HERANTIS PHARMA

In situ regenerative medicine based on leading science

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Herantis Pharma Plc

- Herantis is a public drug development company advancing **two highly differentiated clinical assets for unique market opportunities**
  - **CDNF therapy for Parkinson's Disease**, with potential in treating other neurodegenerative diseases
  - **Lymfactin® gene therapy for secondary lymphedema**
- Both programs originate from scientific discoveries made by **world-leading researchers** at the University of Helsinki, Finland
- Currently funded through clinical PoC, expected in the next 18 months
- Evaluating further financing options

See brief introductory videos on our assets: http://herantis.com/media/videos/

Neuroprotective factor CDNF for stopping the progression of Parkinson's disease

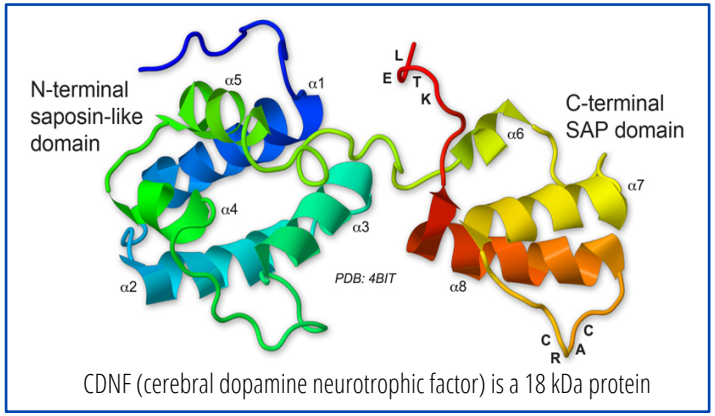
Parkinson's disease (PD)

- PD is the second most common neurodegenerative disease impacting estimated 7 million people
  - Common first symptoms include tremors, slowed movement
- **Available therapies only alleviate motor symptoms of PD**
  - current PD drug market is approximately $3 billion
- Estimated financial burden of PD in Europe: **€13.9 billion**
- Disease-stopping therapy would save the society over **$400,000** per patient* in the USA

*University of Pennsylvania's National Parkinson Foundation

CDNF is a potent neuroprotective factor that promotes neuronal survival

- CDNF is an endogenous protein **promoting the survival and differentiation of neurons**, and the **maintenance of neuronal functions**
  - Protects and recovers dopaminergic neurons from Endoplasmic Reticulum (ER) stress
  - Inhibits formation of toxic α-synuclein oligomers
  - Suppresses neuroinflammation
  - Increases transcription of several genes involved in dopamine synthesis and metabolism

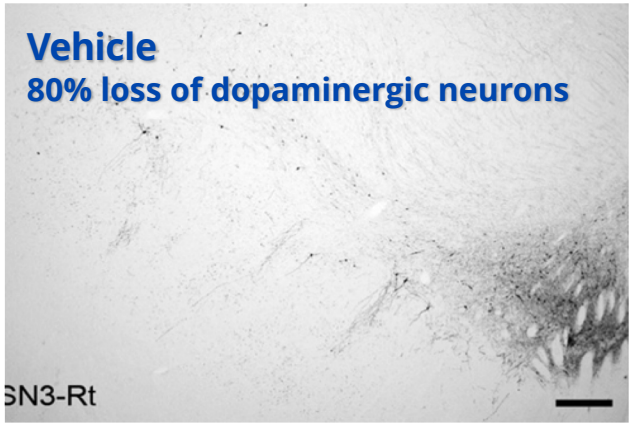


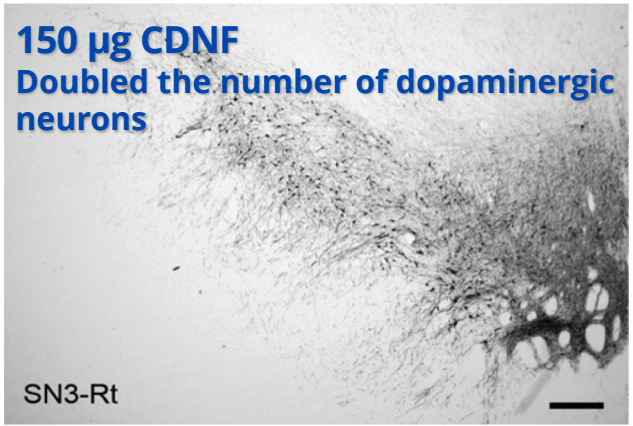
CDNF (cerebral dopamine neurotrophic factor) is a 18 kDa protein

- Based on broad preclinical data **CDNF relieves** both **motor** and **non-motor symptoms** and shows potential to even **stop disease progression**
- CDNF is very distinct from and **superior to conventional neurotrophic factors**

CDNF protects and recovers dopaminergic neurons in non-human primate model of PD

- MPTP neurotoxin induced lesions in rhesus monkeys resulted in 80% loss of dopaminergic neurons in the substantia nigra
- Staining: Tyrosine hydroxylase-staining of lesion-side substantia nigra sections from vehicle and CDNF-treated monkeys
- **Dark color indicate dopaminergic neurons**





- Gross motor functions were improved by 53% (MPDRS*) at three months of dosing compared to vehicle control
- Improvement in fine motor functions (recovery in the use of the affected-side hand in the mMAP** test)

*monkey Parkinsonian disability rating scale
**monkey movement analysis panel

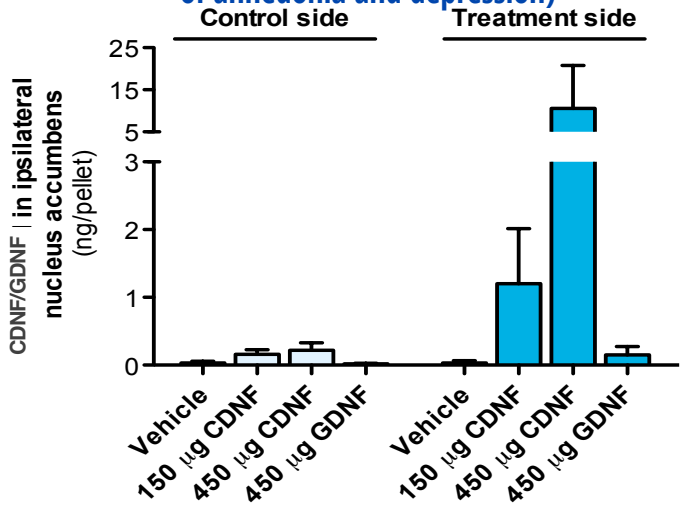
Research collaboration with University of Pittsburgh
funded by Michael J. Fox Foundation

CDNF improves non-motor symptoms in non-human primate model of PD

- MPTP neurotoxin induced PD model in rhesus monkeys
- CDNF-treated monkeys showed significantly reduced depressive behavior (Human Intruder Test)
  - **First treatment that has shown a reduction** in depressive behavior in this unilateral model of PD
- Improved motivation (Wisconsin General Apparatus)
  - Reduced motivation post-MPTP lesion associated with motor dysfunction
  - GDNF* group showed no improvement
  - CDNF-treated groups showed significant improvement in motivation

Findings correlate with elevated CDNF levels in ipsilateral nucleus accumbens

(the primary cognitive processing site for aversion, motivation and reward, also involved in development of anhedonia and depression)



*GDNF = Glial cell-derived neurotrophic factor

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

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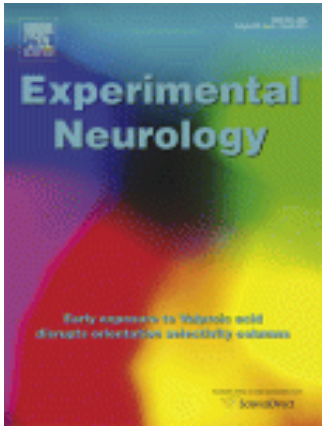
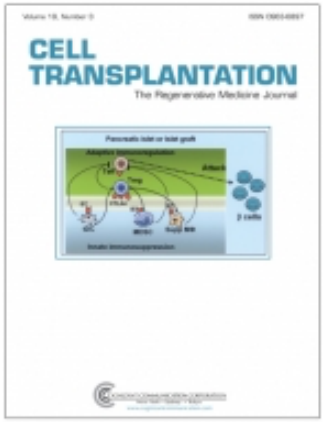
Robust science: *in vivo* data demonstrating MoA

Vol 448, 5 Jul 2007;
Lindholm et al
Novel neurotrophic factor CDNF protects and rescues midbrain dopamine neurons *in vivo*



Vol 228, Issue 1, 2011;
Voutilainen et al
Chronic infusion of CDNF prevents 6-OHDA-induced deficits in a rat model of Parkinson's disease



Vol 21, Issue 6, 2012;
Airavaara et al
CDNF protects the nigrostriatal dopamine system and promotes recovery after MPTP treatment in mice

Vol 11, Issue 6, 2012;
Nadella et al
Transient transfection of human *CDNF* gene reduces the 6-hydroxydopamine-induced neuroinflammation in the rat substantia nigra

CDNF is in a randomized clinical PoC study

- **Randomized, placebo-controlled Phase 1-2** in PD at esteemed centers in EU
  - 18 patients with PD of moderate severity, randomized to 6 on placebo, 12 on the active
  - Topline data expected by end of 2019
- The study is funded by a prestigious Horizon 2020 EU grant: **"Leading science, greatest potential to advance clinical practice"**
- CDNF is administered intracranially once monthly using sophisticated delivery device
  - CDNF does not permeate the BBB
  - A clinically tested drug delivery system (Renishaw Plc) is implanted in a standardized surgery and used for monthly dosing

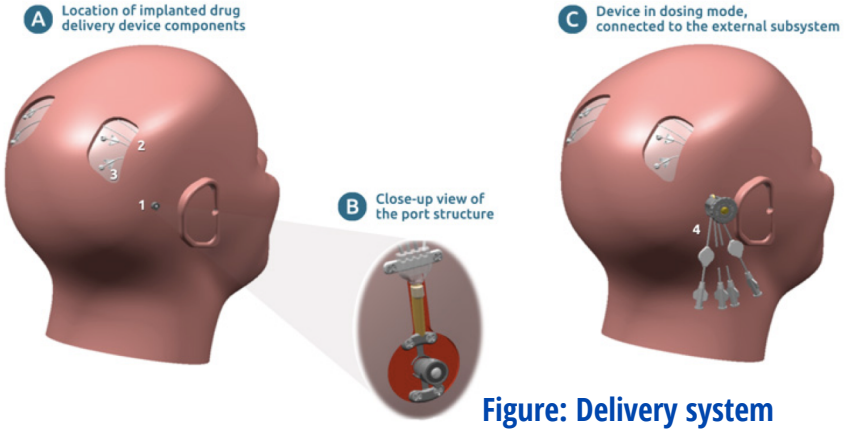
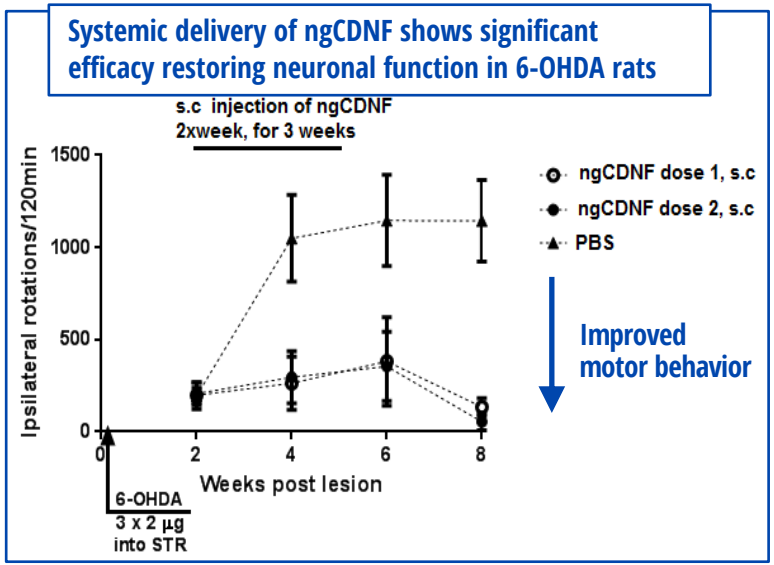


Figure: Delivery system for CDNF dosing

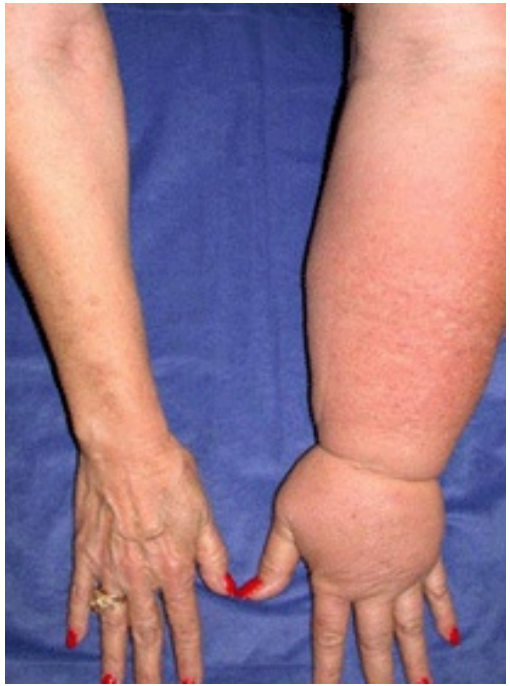
Next generation, non-invasive CDNF ('ngCDNF')

- Professor Saarma's group at the University of Helsinki have **discovered a non-invasive ngCDNF**
  - **Restoration of normal motor function** shown *in vivo* in 6-OHDA PD model with subcutaneous peripheral delivery
  - **Cytoprotective effects of ngCDNF shown**
  - Enormous potential beyond PD: Alzheimer's disease, ALS, stroke
- **Herantis has an exclusive, worldwide ngCDNF license**
  - Non-invasive development program was initiated in Q3/2018



Lymfactin® gene therapy for curing secondary lymphedema

Secondary lymphedema: Disease, Market and Awareness



- **Lymphedema (LE)** is a chronic, progressive swelling of tissue caused by a dysfunction of the lymphatic vasculature
  - Lymphatic system is unable to return interstitial fluid to bloodstream
  - Estimated **140 million people** worldwide have LE; there is no cure
  - Estimated treatment cost **$10,000 per year** in the USA
- **Secondary lymphedema** is caused by e.g. disease, trauma, or surgery
  - **Disabling and disfiguring disease**, which severely affects quality of life
- **Lymphedema awareness is rapidly increasing**
  - Hollywood superstar, lymphedema advocate **Kathy Bates is among the strong LE spokespersons** working with the active patient advocacy group LE&RN

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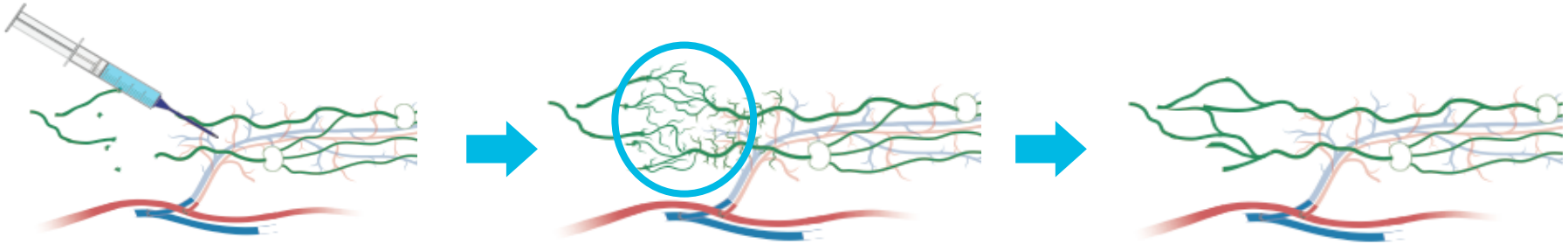
Lymfactin® gene therapy
is designed to repair the cause of secondary lymphedema

- Lymfactin® is a recombinant replication deficient **Adenovirus type 5 gene transfer vector**
- Delivers human VEGF-C growth factor gene to **specifically promote lymphangiogenesis**
- VEGF-C is produced by the human cells in the damaged area where Lymfactin® is administered
- Single-dose treatment with **local and transient VEGF-C expression** for about two weeks



1. Lymfactin® administration

2. VEGF-C expression in the damaged tissue ➔ lymphangiogenesis

3. Functional lymphatic network

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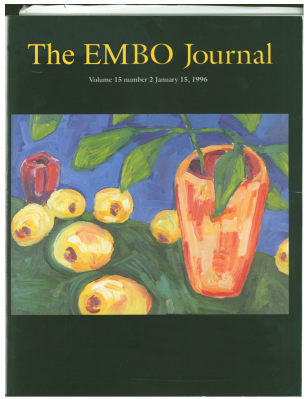
Robust science:
from VEGF-C discovery to adenoviral VEGF-C gene therapy



Vol 15, Issue 2, 15 Jan 1996;
Joukov et al
A novel vascular endothelial growth factor, VEGF-C...

Vol 276, Issue 5317, 30 May 1997;
Jeltsch et al
Hyperplasia of lymphatic vessels in VEGF-C transgenic mice

Vol 5, Issue 1, Jan 2004;
Karkkainen et al
Vascular endothelial growth factor C is required for sprouting...

Vol 18, Issue 14, Nov 2004;
Saaristo et al
Adenoviral VEGF-C and VEGF-C 156S restore drainage of lymphatic fluid across the incision wound

Lymfactin® development

- Currently developed in **breast cancer associated secondary lymphedema (BCAL) in combination with lymph node transfer**
- **Phase 1 completed** in 15 patients with BCAL: Lymfactin® is safe and well tolerated
  - Promising quality-of-life changes observed; however those are uncontrolled data
- Randomized, placebo-controlled **Phase 2 study ongoing**
  - 12 months efficacy data expected by end of 2020
- Estimated **$600M market** in the current indication in USA+EU5*
- Significant potential in other forms of secondary lymphedema
- Naive market with no competitive products

*Market research, Back Bay Life Science Advisors, 2017

Investment opportunity

Investment opportunity

- Herantis' ongoing clinical studies are fully funded
- **Next step:** funding for pivotal / Phase 2-3 of both programs, as well as expanding in further indications and next generation CDNF
- Significant disease modifying potential in **large and well-defined markets**
- Herantis is considering options for further financing such as a US IPO in addition to current listing on Nasdaq First North Helsinki

Herantis Pharma summarized

- Herantis' two lead clinical programs are targeting disease modification and addressing significant unmet medical needs **in large and well-defined markets**
  - **CDNF protein therapy provides a ground-breaking treatment** with broad potential for disease modification in Parkinson's Disease and other neurodegenerative diseases
  - **Lymfactin® gene therapy serves an under-appreciated and significant market need**
- Company is well positioned to reach significant value inflection points in 18 months

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Thank you

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