUC_{inf} (h*ng/ml)	31455	42279
Lambda Z (1/h)	0.268	0.292

- Similar to Part 1, quick absorption also in elderly subjects; plasma peak reached in less than 1 h
- Elimination half-life is slightly longer in elderly subjects (approximately 2.5 h)
- Plasma C_{max} and exposure are higher in females than in males

Part 2 Pharmacokinetic Data Shows Efficient BBB Penetration in Humans



CSF	
Mean concentration (ng/ml)	72.6 (range: 15.2 – 96.9)

- Clear evidence of HER-096 penetrating the blood-brain barrier in humans
- HER-096 (200 mg dose) reaches levels in CSF that, based on preclinical data, are predicted to be in the therapeutic concentration range
- It seems that HER-096 may remain in the CSF longer in humans than expected by the preclinical data

Phase 1a Trial: Conclusions

- Primary endpoint was met
  - Single subcutaneous dose of HER-096 (from 10 to 300 mg) were found to be safe and well-tolerated in healthy subjects
- Secondary endpoints were met
  - Single ascending doses of HER-096 in healthy subjects showed an expected plasma pharmacokinetic profile in both young and elderly healthy subjects
  - Blood-brain barrier (BBB) was tested and demonstrated in elderly healthy subjects, with cerebrospinal fluid (CSF) levels that are in a pharmacologically active range based on preclinical studies
  - In summary, the pharmacokinetic data support moving forward with subcutaneous HER-096 dosing
- Exploratory endpoints
  - Exploratory biomarkers (plasma and CSF) analyses are on-going and data will be reported later

We Have a Strong Data Package on HER-096

- We believe that we have a strong data package on HER-096 to continue clinical development and to advance the partnering process
  - Preclinical evidence of HER-096 therapeutic effects in a Parkinson's disease model (mouse a-synuclein model)
  - The first-in-man (Phase 1a) study data with HER-096: pharmacokinetics and distribution to the central nervous system well aligned with preclinical evidence
  - Clinical experience in Parkinson's patients with CDNF protein that shares the same mechanism of action with HER-096
- Key preclinical data
  - Protection of dopamine neurons, proteostatic effect on α-synuclein, decrease in neuroinflammation
  - Increased brain dopamine level
  - Improvement of motor symptoms

Summary

What we want to achieve with HER-096?

To develop a treatment to slow or stop the progression of Parkinson's disease with symptomatic relief

Evidence of subcutaneous HER-096

- Therapeutic concentration of HER-096 in the central nervous system in humans
- Good safety and tolerability profile in humans
- Therapeutic effects in aged mouse model of Parkinson's disease

Next steps

- Phase 1b to start in 2024 (safety, tolerability of multiple subcutaneous dosing in PD patients)
- Prepare for Phase 2 readiness
- Explore HER-096 in other indications

Strategy

Find a global development partner for HER-096

Thank you!

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