HERANTIS PHARMA

# Toward clinical breakthroughs based on leading science

ABGSC Life Science Summit, 26 May 2020

Pekka Simula, CEO

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# Today's presenter

**Pekka Simula**
*Chief Executive Officer*
*M.Sc. in Physics*
Joined Herantis: 2013

**Previous experience:**

- 2013 - : CEO at Herantis Pharma
- 2012 – 2013: COO at Oncos Therapeutics
- 2009 – 2012: CEO and founder at Oncos Therapeutics
- 2004 – 2008: Global Program Manager at Varian Medical Systems
- 2000 – 2004: Project Director at CRF Health

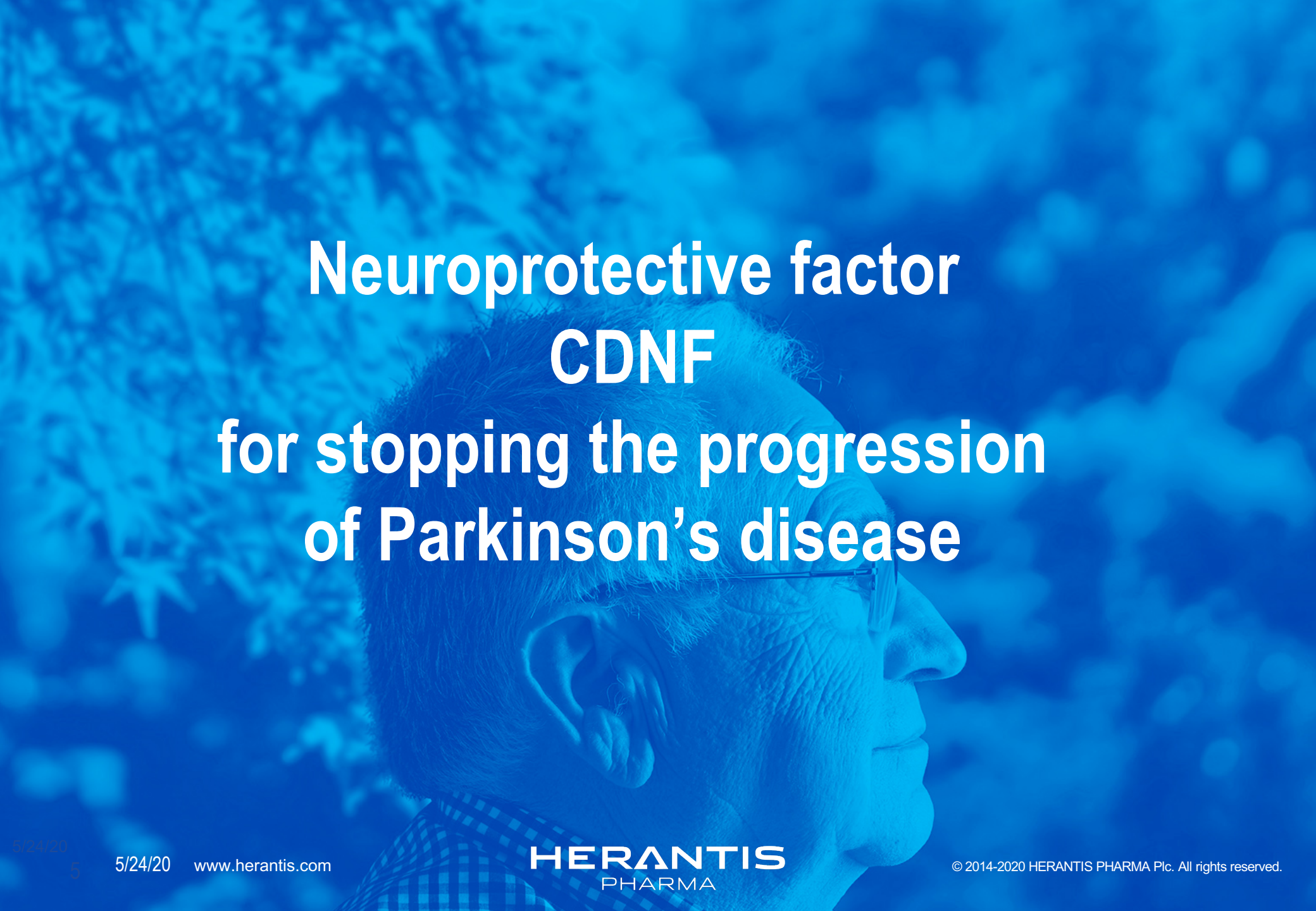
**Other current positions**

- Chairman of Health & Wellbeing Advisory Board of Business Finland
- Chairman of Finnish Biotechnology FIB

# Herantis Pharma Plc

HRTIS Nasdaq First North listed

- 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 world-leading 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 (in Finland and Sweden)



# 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

# Parkinson's is treated with levodopa… since 1960's!

**No real breakthrough in Parkinson's disease…**

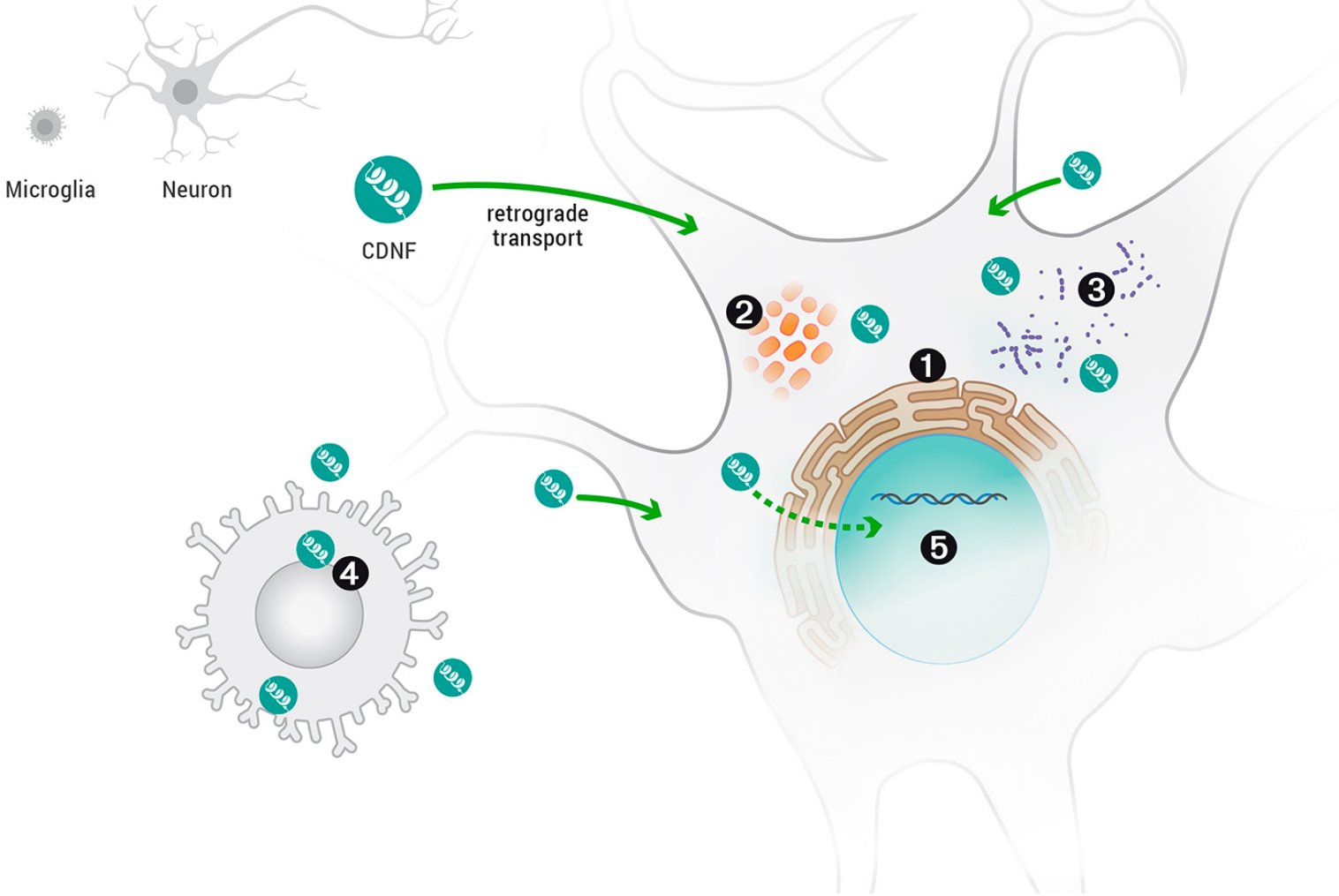
- Levodopa treatment is based on research by Professor Arvid Carlsson (University of Lund)
- Prof. Carlsson conducted first preclinical studies with levodopa in the 1950's, and later received the Nobel price in 2000 on signal transduction in the nervous system

**…but CDNF could change that**

- CDNF is a natural human protein with an important role in neuronal survival
- CDNF is in Phase 1-2 clinical study funded by EU: "**Leading science, greatest potential to advance clinical practice**"
- First results suggest CDNF is safe, with encouraging biological responses; treatments continue through 1H/2020, **12-month data expected in Q3/2020**

Karolinska Institutet · KAROLINSKA UNIVERSITETSSJUKHUSET · TYKS Turku University Hospital · HUS · REGION SKÅNE

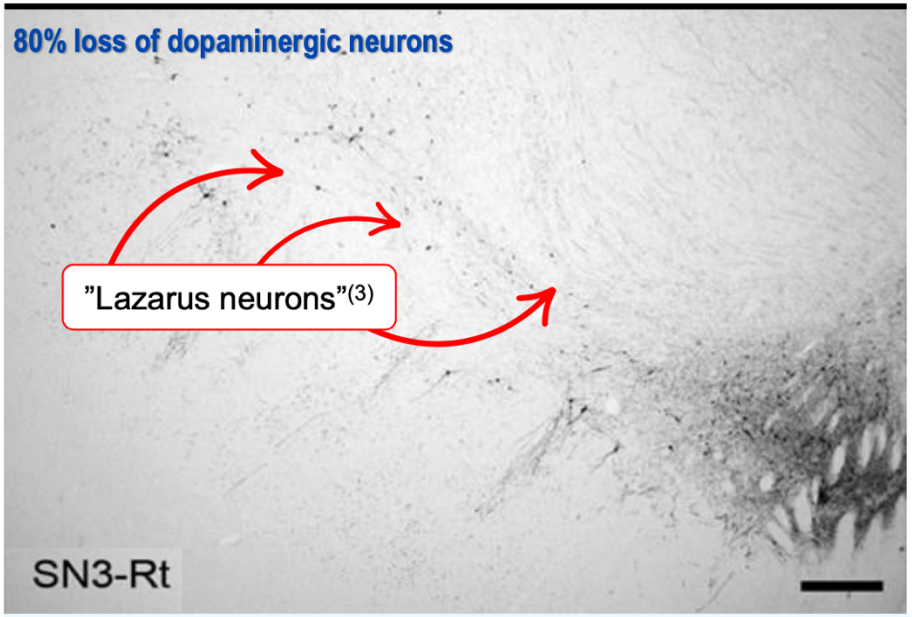
# Herantis' CDNF promotes neuronal survival and recovery through multiple relevant mechanisms




1. 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
4. CDNF suppresses production and secretion of proinflammatory cytokines by glial cells
5. CDNF supports maintenance of neuronal functions by enhancing transcription of genes involved in e.g. dopamine synthesis and metabolism

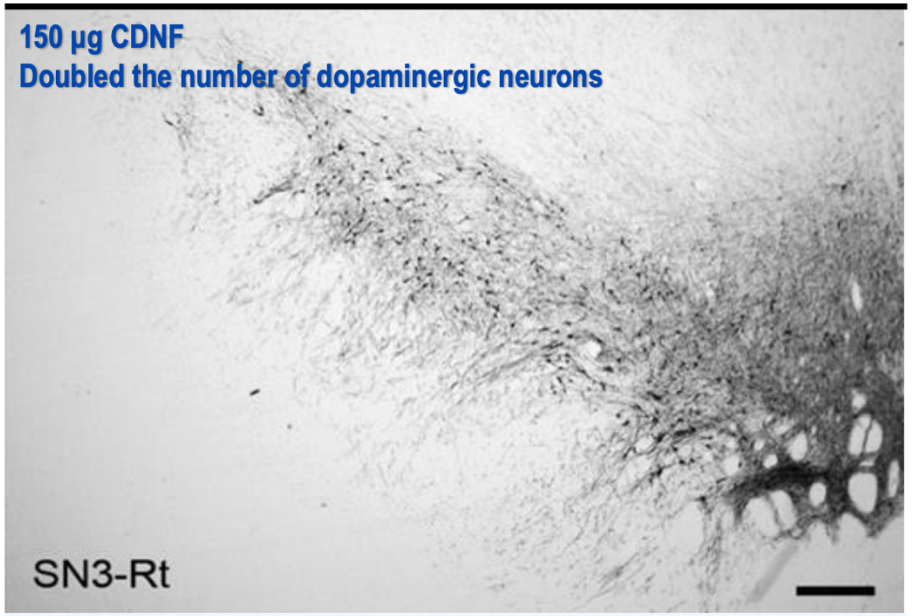
# CDNF doubled the number of functional dopaminergic neurons in preclinical model[1]

**MPTP lesion model of Parkinson's in primates[2]**




- Model: Severe parkinsonism caused in aged primates by MPTP, resulting in significant loss of dopaminergic neurons
- True *neurorestoration* study: Instead of immediate treatment, the lesions were allowed to mature for six weeks before CDNF administration
- Dark staining in the figure indicates dopaminergic neurons: 80% loss corresponds to advancing PD

**CDNF treatment results in significant neurorestoration**



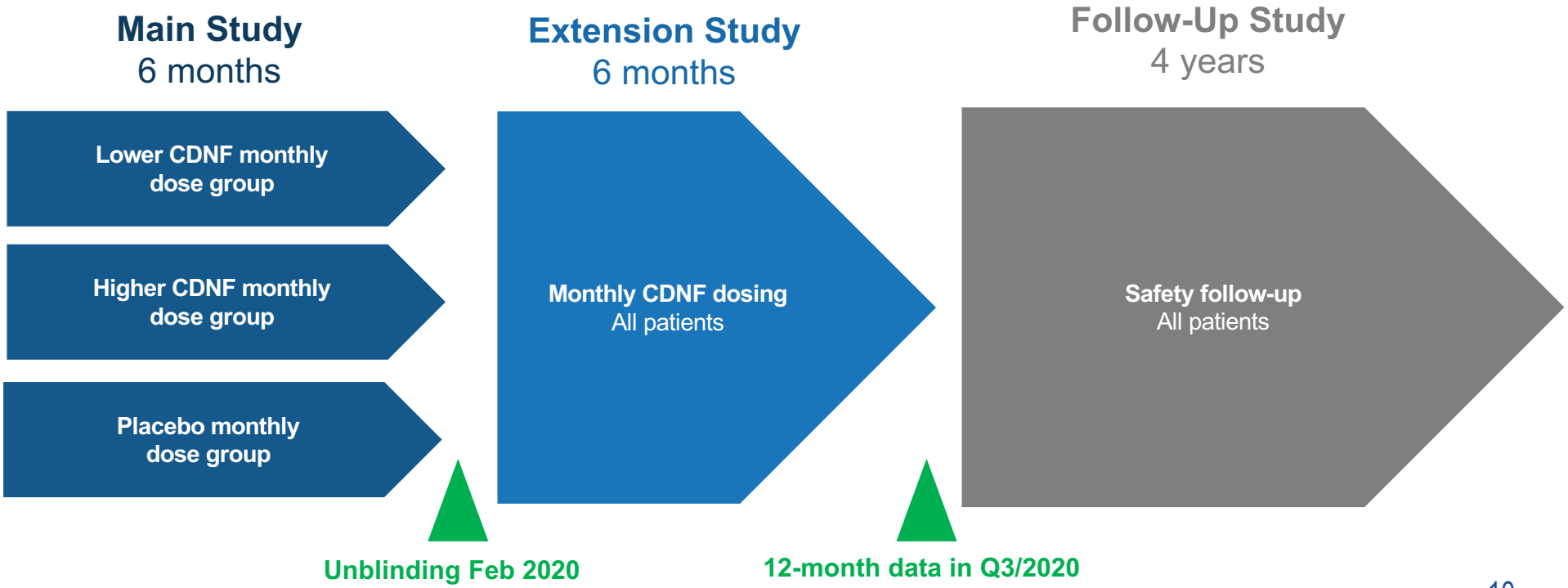

- Three monthly CDNF doses **doubled the number of dopaminergic neurons**
- Significant improvement in gross motor function, fine motor function, and **for the first time in the world**, even in non-motor symptoms
- CDNF can help degenerating and dying 'Lazarus neurons' regain their function

1) Collaboration of University of Pittsburgh and University of Helsinki. 2) MPTP: Chemical compound that causes permanent parkinsonism.
3) "Lazarus neuros" is the term used by Herantis for degenerating neurons that have lost their phenotype (such as ability to produce dopamine)

# Randomized, placebo-controlled Phase 1-2 study with intracerebral CDNF in advanced PD

## Study status in May 2020:

1. All 17 patients have had the surgical procedure for drug delivery device
2. Main study completed (first 6 months of CDNF/placebo dosing)
3. CDNF **safety has been excellent**
4. **Promising efficacy signals** observed in e.g. PET imaging already after 6 months, in patients with advanced PD i.e. very challenging patients for a neuroprotective approach




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

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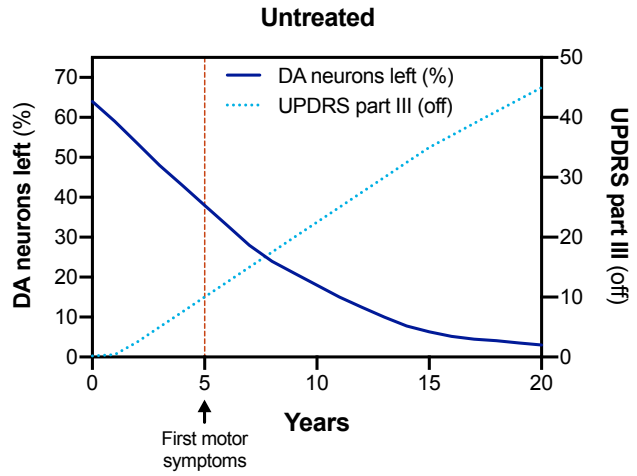
# Current conclusions from Main study (first 6 months)

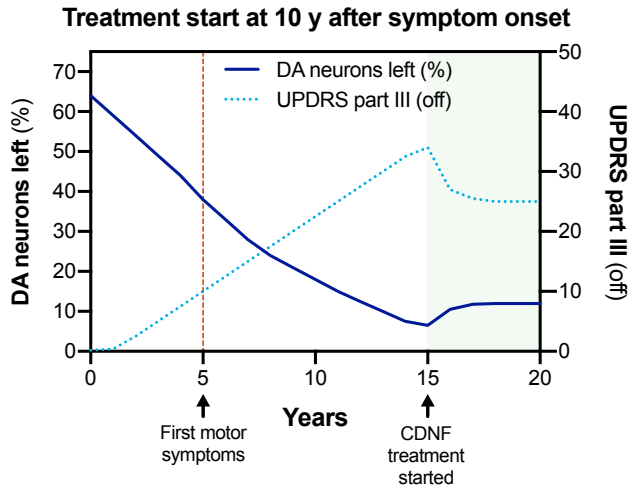
- **Primary endpoint met**: CDNF is safe and well tolerated in **advanced PD patients**
  - → Adverse Events related to the drug delivery device / dosing procedure have been addressed with updated procedures and training
- In one of the two CDNF dose groups, **60% response rate (3/5 patients) in PET imaging**
  - → The best two patients show a **52% increase and a 44% increase** in DAT binding potential
  - → We have seen promising signals in some patients **also in other endpoints**; this is investigated further in the Extension study (full 12 months of treatment)
  - → Promising data keeping in mind these patients have average >10 years motor symptoms; most of their dopaminergic neruons are lost
- **Next read-out expected in Q3 2020** (Extension study, another 6 months of CDNF)
- These initial signals on CDNF are also encouraging for xCDNF, based on the same mechanisms and expected to enable **significantly easier administration**

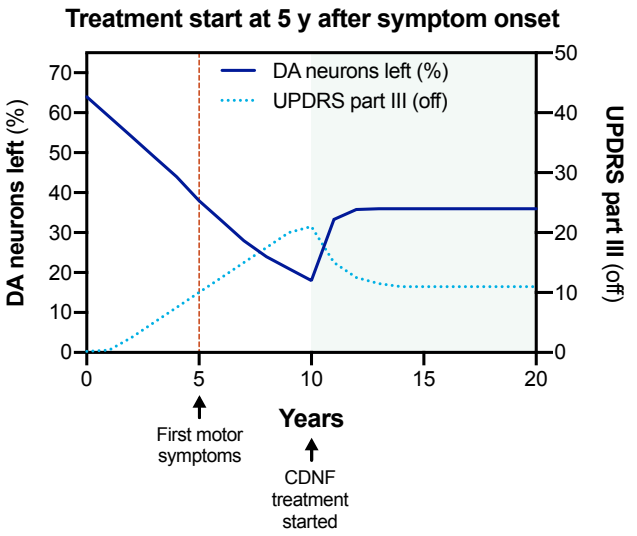
# Planned next step: Phase 2 in earlier stage Parkinson's patients

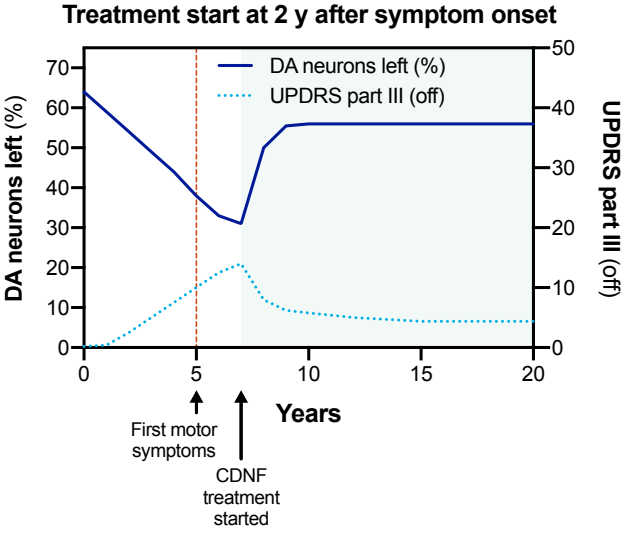
Hypothesis explained in the pictures:

- Symptoms grow worse, i.e. UPDRS score increases, as dopaminergic (DA) neurons continue to decrease
- The clinical relevance of neurorestorative CDNF treatment is expected to increase significantly if started at earlier stage of the disease: more DA neurons restored and protected → less symptoms

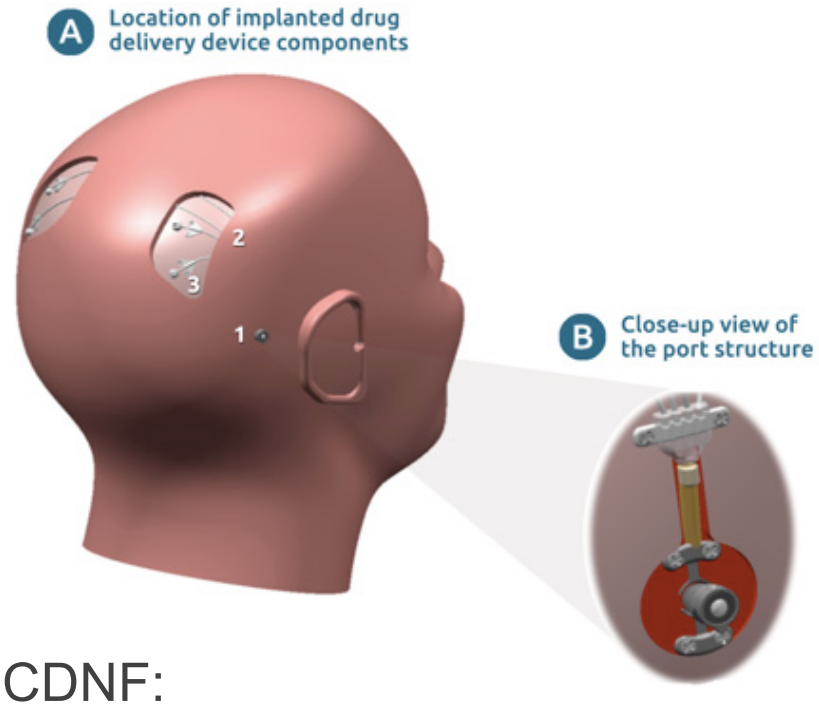


# Leveraging CDNF results: Next generation xCDNF




- 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 → **much simpler administration**
  3. Have potential in several indications beyond PD: E.g. Alzheimer's, ALS, stroke

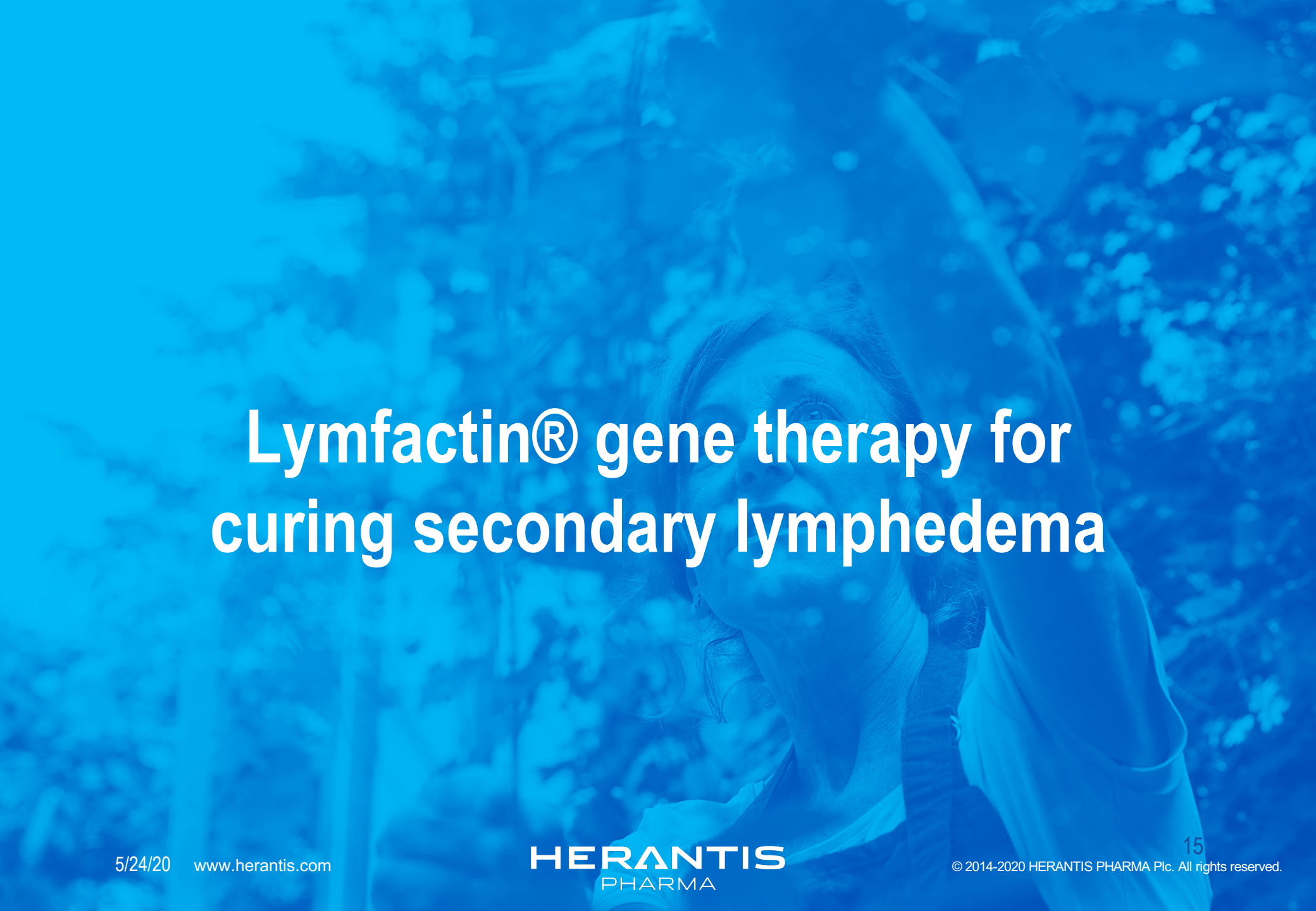
➢ **Based on current data xCDNF could be administered as easily as insulin**

# Few PD therapies with disease-modifying potential

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

| | HERANTIS PHARMA | MEDGENESIS | Roche | Calico | BIOARCTIC | Integrative Research Laboratories | Voyager THERAPEUTICS |
|---|---|---|---|---|---|---|---|
| **Therapies** | CDNF/xCDNF | GDNF | PRX002 | ISRIB | ABBV-0805 | Mesdopetam (IRL790) | VYAADC-01 |
| **Phase** | Phase 1-2 / Discovery | Phase 2 | Phase 2, missed primary endpoint | Preclinical | Phase 1 | Phase 2 | Phase 2 |
| **Mechanism of Action** | Multi-modal: Reduction of ER stress, α-syn aggregation and toxicity | Activates GFRα/Ret signaling | Reduction of α-synuclein | Activates eIF2B to reduce integrated stress response | Reduction of α-synuclein | D3 receptor antagonist (for levodopa-induced dyskinesia) | Provides dopa decarboxylase gene to putamen |
| **Molecule type** | Protein / Peptide | Recombinant Protein | Monoclonal Antibody | Small Molecule | Monoclonal Antibody | Small Molecule | Gene Therapy |
| **Route of Administration** | Intracerebral / Peripheral | Intracerebral | Intravenous | Intravenous | Intravenous | Oral | Intracerebral |
| **Disease Modifying** | ✓ | ✓ | ✓ | ✓ | ✓ | ✗ | ✗ |

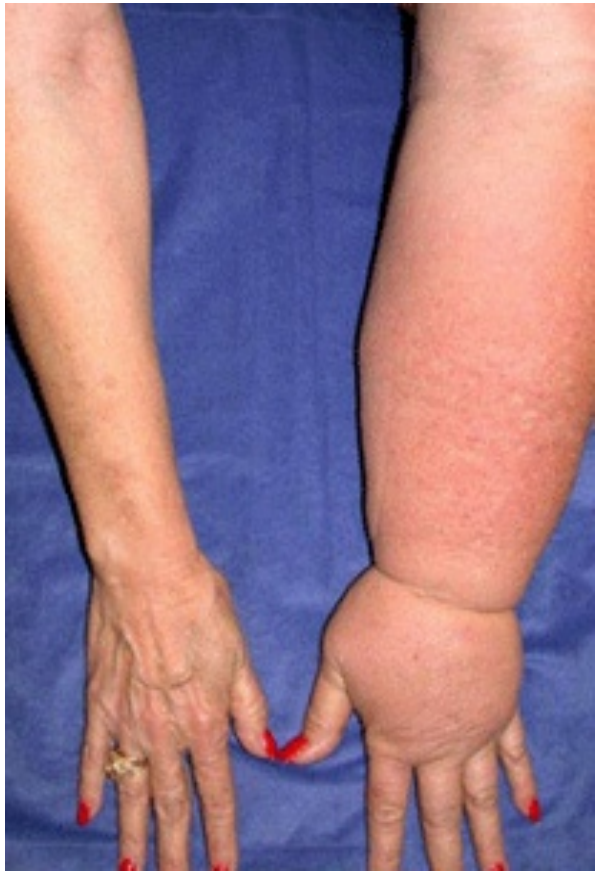
**Few PD therapies in development are potentially disease modifying, and among those we believe CDNF has the most compelling mechanism**



# Lymfactin® gene therapy for curing secondary lymphedema

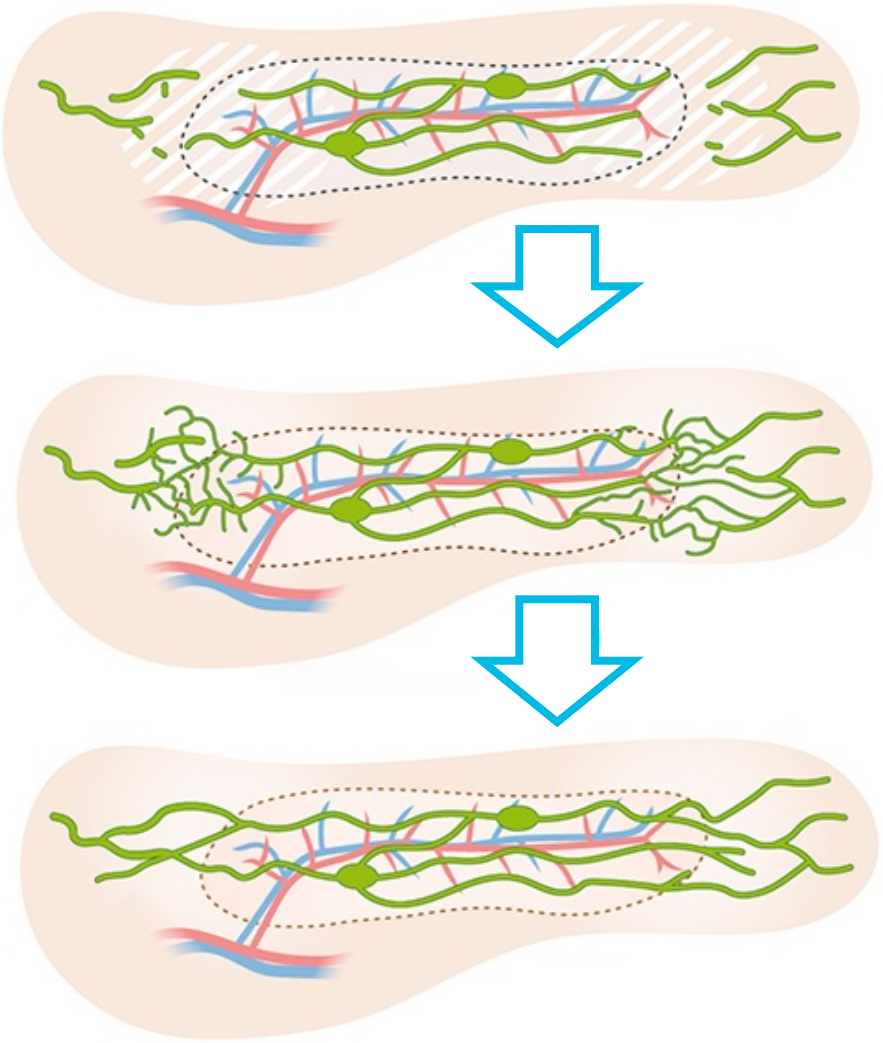
# Secondary lymphedema

- Lymphedema (LE) is chronic, progressive swelling due to accumulation of lymph
  - → Disabling and disfiguring disease
  - → No approved drugs for treatment
- Herantis' Lymfactin® is a gene therapy that aims to **repair the lymphatic system**
  - → Targeted as the **first lymphedema drug** and the **first curative treatment of secondary lymphedema**



# 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



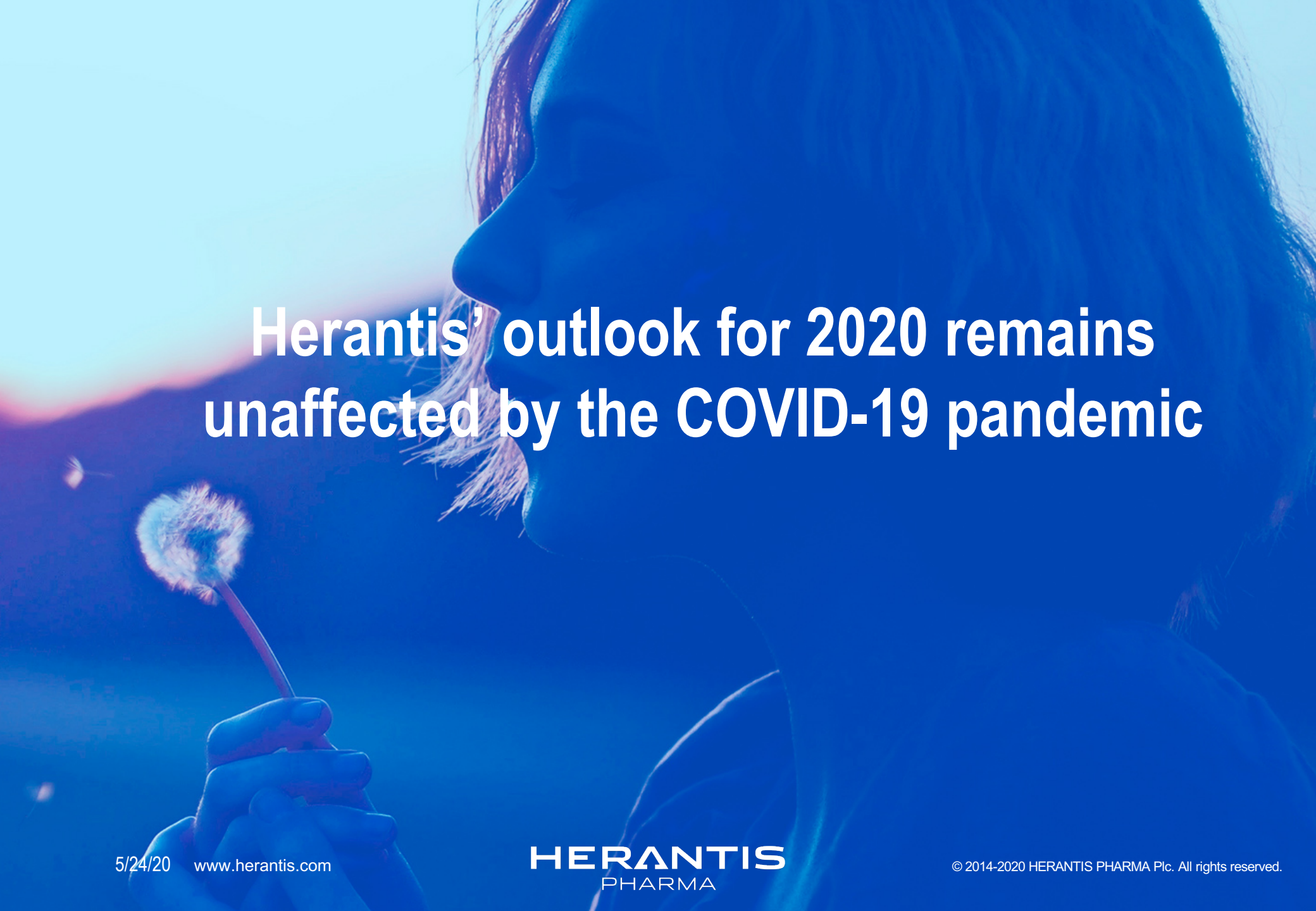
# Lymfactin® development

- Currently planning a Phase 3 study (EU & USA)
- Phase 2 study AdeLE in patients with breast cancer associated LE (BCAL): All treatments completed, in 12-month blinded follow-up
  - → Adjunct to lymph node transplantation surgery, which aims to relieve symptoms
  - → Study centers: 5 university hospitals in Sweden and Finland
- Phase 1: Safety established in the same patient group & setup
  - → Promising improvements observed in signs and symptoms of LE after 12-month follow-up (uncontrolled data)

- **Phase 2 study: 39 patients randomized in Lymfactin® vs. placebo groups**
- **Topline results expected in Q1/2021 (after 12-month blinded 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*
  - → Expansion potential in other LE
- Lymphedema awareness increases
  - → Herantis is a partner of LE&RN, international patient advocacy group
  - → Hollywood superstar Kathy Bates is an active LE&RN spokesperson



# Herantis' outlook for 2020 remains unaffected by the COVID-19 pandemic



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# Expected news flow: Approaching key milestones

## H1 2019

- ✓ 3/2019: Directed share issue, introducing Swedbank Robur Medica as new anchor investor
- ✓ 4/2019: Positive 12-month follow-up review from Phase 1 clinical study of Lymfactin®

## H2 2019

- ✓ 12/2019: Swedish IPO (Nasdaq First North Stockholm) with oversubscribed share issue
- ✓ 12/2019: Lymfactin® Phase 2 clinical study completed patient recruitment and all patient treatments
- ✓ 12/20919: The Main part of the Phase 1-2 clinical study in Parkinson's completed patient treatments
- ✓ 12/2019: Three lead candidates selected for non-invasive next-generation xCDNF development

## H1 2020

- ✓ 2/2020: Positive topline results from first 6 months of Phase 1-2 clinical study in Parkinson's
- ✓ 4/2020: Board of directors strengthened by introduction of Mats Thorén; Timo Veromaa elected Chairman
- Management strengthened for next growth stage by appointing Dr. Craig Cook as CEO

## H2 2020 onwards

- Q3/2020: Results from 12 months of Phase 1-2 clinical study in Parkinson's
- Q1/2021: Unblinding and topline data of Phase 2 clinical study with Lymfactin®
- Subject to clinical study results: Further details on next steps in clinical development

# Preparing for next stage of company development: Dr. Craig Cook joining as CEO in July 2020

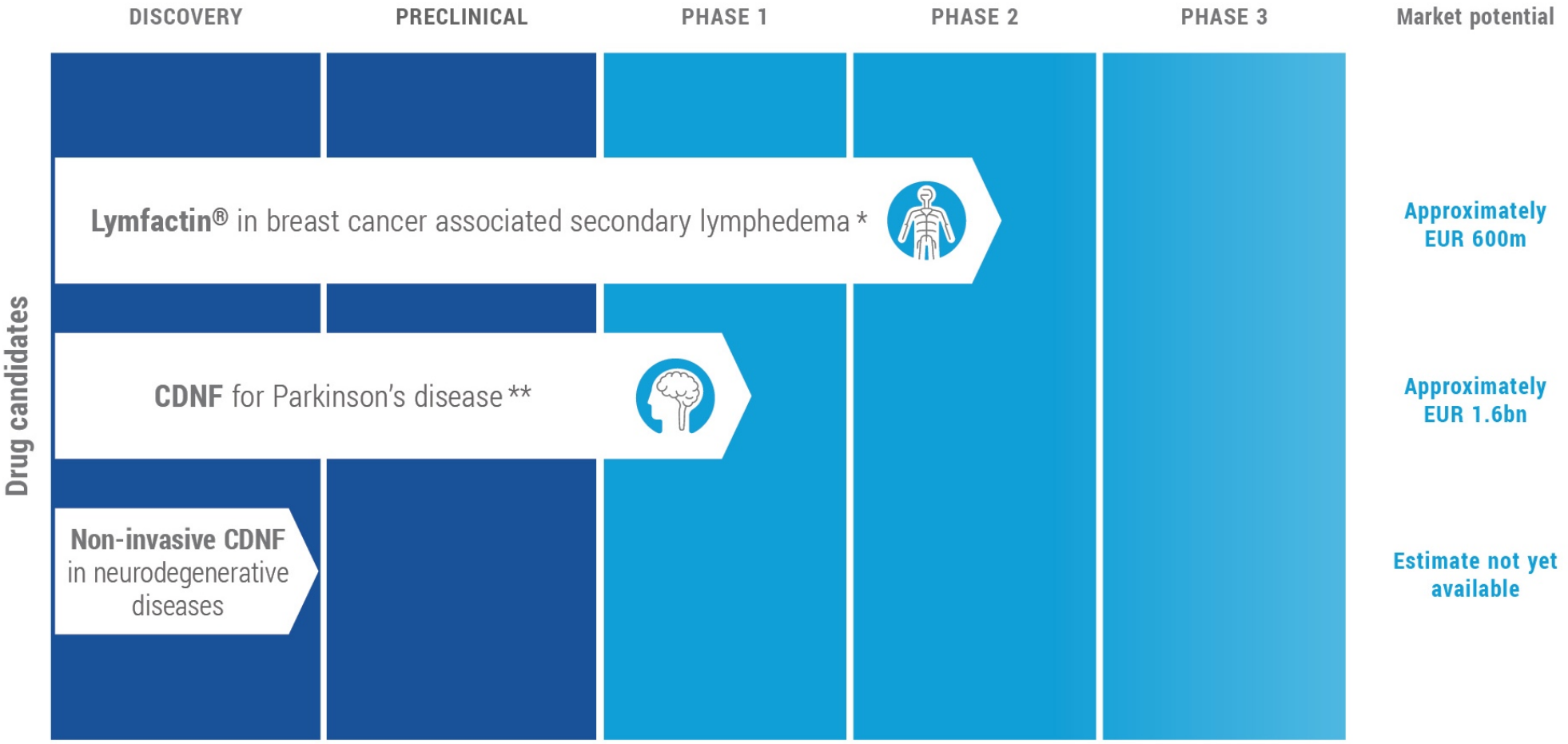
**Company announcement 11 May 2020:**

- **Herantis prepares for next stage of company development** by appointing Dr. Craig Cook as CEO
- Craig has significant international expertise in business development, clinical stage drug development and capital markets (NASDAQ US & London)
- Craig will join 1st Jul 2020; the current CEO, Pekka Simula, will continue as CEO until then
- Pekka will support Craig during a three-month handover period until end of Sep 2020 to ensure smooth transition
- Craig brings more than 20 years of experience in international pharmaceutical and biotech industry:
  - Eli Lilly, Johnson & Johnson, Novartis, EMD Serono
  - CEO of Midatech, a UK-based company focused on delivering innovative oncology and rare disease products to patients
  - Multiple therapeutic areas including CNS and immunology

# Management, shareholders, and financials

- Funded to reach read-outs in the ongoing clinical studies with CDNF (Parkinson's disease) and Lymfactin® (secondary lymphedema)
- Cornerstone investor in last directed issues (3/2019 and 12/2019) was Swedbank Robur's global healthcare fund Medica
- International and experienced Board of Directors
- Herantis' management has actively purchased shares both from the market and participated in share issues

# 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

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# Thank you

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