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Basic research translated into therapy for brain diseases

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- Early stage drug development company – no sales! Focus and expertise in:
  - Finding promising drug candidates especially from universities
  - Continuing where academic funding typically ends:
    - Drug manufacturing
    - Preclinical development
    - Early clinical studies aiming at clinical proof-of-concept
    - Finding the money to complete all of the above
    - Finding commercial partners for late stage development

- Focus in developing growth factor-based therapies in indications with significant unmet clinical needs
  - CDNF (from Professor Mart Saarma's group): Parkinson's disease
  - Lymfactin (from Professor Kari Alitalo's group): Secondary lymphedema

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Case example: Parkinson's disease

- Parkinson's disease (PD) is a progressive neurodegenerative disease, which cannot be cured
  - Common early symptoms include tremors, slowed movement, impaired balance
  - Non-motor symptoms such as depression, sleep disorders, sexual dysfunction as the disease progresses; often even more disruptive to quality-of-life than motor symptoms
  - Estimated 7.000.000 patients worldwide
  - Europe's financial burden caused by PD in 2010: €13,9 billion

- Available PD treatments are symptomatic and only help the motor symptoms caused by disease
  - Two huge unmet clinical needs: Addressing non-motor symptoms, and slowing down or stopping disease progression

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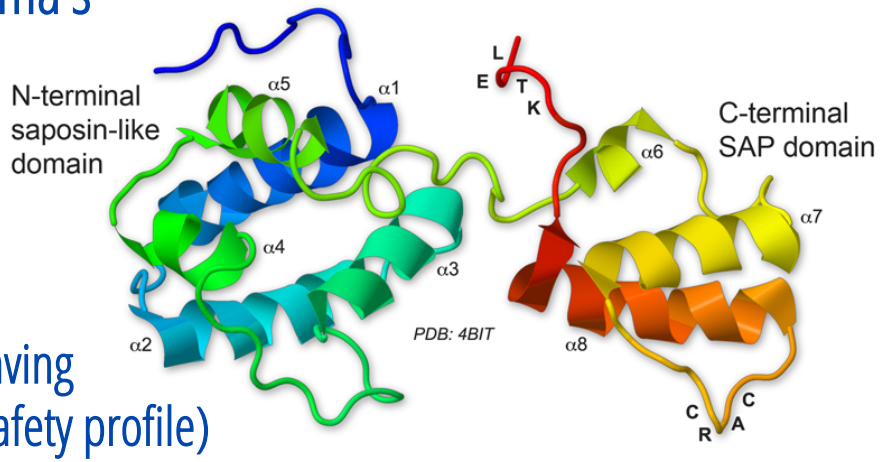
Development of potential PD drug : Where does it start?

- New protein identified by professor Mart Saarma's group at the University of Helsinki: CDNF, Cerebral Dopamine Neurotrophic Factor
  (Lindholm et al, Nature 448: 73-77, 2007)
  - ✓ Found in normal human plasma and CSF
  - ✓ Described as a CNS-specific neurotrophic factor leaving peripheral neurons unaffected (benign expected safety profile)



- Early finding: CDNF protects dopaminergic neurons
  - ✓ Link to Parkinson's disease: PD is caused by the death of dopaminergic neurons
  - ✓ Seems more potent than similar clinically tested compounds such as GDNF

→ Potentially interesting drug candidate for Parkinson's disease?

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CDNF in Parkinson's: How to get from bench to bed-side?

- Drug development always requires clinical studies
  - Clinical studies always require an extensive preclinical regulatory program of little scientific interest
  - Ballpark budget estimate for a novel biological PD drug candidate from academia through a first clinical study: € 10 million → definitely out of reach by academic funding
  - Two usual options remain for academic groups:

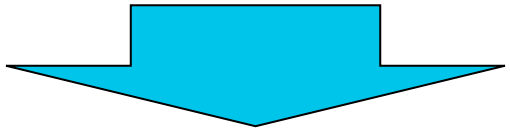
1. Find a commercial partner

- Very challenging for biological compound with a novel mechanism-of-action
- Development will be slow even in terms of drug development
- Risks may be considered too high

OR

2. Found a startup company

- Very challenging to find investors for same reasons
- Keeps development in the hands of the inventors



Herantis Pharma founded in 2008 as Hermo Pharma Ltd

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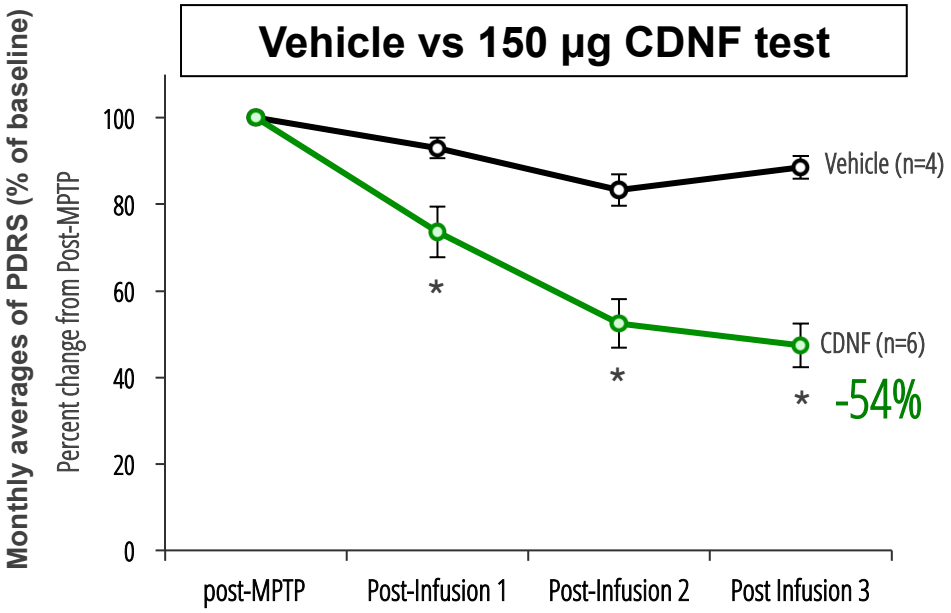
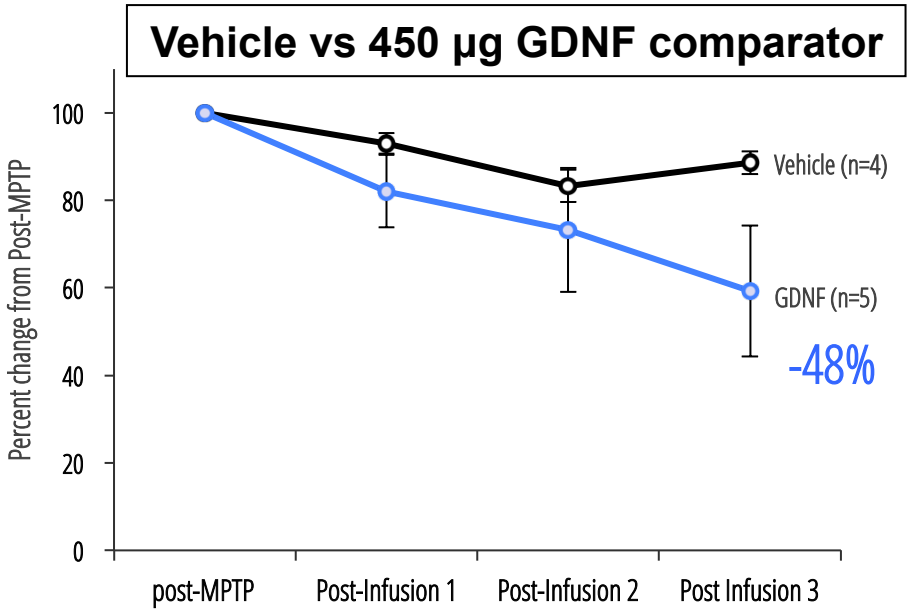
Thanks to investments in the company, and Michael J. Fox Foundation grant to professor Mart Saarma, new really exciting data were created

Non-human primate study in collaboration with University of Pittsburgh, MPTP lesion PD model

- Monthly intermittent infusions of CDNF strongly improve motor function (figure)
- CDNF also significantly reduced depressive behavior in the human intruder test
  - No other treatment has shown a reduction in depressive behavior in this unilateral PD model
- CDNF also improved motivation; positive control (GDNF) showed no improvement





Approaching a First-in-Human clinical study of CDNF

Patience and preclinical development has lead to readiness of first-in-human clinical study

- Funding for the study already secured by an investment round in 2014, and Tekes R&D loan

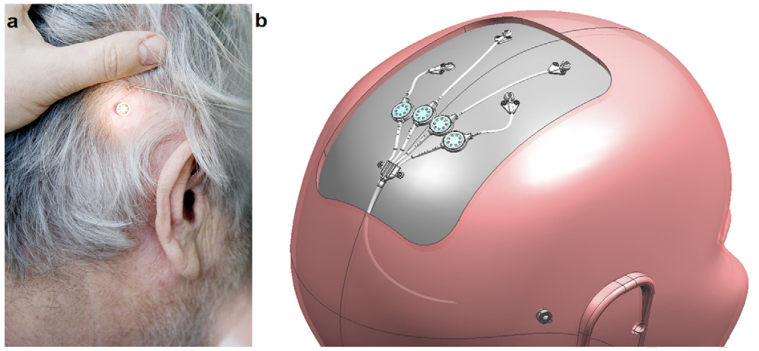
A Phase I-II, randomized, double-blind, placebo-controlled, partial cross-over, safety study

- Primary objectives are safety and tolerability
- Secondary objectives aim to also show benefits of the treatment
  - For instance advanced PET imaging based assessments
- Study to be conducted in 18 patients with idiopathic Parkinson's disease
- 4 study sites selected: Helsinki, Turku, Stockholm, Lund
  - Helsinki has the required surgical expertise in Parkinson's disease
  - Turku has a world-class PET imaging center

Planned clinical administration of CDNF

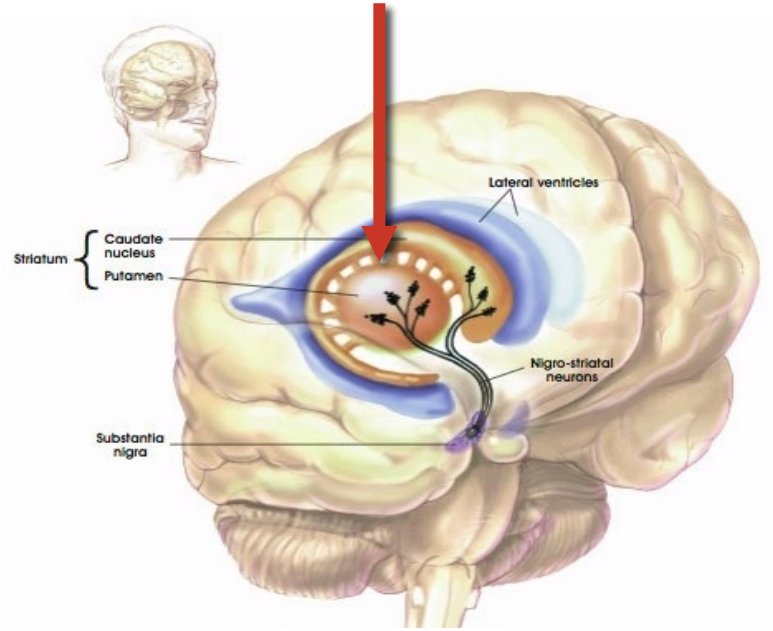
- Therapeutic proteins need special methods of delivery in order to cross the blood-brain barrier
- In Parkinson's disease, dopaminergic neurons degenerate in a highly localized area of the brain
  → localized administration by infusion feasible
- First-in-human studies with CDNF will be carried out using neurosurgically implanted catheters (bilateral, putamen) to maximize efficacy
  - ✓ The surgical procedure is similar to implantation of deep brain stimulators (DBS), which have become a standard therapy in PD with >100,000 devices implanted to date
- British company Renishaw Plc develops a drug delivery system (DDS) suitable for monthly intermittent Convection Enhanced Delivery (CED) to the putamen
  - ✓ Diffusion in the target organ/infusion site (putamen) is critical for efficacy
  - ✓ CDNF has ~2x larger volume of diffusion in brain than GDNF

Figure: Illustration of a way to administer CDNF



Barua et al. J. Neurosci. Methods 214: 223-232, 2013.

1-2 intraputamenal catheters
(per hemisphere) connected to a
transcutaneous bone-anchored port



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Development schedule in Parkinson's disease

- Herantis intends to submit Clinical Trial Applications by the end of 2015
  - Quite uniquely Finnish study: CDNF found and patented in Finland, developed by a Finnish company, manufactured in Finland, clinical study planned to be conducted in Finland (and Sweden)
- Patient recruitment hoped to start in 1H/2016
- Even if the regulatory processes are completed in schedule a lot of patience is still required: Topline data expected by end of 2017
- Thereafter, with strong data, the sky is the limit…
  - Development costs will be sky high…
  - And the potential results will be sky high. CDNF could change the lives of millions of patients and their families

We hope to continue further work in other indications – case ALS

ALS is an aggressive motoneuron disease with no cure. In preclinical studies, a single CNDF injection has prolonged survival and reduced symptoms in a mouse model of ALS.

- Estimated 140,000 diagnosed cases per year worldwide
- First symptom typically weakness of limb muscles
  - Disease progression causes difficulty in moving, speaking, swallowing, and eventually breathing, leading to death typically in 2-5 years from diagnosis
  - Huge unmet clinical need – no known treatments that provide essential help
- Financial burden of motoneuron diseases in Europe: €7.7 billion
- Herantis plans to proceed to clinical development if funding for a development program can be secured
  - Finland has great ALS expertise – how to ensure development continues here?

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Thank you

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