HERANTIS PHARMA

Toward clinical breakthroughs based on leading science

Life Science Investorkonference, Copenhagen 18 Sep 2019 Pekka Simula, CEO

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Herantis Pharma Plc

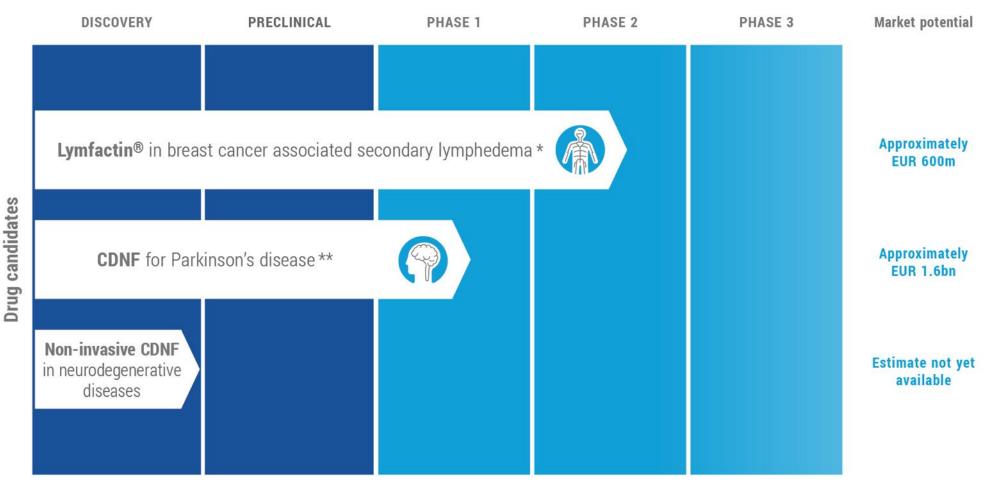


- Herantis Pharma is a public drug development company with two highly differentiated assets for unique market opportunities:
 - → CDNF to **stop progression of Parkinson's disease**, with disease-modifying potential also in other neurodegenerative diseases
 - → Lymfactin® gene therapy targeted as first curative treatment of secondary lymphedema
- Programs originate from scientific discoveries made by worldleading researchers, published in Nature and Science
- Both assets are in clinical PoC studies; the company is fully funded to reach unblinding in both randomized trials
- Listed in Nasdaq First North Helsinki

→ Considering dual-listing in Sweden, one of Europe's most active markets



CDNF and Lymfactin® are in placebo-controlled studies that target significant unmet needs

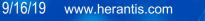


* Randomized, double-blind, placebo-controlled Phase 2 clinical study ** Randomized, double-blind, placebo-controlled Phase 1/2 clinical study



Neuroprotective factor CDNF

for stopping the progression of Parkinson's disease

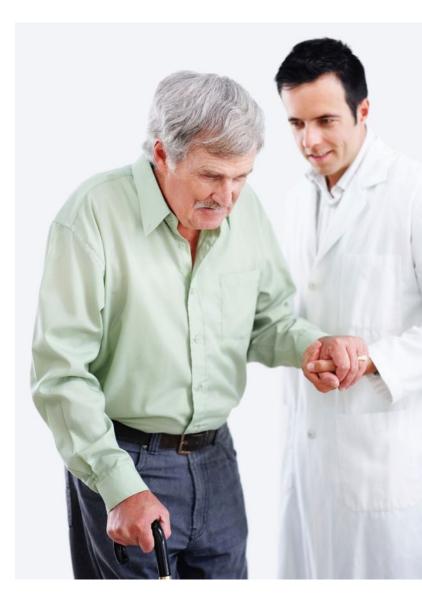




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Parkinson's disease (PD)

- Second most common neurodegenerative disease impacting 7-10 million people
- Current therapies only alleviate motor symptoms of PD
- Estimated annual financial burden of PD is \$50 billion
- Progression-stopping therapy would save the society over
 \$400,000 per patient in the USA*



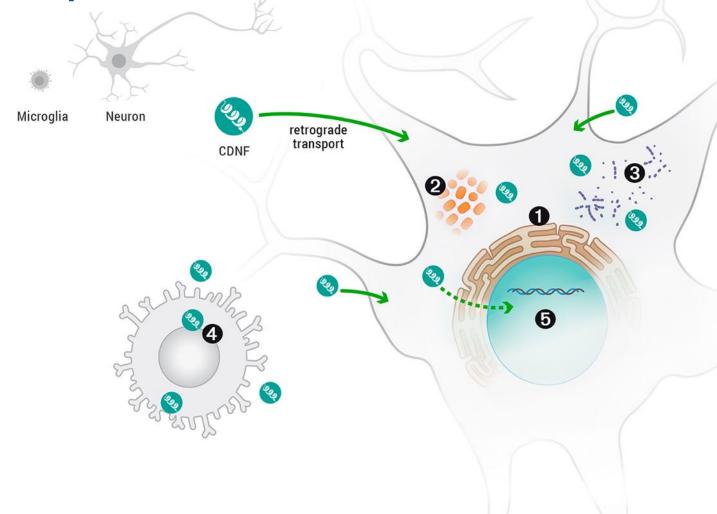
*University of Pennsylvania's National Parkinson Foundation



CDNF promotes neuronal survival and recovery through multiple relevant mechanisms

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• CDNF promotes neuronal survival and functionality by reducing endoplasmic reticulum (ER) stress

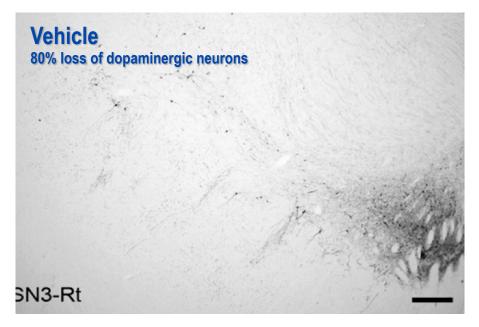
2 CDNF promotes neuronal survival by activating Protein Kinase B (Akt)

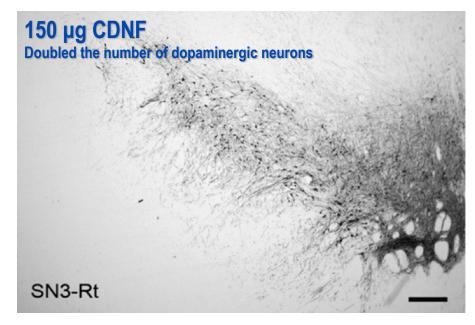
3 CDNF inhibits α-synuclein oligomerization and toxicity

CDNF suppresses production and secretion of proinflammatory cytokines by glial cells

G CDNF supports maintenance of neuronal functions by enhancing transcription of genes involved in e.g. dopamine synthesis and metabolism

CDNF doubled the number of neurons in a PD model*





- Disease model: MPTP lesion model in aged Rhesus monkey
- Three monthly CDNF doses doubled the number of DA neurons
- Significant improvement in gross motor function, fine motor function, and for the first time in the world, non-motor symptoms

* Research collaboration with University of Pittsburgh funded by Michael J. Fox Foundation



CDNF may change how patients live with PD

Currently in Phase 1-2 clinical study funded by EU: "Leading science, greatest potential to advance clinical practice"



Study fully recruited: 17 patients randomized in CDNF vs. placebo groups

- Topline results expected by end of 2019
- > First-in-human study in advanced PD patients \rightarrow Primary endpoint is safety



Objectives of ongoing phase 1-2 CDNF study in PD*

Herantis has been applauded on the design of the FIH study for including placebo control, and an advanced PET imaging endpoint

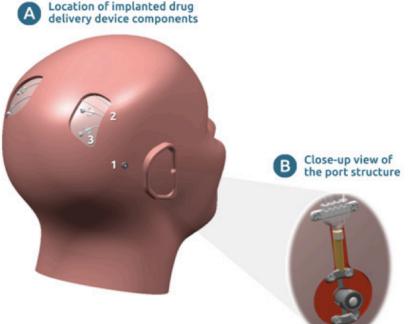
- Primary objectives:
 - \rightarrow Safety and tolerability
- Secondary objectives (Functional and biomarkers):
 - \rightarrow UPDRS motor score and total score
 - \rightarrow TUG test
 - \rightarrow PDQ-39 quality-of-life questionnaire
 - \rightarrow CGI-I
 - → Brain PET measuring nigrostriatal DAT availability (presynaptic terminals)
 - \rightarrow CSF levels of α -synuclein (total, serine 129 ph., oligometric)
 - → Activity measurement by Parkinson's KinetiGraph[™] actigraphy device

*EudraCT number: 2015-004175-73, NCT number: 03295786



Next generation: xCDNF

 Common challenge in brain diseases is drug delivery in the brains → CDNF is dosed with sophisticated medical device



- We have shown that certain fragments of CDNF:
 - 1. Retain its biological activity (comparable efficacy in PD models)
 - 2. Penetrate the BBB \rightarrow much simpler administration
 - 3. Have potential in several indications beyond PD: E.g. Alzheimer's, ALS, stroke

Based on current data xCDNF could be administered as easily as insulin



CDNF has a uniquely compelling mechanism among the few therapies with disease-modifying potential

Many PD therapies target dopamine-based mechanisms for motor symptom relief

	ACØRDA	Neuro Derm	PHARMA	
Therapies	CVT-301	ND-0612	ODM-104	VYAADC-01
Phase	Phase 3	Phase 3	Phase 2	Phase 2
МоА	Increases dopamine concentration	Increases dopamine concentration	COMT inhibitor that prolongs dopamine presence in brain	Provides dopa decarboxylase gene to putamen
Molecule Type	Small Molecule	Small Molecule	Small Molecule	Gene Therapy
RoA	Inhaled L-dopa	Long acting intravenous L- dopa	Oral	Intracerebral
Disease- Modifying	×	×	×	×

Few therapies are potentially disease modifying, and among those CDNF has the most compelling mechanism

HERANTIS	MEDGENESIS	Roche	Calico
CDNF / xCDNF	GDNF	PRX002	ISRIB
Phase 1-2 / Discovery	Phase 2	Phase 2	Preclinical
Multi-modal: Reduction of ER stress, α-syn oligomerization and toxicity	Activates GFRα/Ret signaling	Reduction of α- synuclein	Activates eIF2B to reduce integrated stress response
Protein / Peptide	Recombinant Protein	Monoclonal Antibody	Small Molecule
Intracerebral / Subcutaneous	Intracerebral	Intravenous	Intravenous
\checkmark	\checkmark	\checkmark	\checkmark



Lymfactin® gene therapy for curing secondary lymphedema



Secondary lymphedema

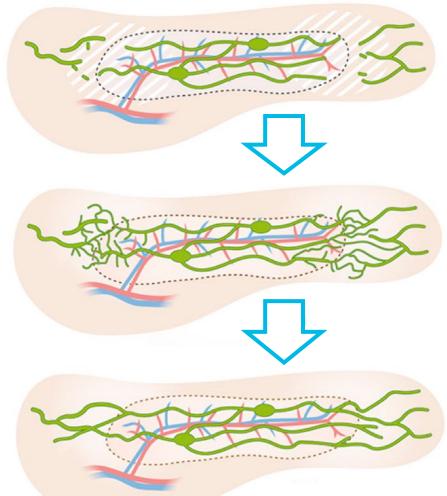
- Lymphedema (LE) is chronic, progressive swelling due to accumulation of lymph
 - \rightarrow Disabling and disfiguring disease
 - \rightarrow No approved drugs for treatment
- Herantis' Lymfactin® is a gene therapy that aims to repair the lymphatic system





Lymfactin®: VEGF-C gene therapy to reconstitute the lymphatic system

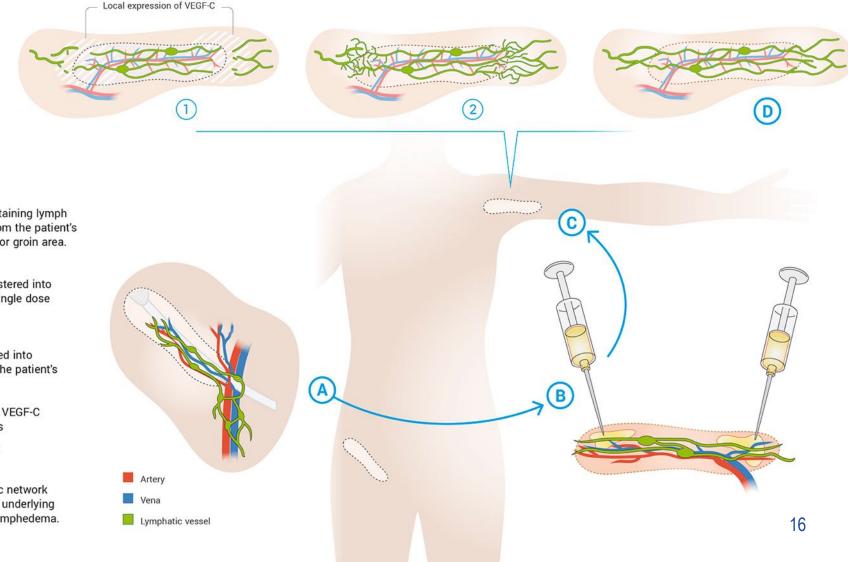
- 1. A single Lymfactin® injection results in local VEGF-C expression for about 2 weeks
- 2. VEGF-C is the natural human protein that promotes the **growth of lymphatic capillaries**
- 3. Lymphatic capillaries mature into functional lymphatic vessels, reconstituting the lymphatic system





First target: Breast cancer associated LE (BCAL)

Adjunct therapy for patients undergoing lymph node transplantation



- A. A soft tissue flap containing lymph nodes is harvested from the patient's lower abdominal wall or groin area.
- **B.** Lymfactin® is administered into the flap *ex vivo* as a single dose administration.
- **C.** The flap is transplanted into the axillary region of the patient's affected upper limb.
 - 1. Local expression of VEGF-C for about two weeks
 - 2. Lymphangiogenesis
- D. A functional lymphatic network is formed treating the underlying cause of secondary lymphedema.

Lymfactin[®] development

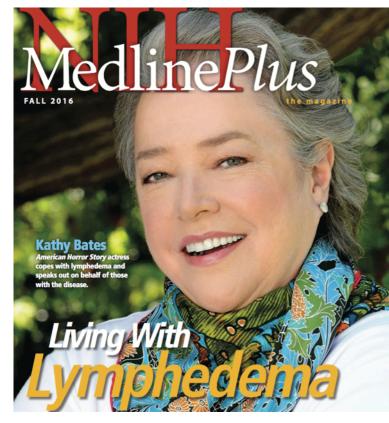
- Actively recruiting patients with breast cancer associated LE (BCAL)
 - → Adjunct to lymph node transplantation surgery, which attempts to relieve symptoms
 - \rightarrow Study centers: 5 university hospitals in Sweden and Finland
- Safety established in Phase 1 study with same setup
 - → Promising improvements observed in signs and symptoms of LE (uncontrolled data)

- Target: 40 patients randomized in Lymfactin[®] vs. placebo groups
 Topline results expected by end of 2020 (12-month follow-up)
- Primary endpoints: Efficacy in signs and symptoms of LE



Lymphedema: Market and awareness

- 140 million LE patients worldwide
- Annual cost of lifelong symptomatic treatment \$10,000 - \$20,000 (USA)
- €600M market for Lymfactin® as an adjunct therapy in BCAL*
 - \rightarrow Significant potential in other lymphedemas
- Lymphedema awareness increases
 - → Herantis is a partner of LE&RN, international patient advocacy group



 \rightarrow Hollywood superstar Kathy Bates is an active LE&RN spokesperson



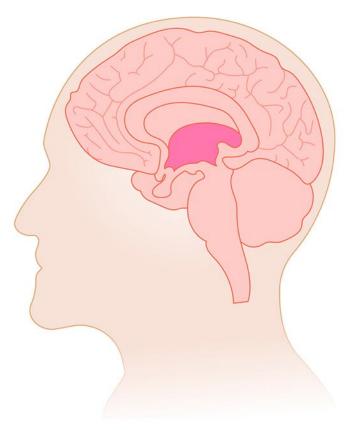
Summary

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Herantis Pharma

- Targeting disease modification in significant unmet medical needs, large and well-defined markets
- Programs based on internationally renowned science published in Nature and Science
- Funded to **reach unblinding** in two randomized clinical studies
- Considering possible dual listing in First North Sweden in 2019





About Herantis' management and shareholders

- International and experienced Board of Directors
- Herantis' management has actively purchased shares both from the market and participated in share issues
- All insider trading published on the company's website
- Cornerstone investor in last funding round (3/2019) was Swedbank Robur's global healthcare fund, Medica



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Thank you

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