HERANTIS PHARMA

Herantis Corporate Presentation

September 2021

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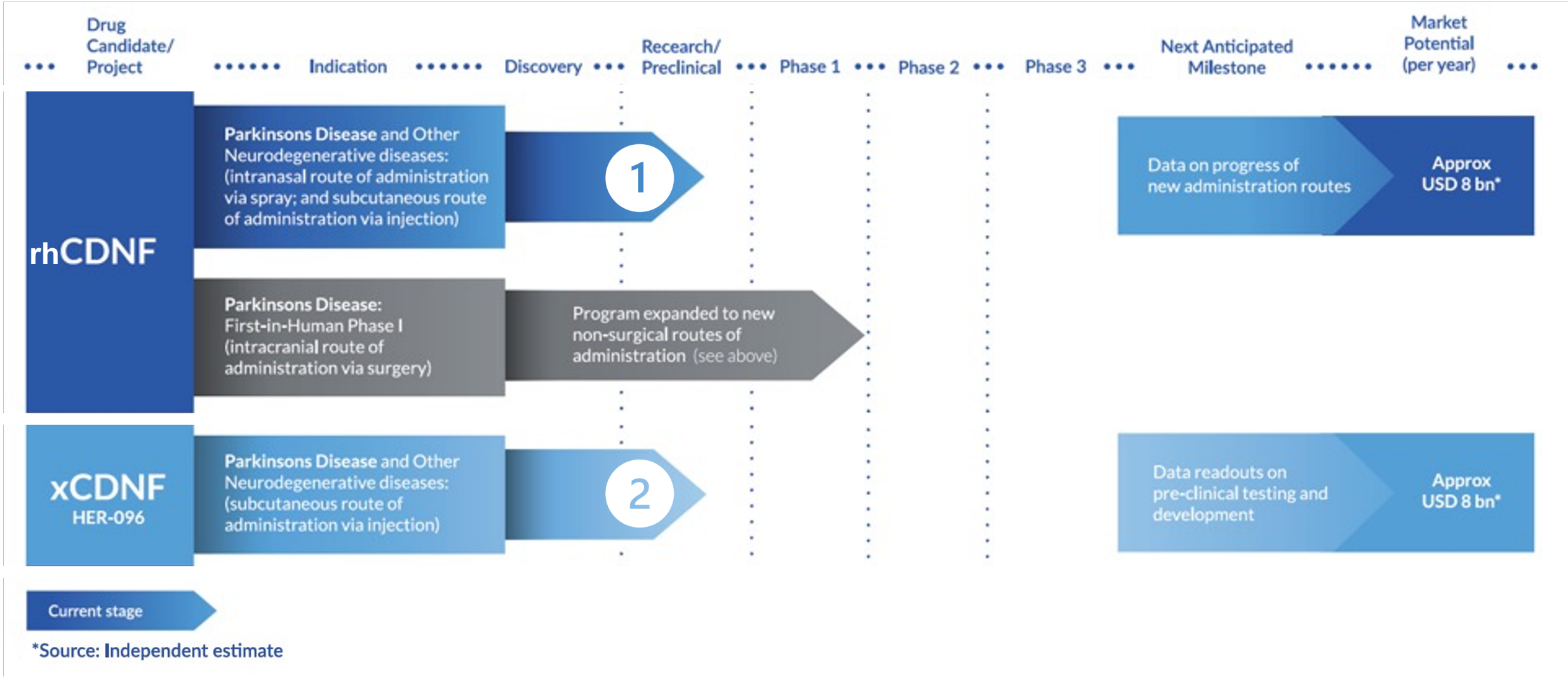
Company Overview

- Headquartered in Helsinki, listed on Nasdaq First North Finland and Sweden
- Founded 2008, IPO 2014 (Finland) 2019 (Sweden), €63m raised to date, €15m in 2020
- Research focus is assets that modify human pathology as result of protein dysregulation
- Disease focus is on Parkinson's and other neurodegenerative diseases
- Looking to bring treatments for these diseases into 21st century
- More than a decade of R & D now yielding compelling dataset supporting clinical, imaging, biomarker, and genetic footprint

Pipeline Fully Focused On Neurodegenerative Diseases



CDNF = Cerebral Dopamine Neurotrophic Factor

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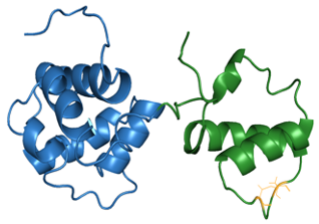
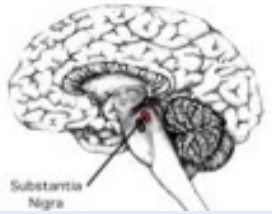
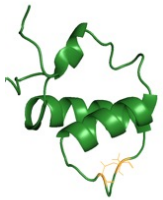
Two Stand Alone Molecules, Same MoA, Same Target … Individual Approaches

rhCDNF
Protein, clinical stage Phase I data on molecule, intranasal spray administration





xCDNF (HER096)
Chemical, pre-clinical stage. subcutaneous administration



Target Disease - Parkinsons

Target Organ - Brain

Target Pathology - Proteostasis

Clinical Safety & Efficacy Data In Humans

Generated in rhCDNF Ph I program, applicable to both molecules

Pre-Clinical Safety & Efficacy Data In Animals

Blood Brain Barrier Crossing

Route of Administration

Molecule

Yes

Yes

As per CDNF

Yes

Unknown

Confirmed

Nasal Spray

Skin Injection

Recombinant Protein

Chemical Peptidomimetic

Key: Distinct Elements
Common Elements

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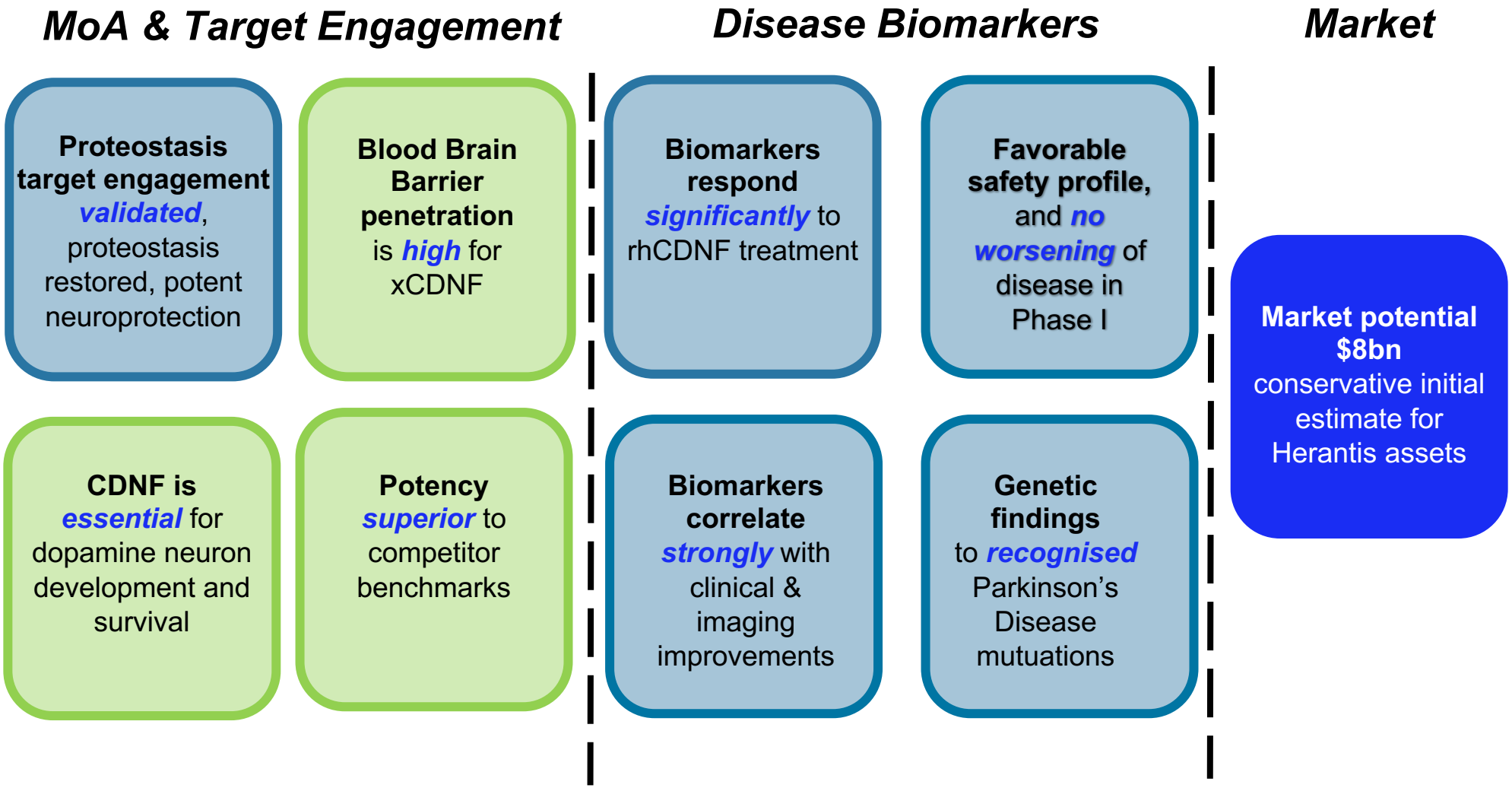
rhCDNF and xCDNF Data Continues To Build



Key:
Human data
In-vivo data

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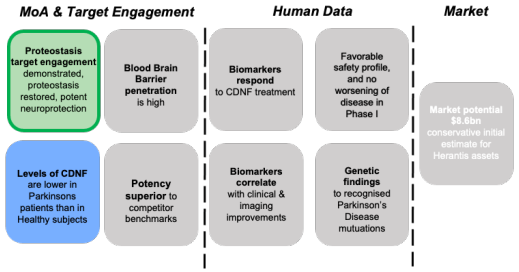
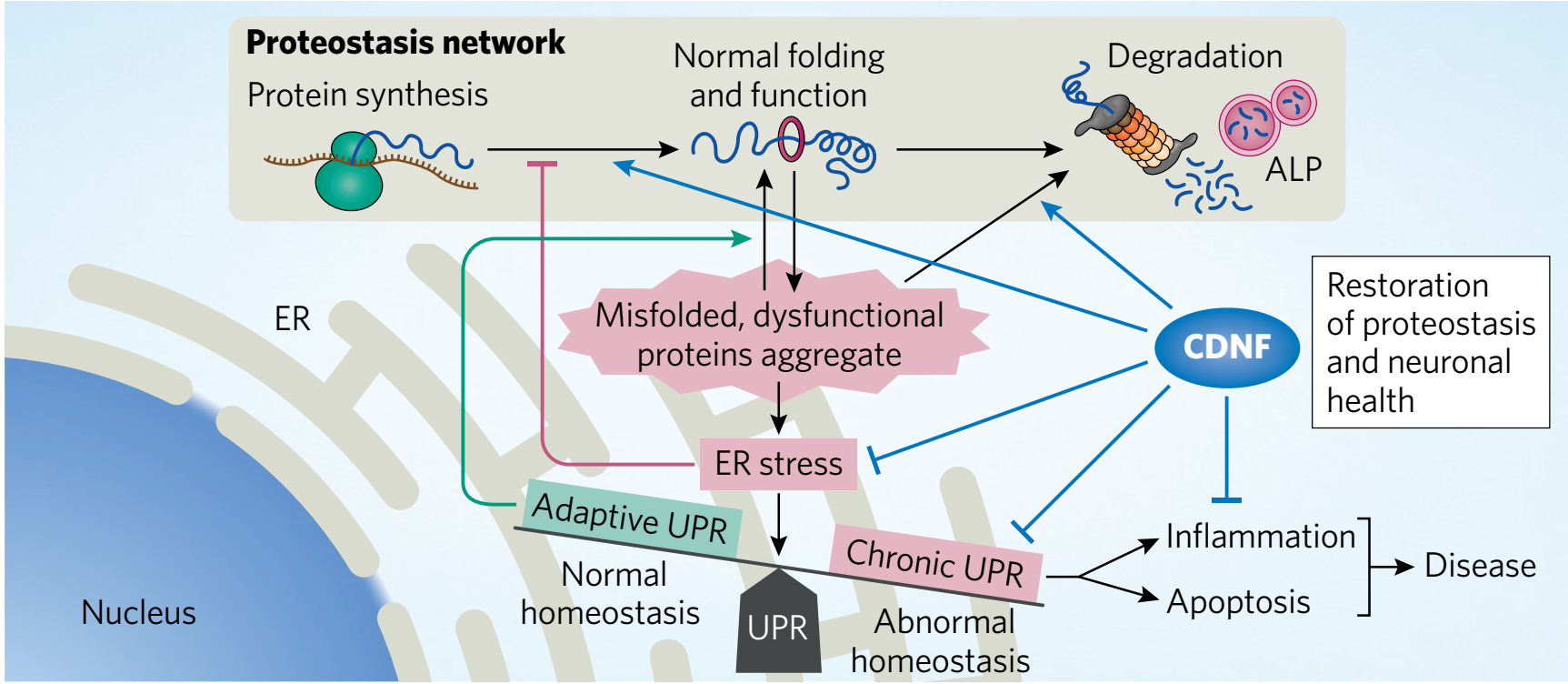
CDNF Targets Core Pathology Of Parkinson's Disease – Proteostasis



- Proteostasis regulates proteins in body and influences the fate of every protein from synthesis to degradation
- Its failure is implicated with the development of neurodegenerative diseases such as Parkinson's



www.nature.com

- ***rhCDNF and xCDNF designed to restore the protective effects of proteostasis***

Fig. 1 | CDNF and proteostasis. The proteostasis network maintains a functional proteome in cells. Dysregulated proteostasis plays a major role in development of disease. In Parkinson's disease, accumulation of misfolded proteins induces endoplasmic reticulum (ER) stress leading to reduced protein synthesis and activation of the unfolded protein response (UPR), which if prolonged leads to apoptosis. CDNF acts to normalize proteostasis by restoring adaptive UPR signalling, supporting cell survival and normal degradation of misfolded proteins.

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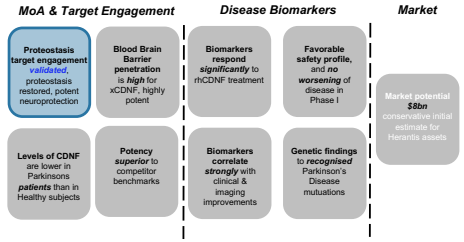
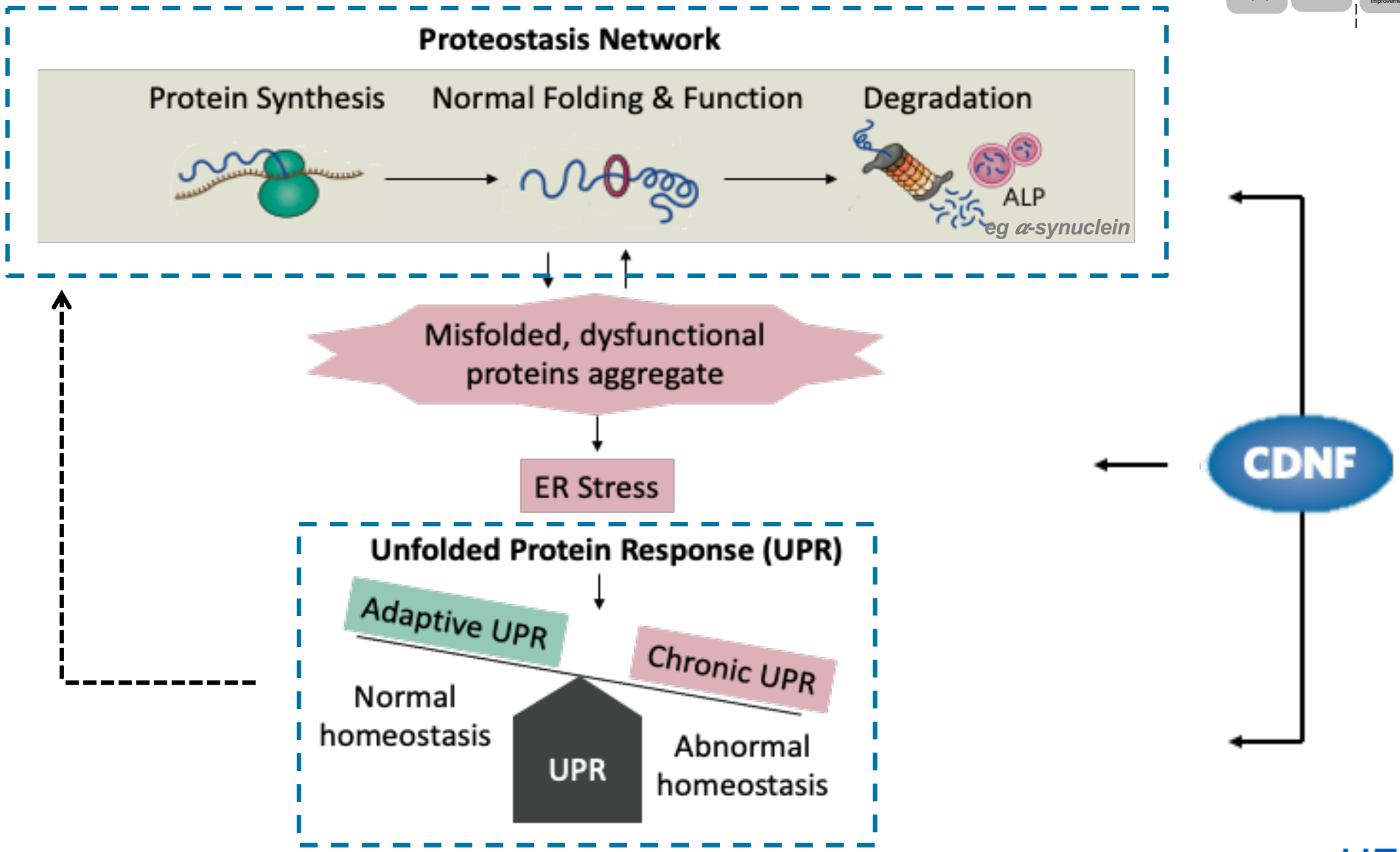
rhCDNF/xCDNF Act Powerfully On Proteostasis





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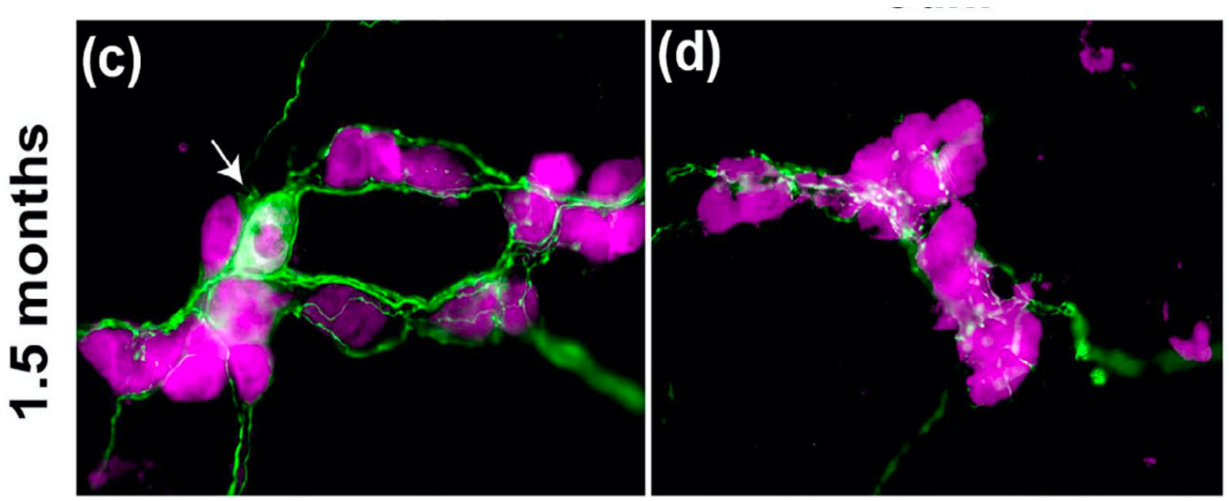
CDNF Is Essential For Enteric Dopamine Neuron Development And Survival

- Dopaminergic neurons occur in highest concentration in brain and gut areas of body
  - Role of CDNF can be observed in both brain and gut dopamine neurons
- CDNF deficient mice show degeneration of gut dopamine neurons
  - Results in impairment of gastrointestinal function and colonic expulsion
  - Such Non-Motor Symptoms (NMS) – eg constipation due to impaired gastrointestinal function - are a major determinant of progression of overall disability and quality of life in Parkinson's disease and often precede motor symptoms

Degeneration of gut dopamine neurons in CDNF$^{-/-}$ mice



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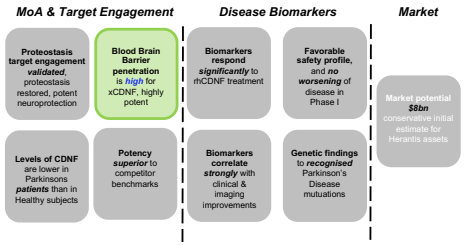
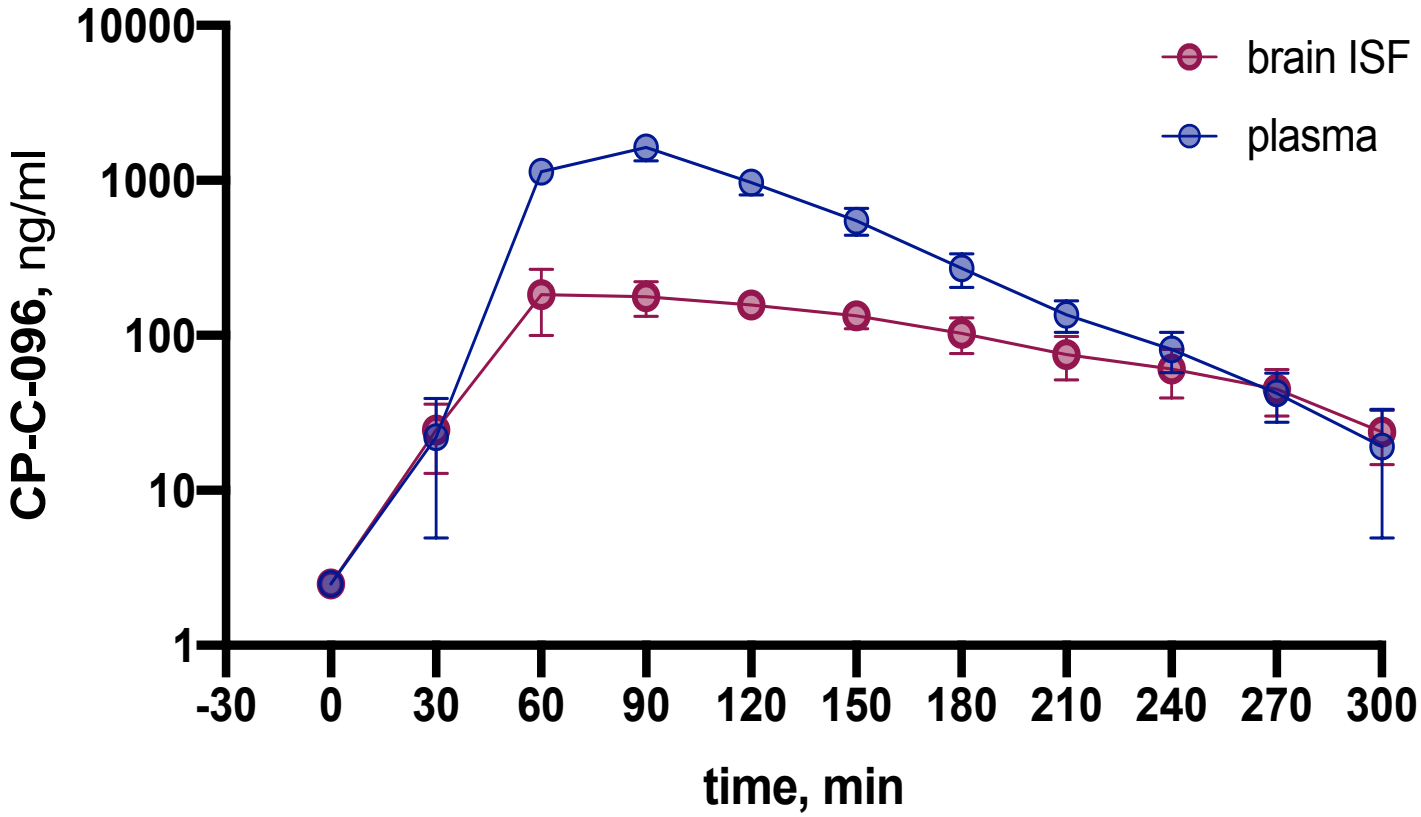
xCDNF (HER096) Convincingly Penetrates Blood Brain Barrier After Simple Skin Injection



DUAL (BRAIN AND PLASMA) MICRODIALYSIS STUDY IN MICE



$K_{p,uu,brain}$ = 0.216

ie: 22% brain-to-plasma ratio

Achieves Therapeutic Levels + Extended Half Life In Vivo

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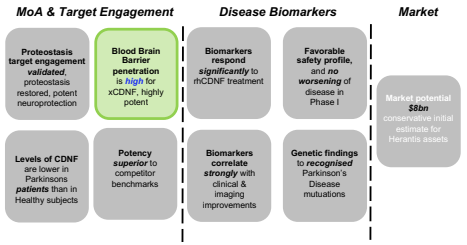
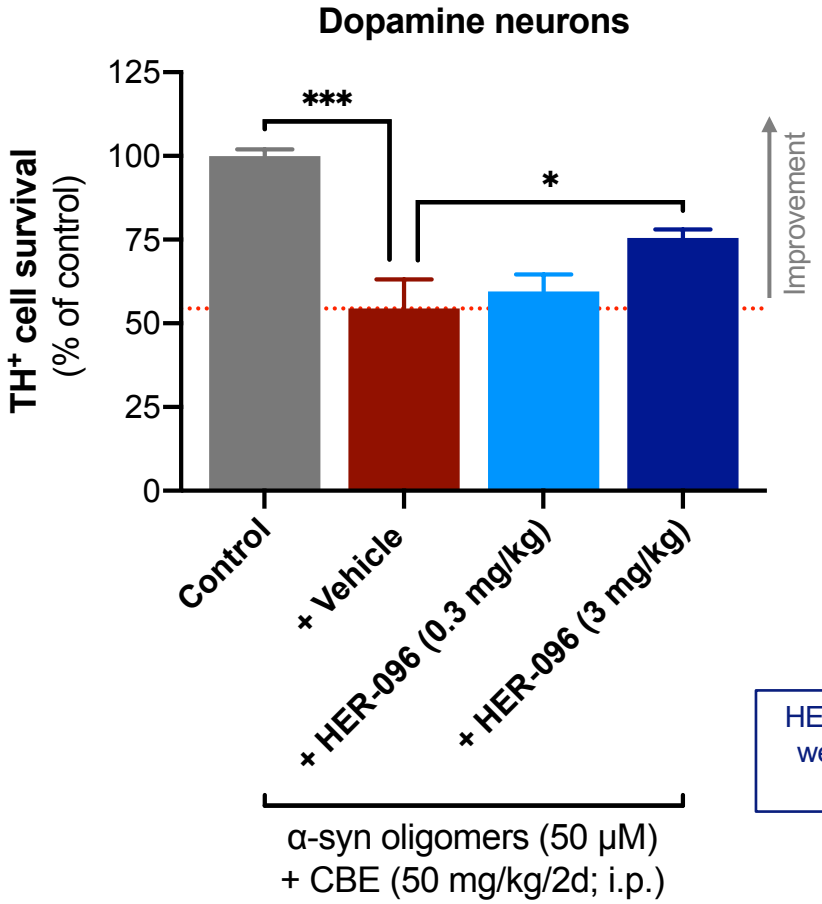
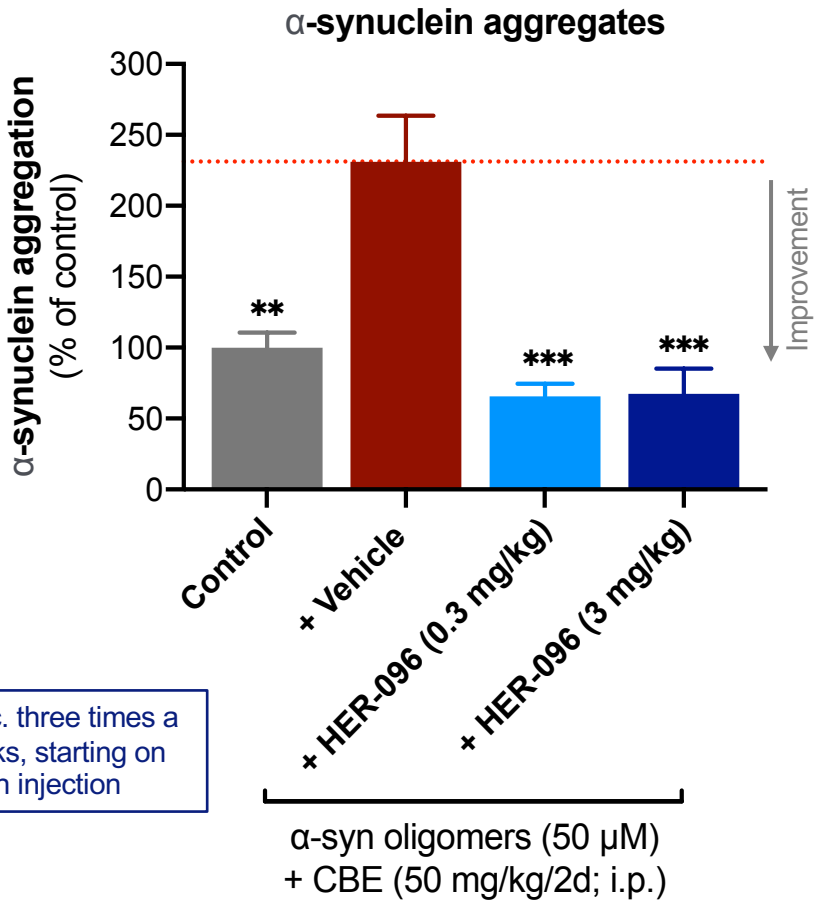
xCDNF (HER096) Potent Protection Of Dopamine Neurons + Significantly Reduces α-Synuclein Aggregates In Vivo



High protection of dopamine neurons, plus almost complete eradication of α-synuclein aggregates



HER-096 dosed s.c. three times a week for four weeks, starting on the day of aSyn injection



STUDY: Test compound CP-C-096 was administrated subcutaneously in dose 1mg/kg or 10 mg/kg three times per week for four weeks starting from the day of a-synuclein oligomers injection. Animals were sacrificed at day 28 after the model initiation, and neuronal survival and alpha-synuclein aggregation in substantia nigra were assessed by immunohistochemistry (n=5). *p<0,05 ANOVA with post-hoc Fisher's test versus group treated with vehicle.

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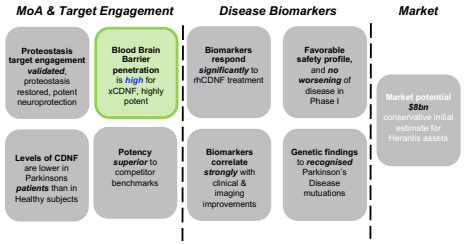
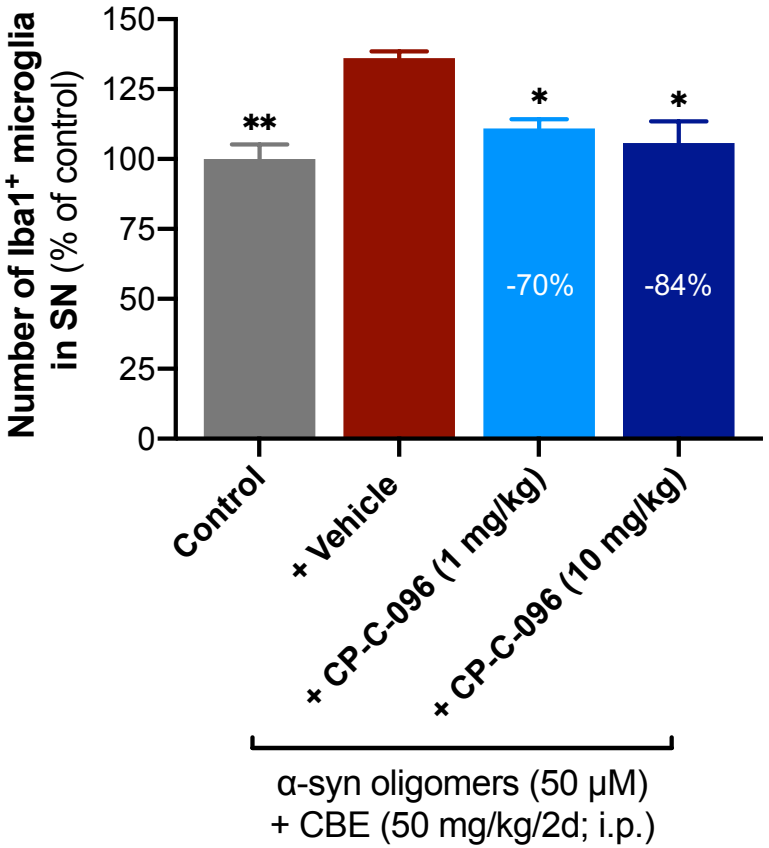
xCDNF (HER096) Potent Impact On Key Pathologies Of Parkinsons

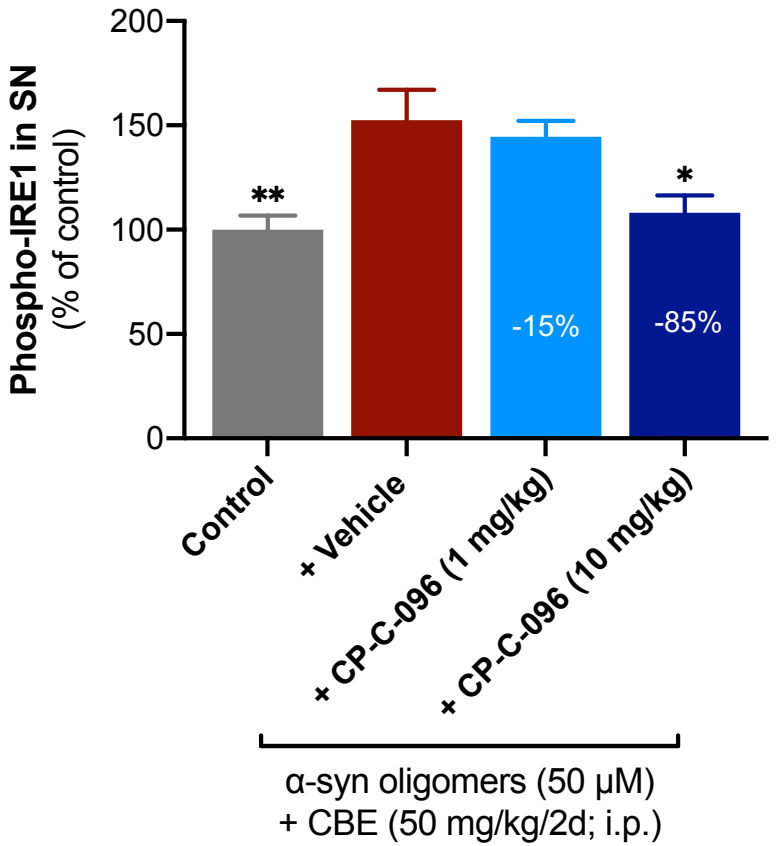


Attenuates Unfolded Protein Response And ER Stress, Thus Reduces Cell Death
>80% reduction of key neuroinflammatory/microgliosis marker, and 85% and 52% reductions of activated IRE1 and ATF6

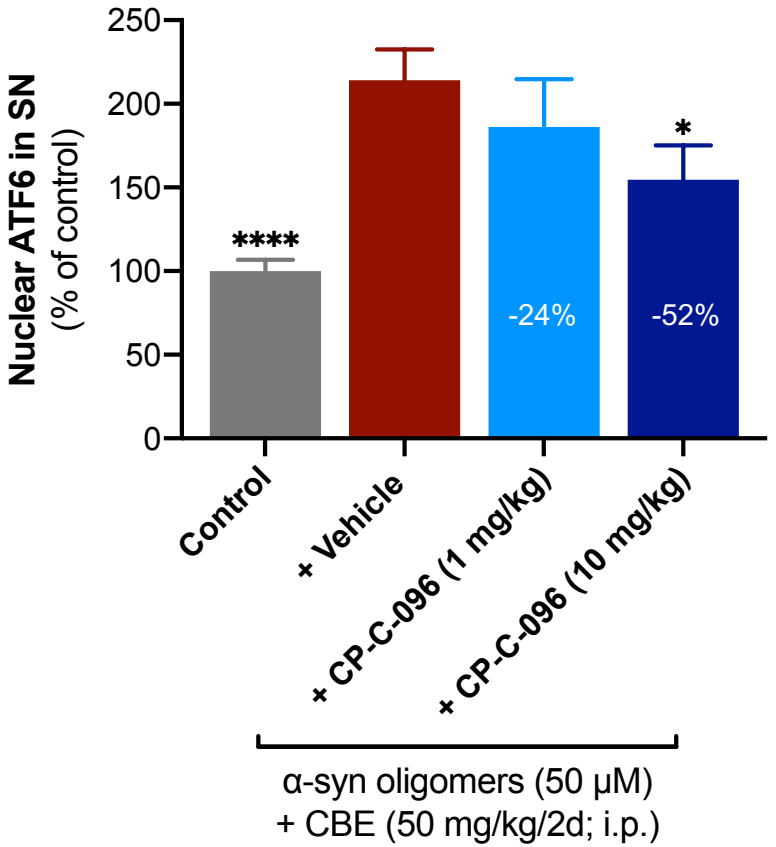
Microgliosis



Activation of the IRE1 pathway of UPR



Activation of the ATF6 pathway of UPR



STUDY: Test compound CP-C-096 was administrated subcutaneously in dose 1mg/kg or 10 mg/kg three times per wek for four weeks starting from the day of a-synuclein oligomers injection. Animals were sacrificed at day 28 post-aSyn injection, and microglia activation and selected UPR markers (ATF6, phospho-IRE1) in substantia nigra were assesed by immunohistohemistry (n=5). *p<0.05 ANOVA with post-hoc Fisher's test versus group treated with vehicle.

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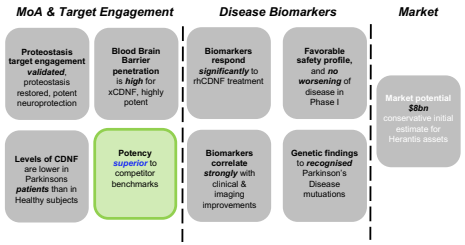
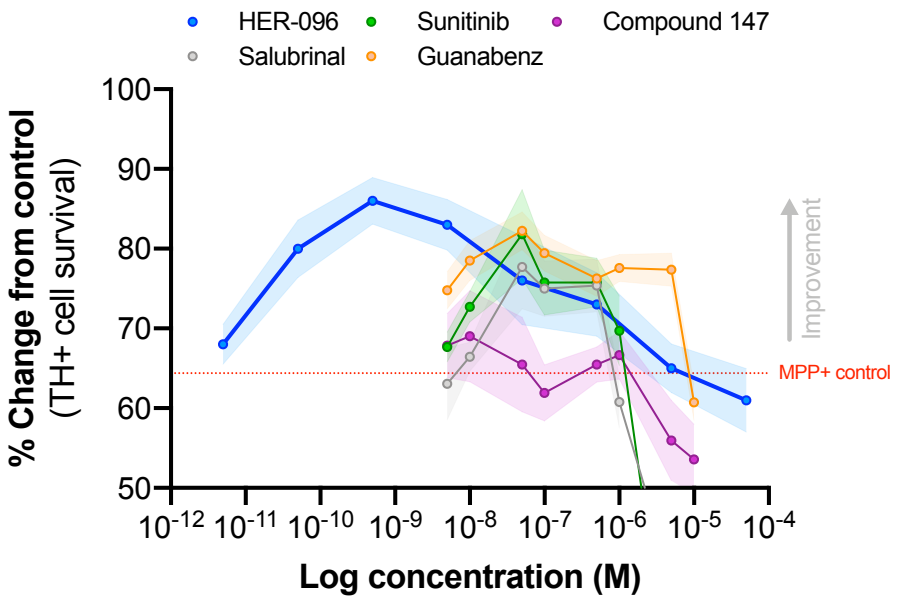
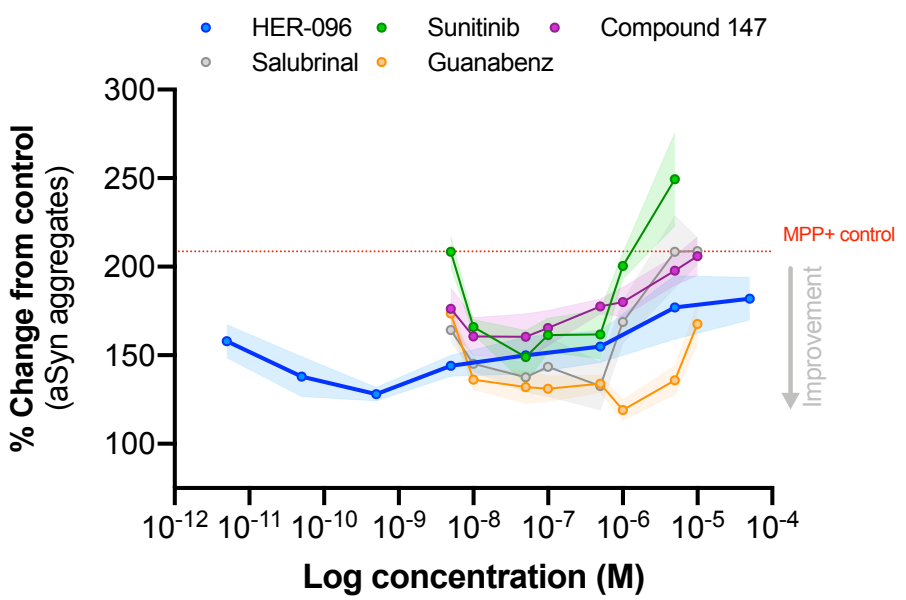
HER-096 Has Superior Pharmacological Properties When Compared to Several Other UPR Modulating Compounds



DOPAMINE NEURON SURVIVAL



ALPHA-SYNUCLEIN AGGREGATION



- HER-096 has superior potency and significantly wider therapeutic window of activity compared to sunitinib (IRE1), Compound 147 (ATF6), salubrinal (PERK) and guanabenz (PERK).

Sunitinib is an FDA-approved multi-target kinase inhibitor that modulates IRE1α kinase and RNase activities (Korennykh et al. Nature 457: 687-694, 2009; Ali et al. EMBO J 30: 894-905, 2011).
Salubrinal is a selective inhibitor of eIF2α dephosphorylation (PERK pathway) that protects cells from ER stress (Boyce et al. Science 307: 935-939, 2005).
Guanabenz is an inhibitor of eIF2α dephosphorylation (PERK pathway; Tsaytler et al. Science 332: 91-94, 2011).
Compound 147 is an ATF6 activator (Paxman et al. eLife 7: e37168, 2018).

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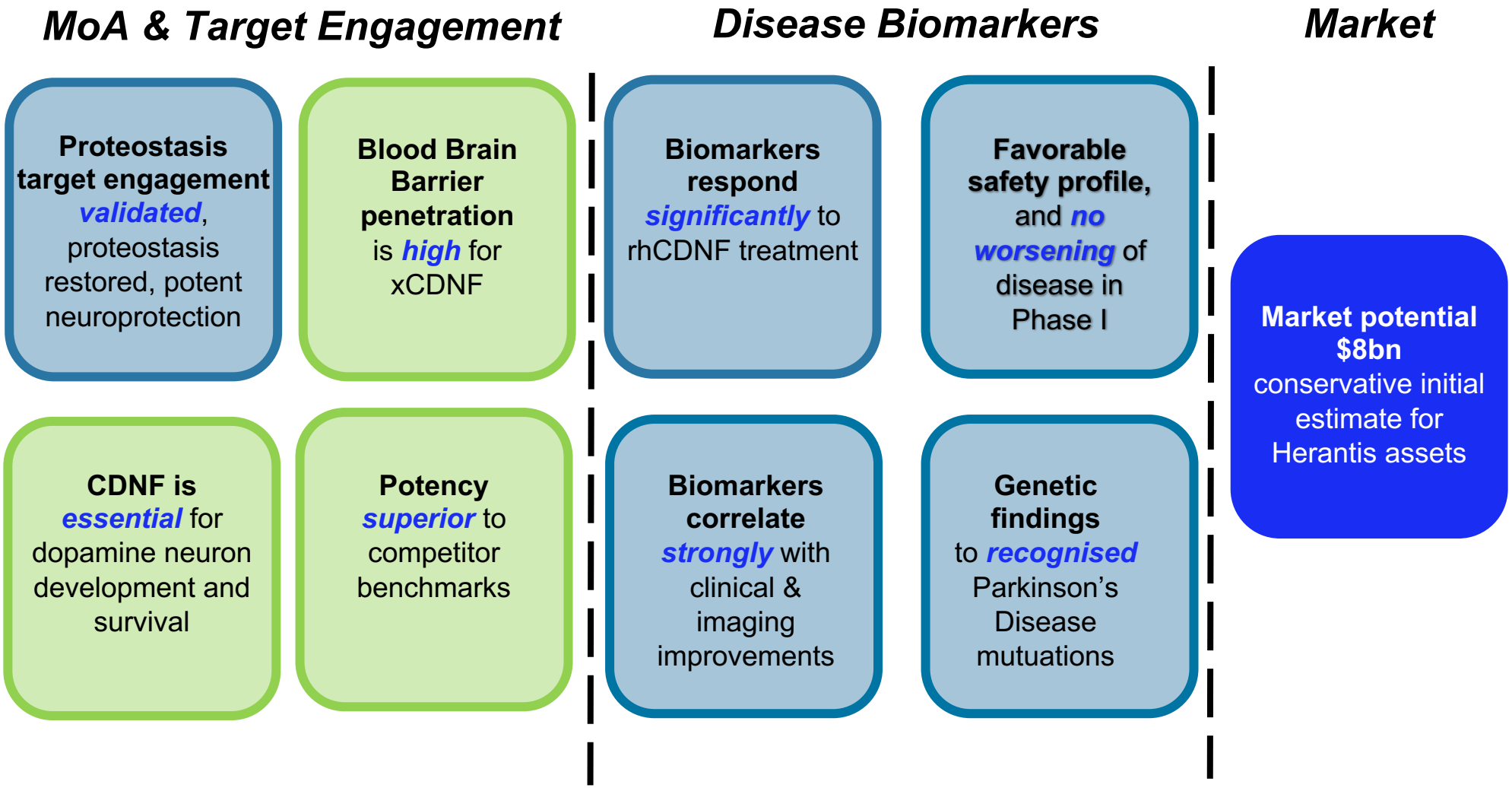
rhCDNF and xCDNF Data Continues To Build



Key:

Human data

In-vivo data

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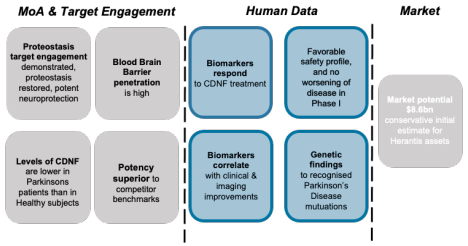
rhCDNF Treatment Effects On Disease Biomarkers In Humans



- Biomarkers in Cerebrospinal Fluid (CSF) change in response to rhCDNF treatment in some patients
- Correlated with improvements in motor function and biological dopamine signals
- Some subjects found to carry mutation etiopathologically related to Parkinsons - LRRK2, GBA
- Biomarker profiling suggests modulation of proteostasis in response to rhCDNF treatment
- Direct molecular interaction with alpha-synuclein

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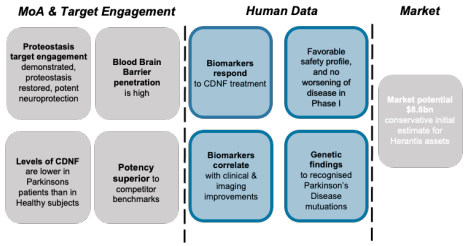
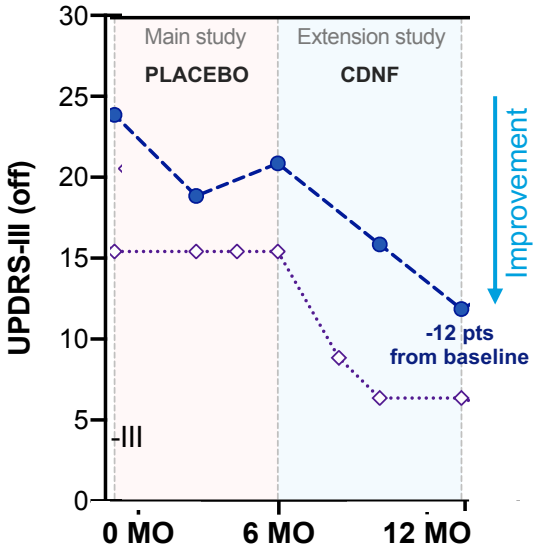
Data Linking Clinical + Imaging + Biomarker + Genetics Following Treatment With rhCDNF



- 60+ year
- Disease duration: 10 years (from first motor symptoms)
- 6 months placebo, followed by 6 months rhCDNF

1

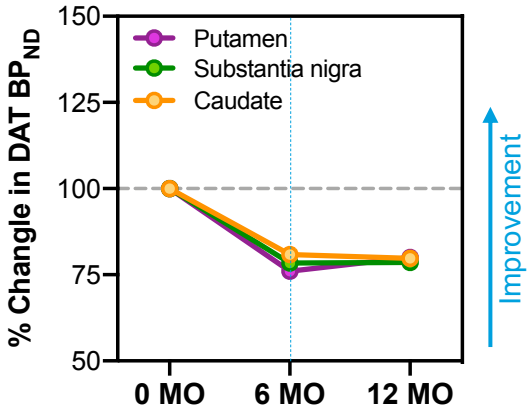
Motor Score



Significantly improved motor score following commencement of rhCDNF treatment at 6 months

2

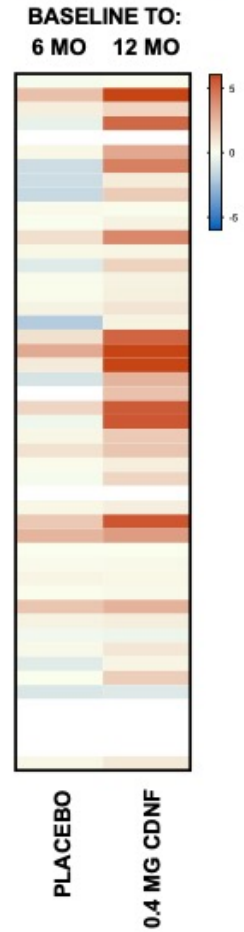
Imaging



Stabilising / increasing dopamine signal following commencement of rhCDNF treatment at 6 months

3

CSF Proteomic profile

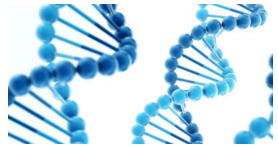


Strong response signal in disease and proteostasis relevant markers

4

Genotype

LRRK2 (G2019S)



Genetic mutation related to Parkinsons Disease

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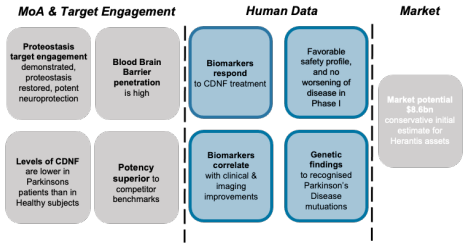
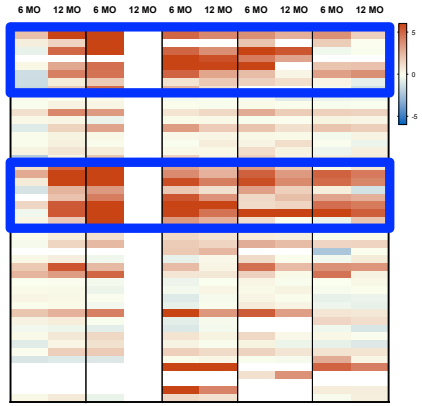
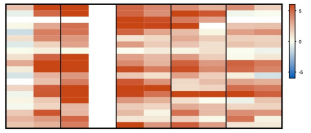
A Distinctive Biomarker Signature: Twenty Disease Related CSF Proteins Show Similar Pattern of Change in the “Responders”





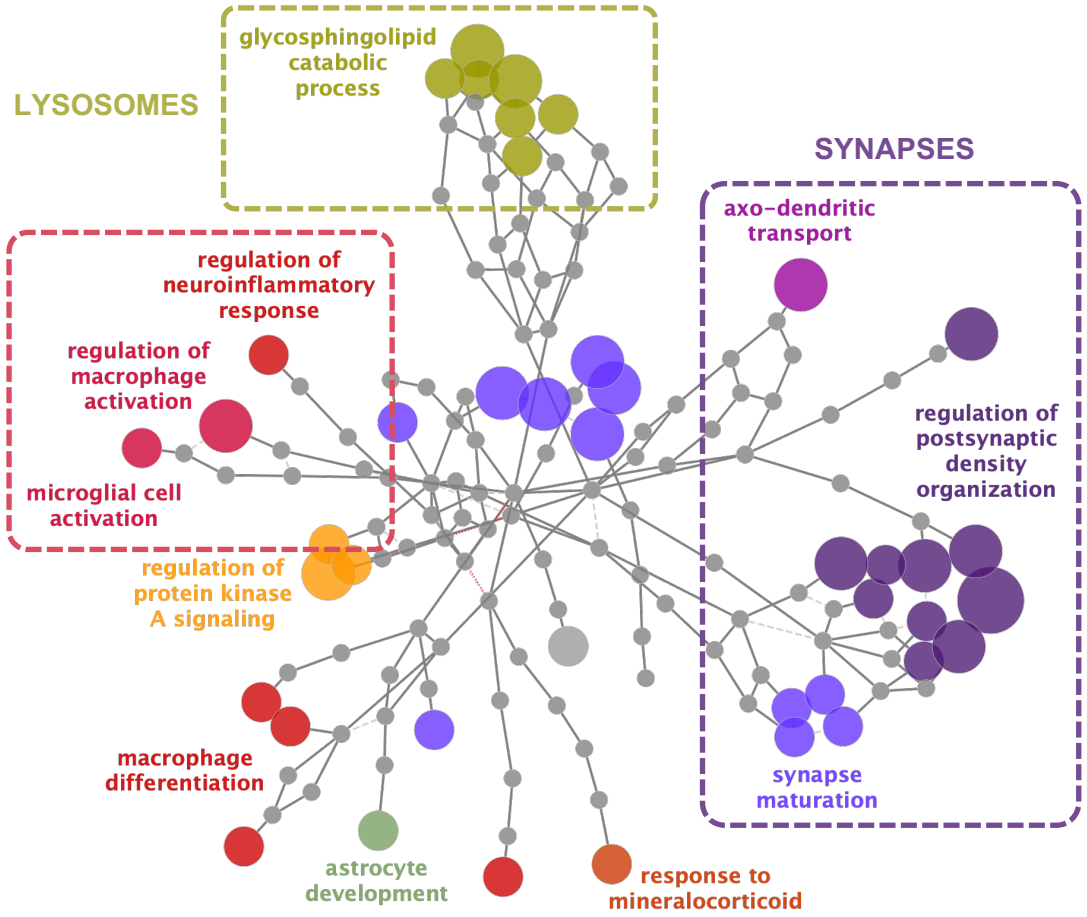
Markers that changed at least 2-fold vs baseline in at least three patients in at least one timepoint.



20 CSF proteins

- The 20 CSF proteins that change in concert share several functional associations:
  - Lysosome function/autophagy [6 of 20 (30%) markers that changed in concert in ”responders”]
  - Neuro-inflammation immune response, neutrophil activation [6 of 20 (30%)]
  - Synapse neuronal cell adhesion and synapse assembly [3 of 20 (15%)]

Functional association: Gene Ontology (GO) term enrichment analysis of the 20 CSF proteins



Pathway analysis done in Cytoscape v3.8.2 with ClueGO plugin (Bindea et al. Bioinformatics 25:1091–1093, 2009).

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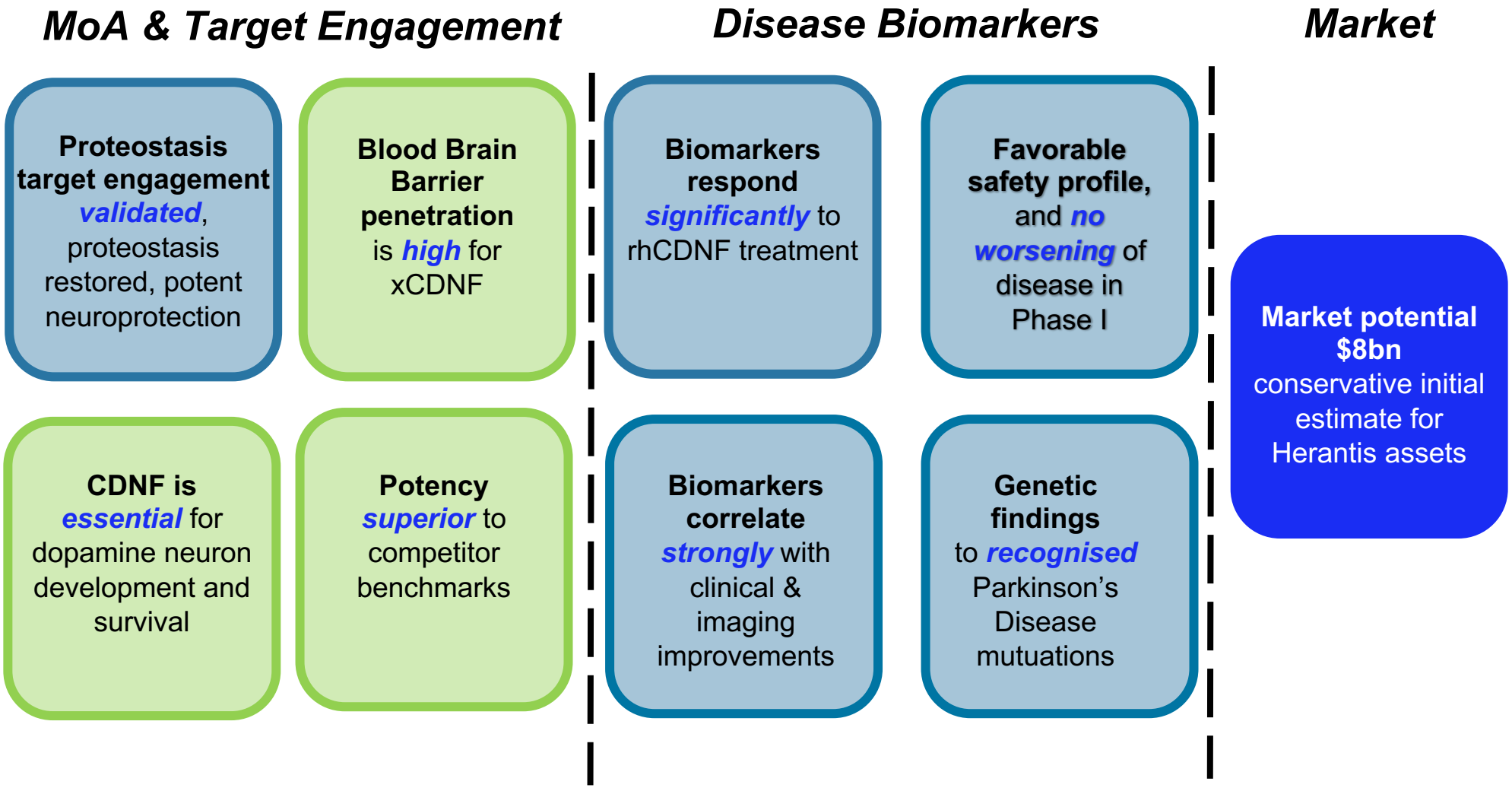

Key:
Human data
In-vivo data

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Parkinson's Disease – Urgent Need For Disease Modifying Treatments

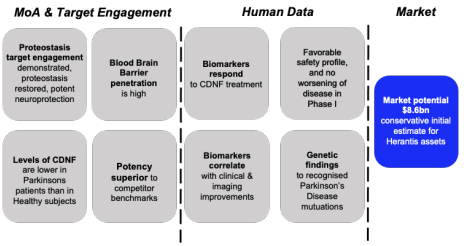
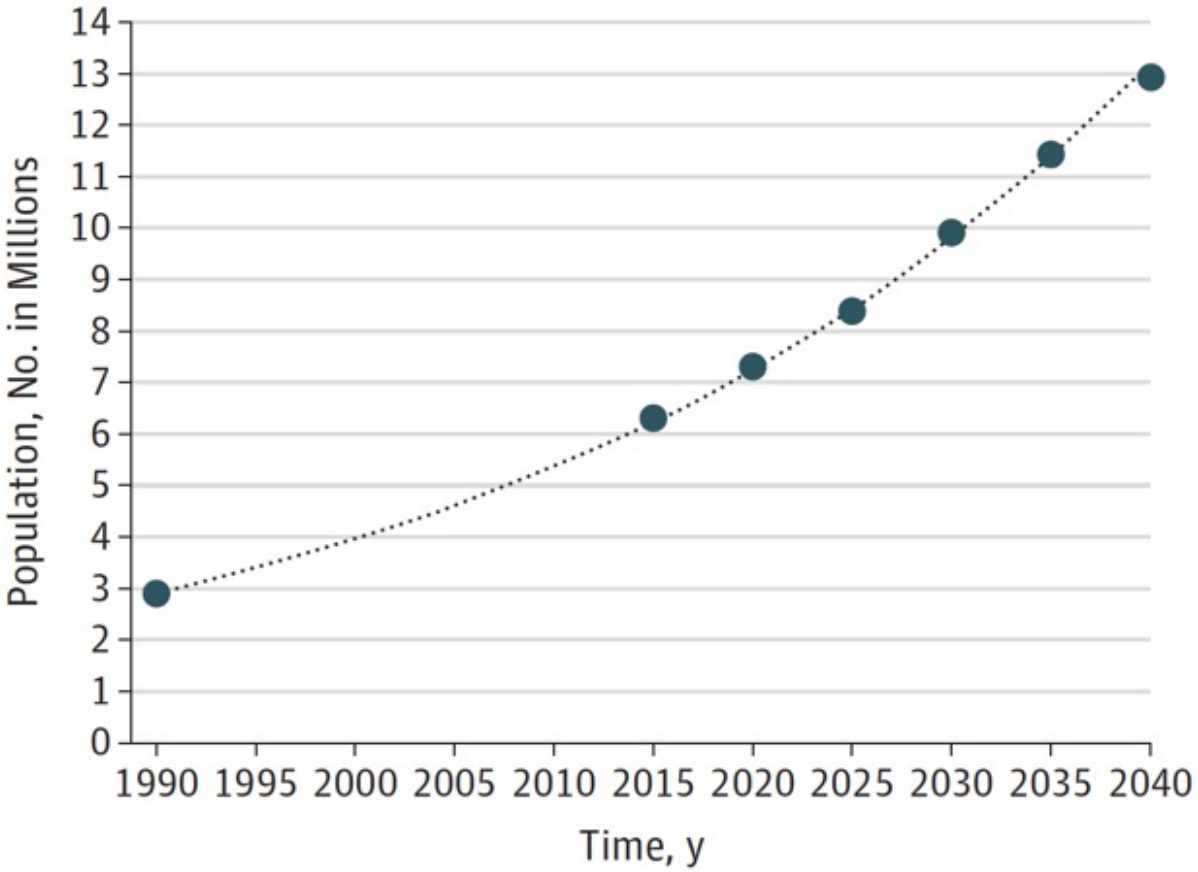


Figure. Estimated and Projected Number of Individuals With Parkinson Disease, 1990-2040



Viewpoint: E.Ray Dorsey. MD, Bastiaan Bloem, MD, PhD

- **Exploding incidence of Parkinson's worldwide … of 'pandemic proportions'**
- **Combination of man-made and genetic factors**

[1] European Parkinson's Disease Association www.epda.eu.com

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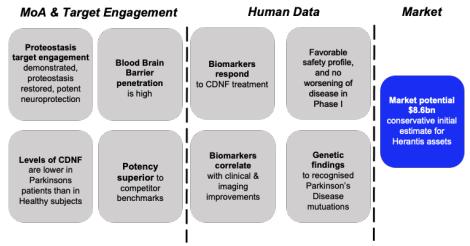
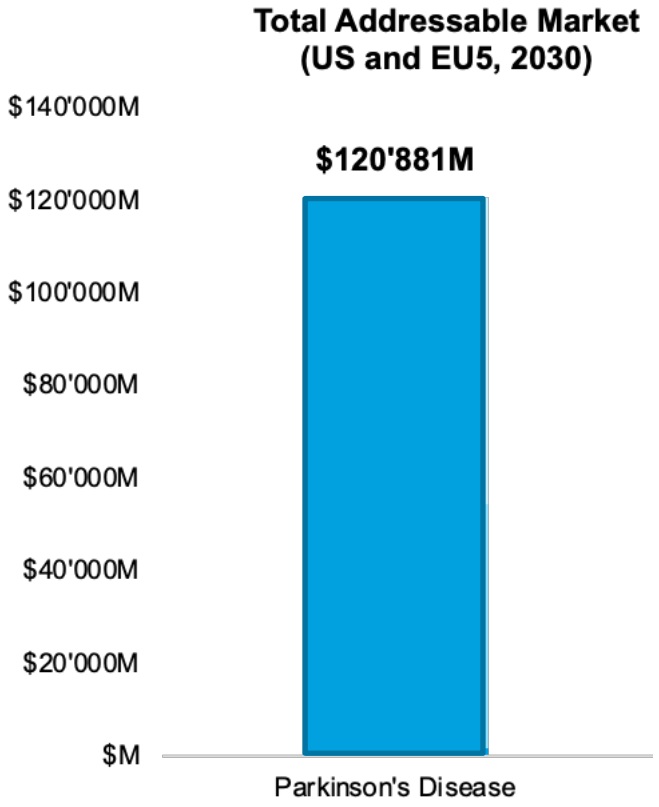
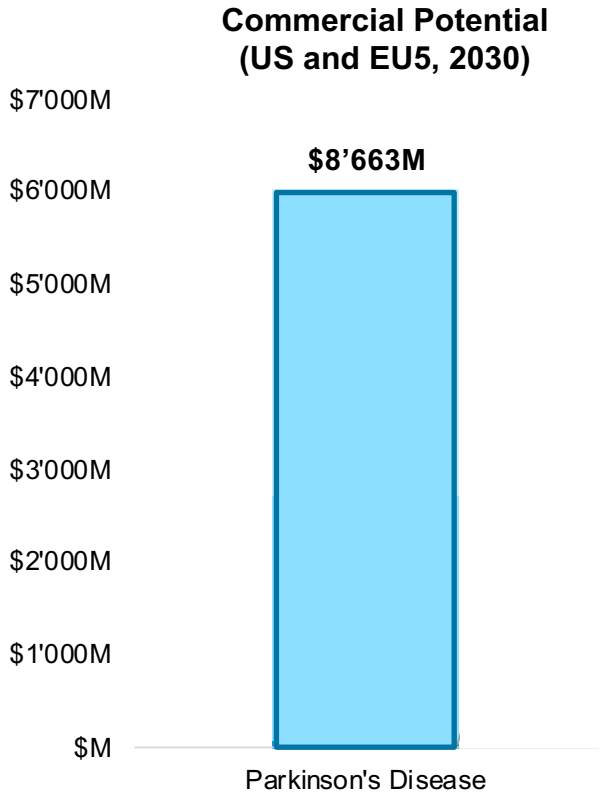
Compelling Commercial Opportunity For Disease Modifying rhCDNF/xCDNF





Overall, the TAM for Parkinson's disease represents a ~$120B market in 2030



For CDNF/xCDNF, Parkinson's disease represents at least a ~$8B commercial opportunity in 2030

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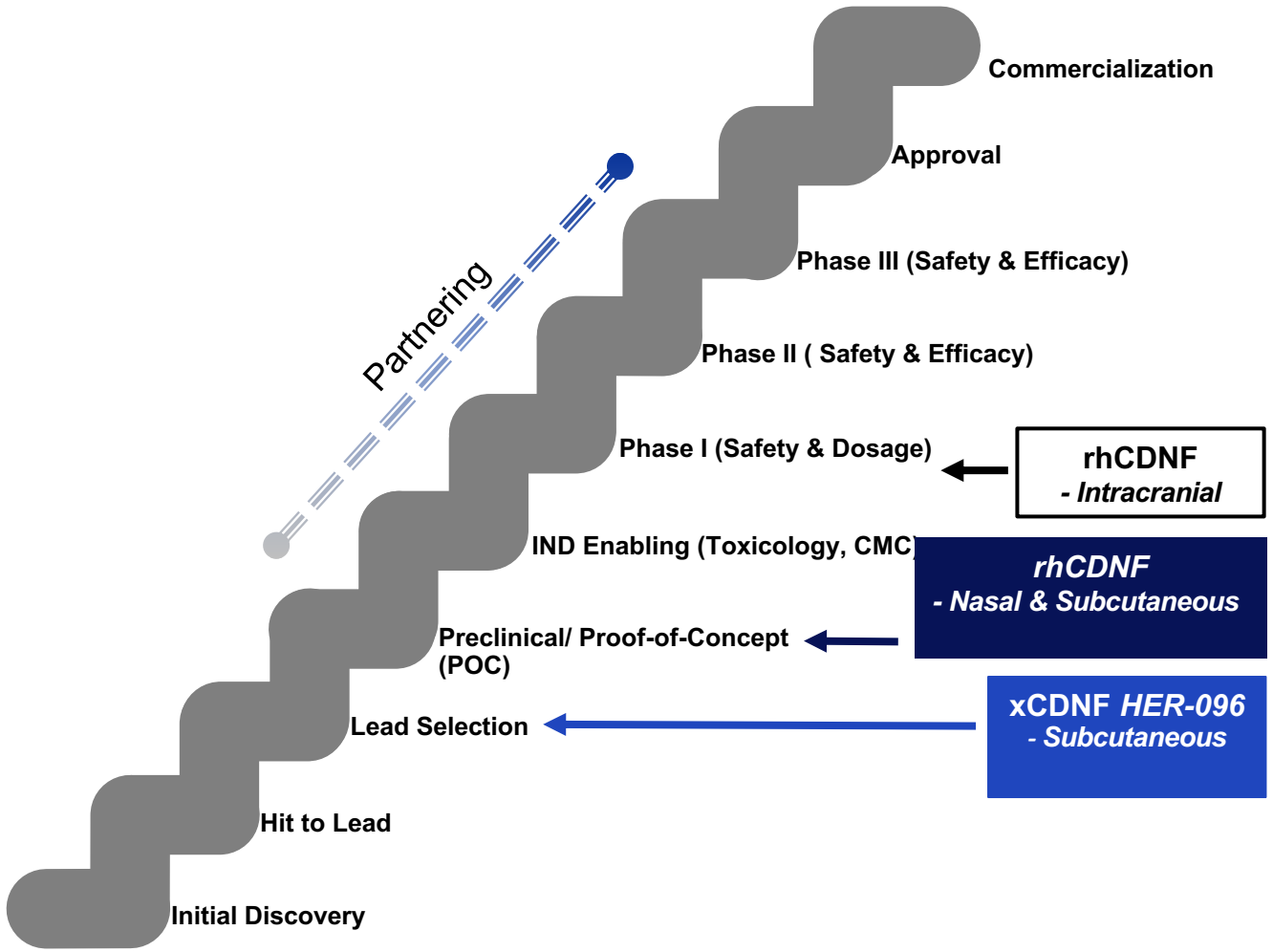
Timelines & Some Of The Key Planned Milestones



2H 2021	Parkinson's Disease and other neurodegenerative diseases	rhCDNF:	Intranasal administration formulation milestones
2H 2021	Parkinson's Disease	xCDNF (HER-096)	Pre-clinical efficacy and additional PoC milestones
1H 2022	Parkinson's Disease and other neurodegenerative diseases	rhCDNF:	Pre-clinical efficacy and PoC milestones
1H 2022	Parkinson's Disease	xCDNF (HER-096)	IND enabling and toxicology milestones
2H 2022	Parkinson's Disease and other neurodegenerative diseases	CLINICAL:	Observational biomarker study in PD patients

Program Development Milestones ← → **Newsflow 2021/22**

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Conclusion: Why rhCDNF & xCDNF(HER096) Are So Compelling!

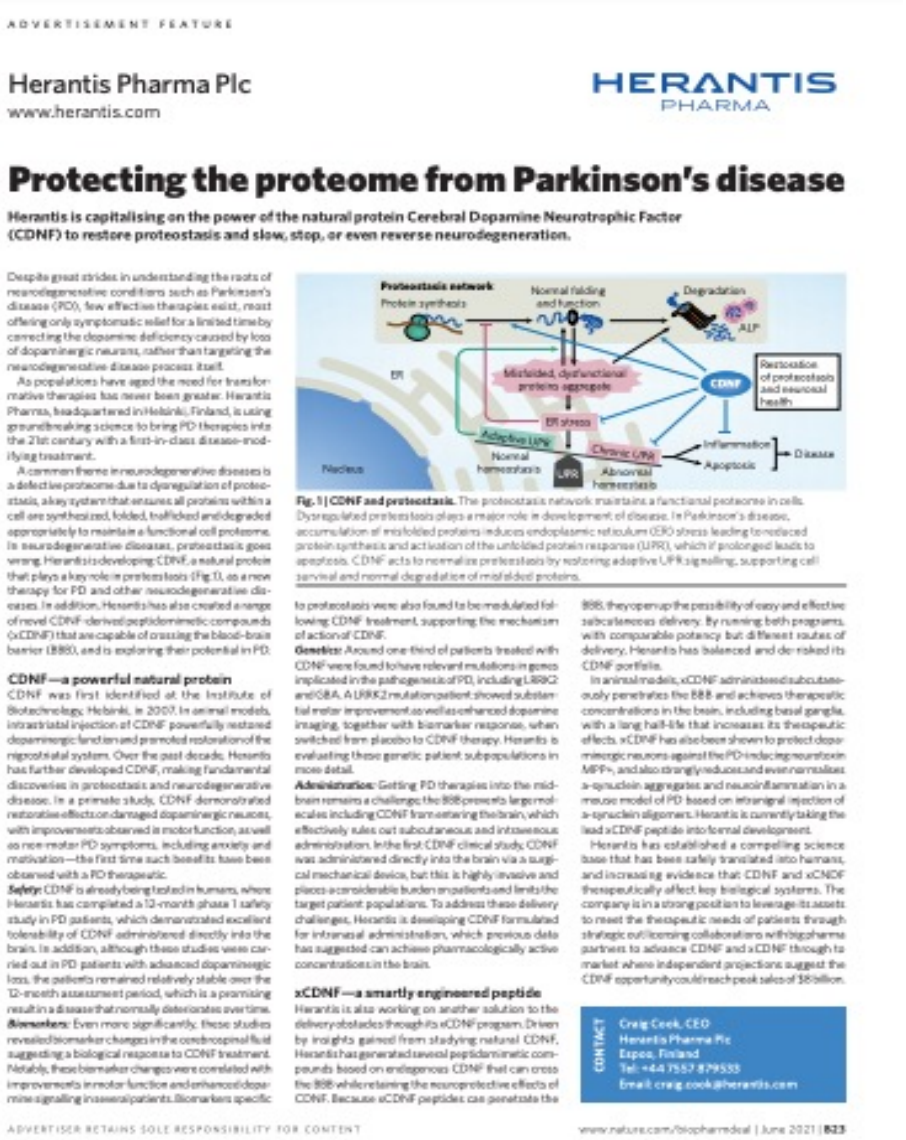
- **Powerful validated MoA and scientific merit**
  - *Restores proteostasis, needed for neuronal survival, convincingly crosses BBB*
- **Unparalleled biomarker data**
  - *Strong impact on markers of disease; clear correlation with clinical & imaging improvements*
- **Significant market opportunity**
  - *Parkinson's pandemic equates to multi $bn dollar need*
- **Rich potential newsflow**
  - *Several near and medium term milestones anticipated*

Herantis Pharma Featured in the June 2021 Nature Journal

Nature Magazine's BioPharma Dealmakers June 2021 edition which focuses on the latest developments in CNS.

The Herantis article, titled, *Protecting the proteome from Parkinson's disease,* details how Herantis is capitalizing on the power of the natural protein Cerebral Dopamine Neurotrophic Factor (CDNF) to restore proteostasis and slow, stop, or even reverse neurodegeneration.

The complete article is available in print and in digital format and can be viewed via the following link: www.nature.com/articles/d43747-021-00070-6



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Protecting the proteome from Parkinson's disease

Herantis is capitalising on the power of the natural protein Cerebral Dopamine Neurotrophic Factor (CDNF) to restore proteostasis and slow, stop, or even reverse neurodegeneration.

Despite great strides in understanding the roots of neurodegenerative conditions such as Parkinson's disease (PD), few effective therapies exist, most offering only symptomatic relief for a limited time by correcting the dopamine deficiency caused by loss of dopaminergic neurons, rather than targeting the neurodegenerative disease process itself.

As populations have aged the need for transformative therapies has never been greater. Herantis Pharma, headquartered in Helsinki, Finland, is using groundbreaking science to bring PD therapies into the 21st century with a first-in-class disease-modifying treatment.

A common theme in neurodegenerative diseases is a defective proteome due to dysregulation of proteostasis, a key system that ensures all proteins within a cell are synthesized, folded, trafficked and degraded appropriately to maintain a functional cell proteome. In neurodegenerative diseases, proteostasis goes wrong. Herantis is developing CDNF, a natural protein that plays a key role in proteostasis (Fig 1), as a new therapy for PD and other neurodegenerative diseases. In addition, Herantis has also created a range of novel CDNF-derived peptidomimetic compounds (xCDNF) that are capable of crossing the blood–brain barrier (BBB), and is exploring their potential in PD.

CDNF—a powerful natural protein

CDNF was first identified at the Institute of Biotechnology, Helsinki, in 2007. In animal models, intrastriatal injection of CDNF powerfully restored dopaminergic function and promoted restoration of the nigrostriatal system. Over the past decade, Herantis has further developed CDNF, making fundamental discoveries in proteostasis and neurodegenerative disease. In a primate study, CDNF demonstrated restorative effects on damaged dopaminergic neurons, with improvements observed in motor function, as well as non-motor PD symptoms, including anxiety and motivation—the first time such benefits have been observed with a PD therapeutic.

Safety: CDNF is already being tested in humans, where Herantis has completed a 12-month phase 1 safety study in PD patients, which demonstrated excellent tolerability of CDNF administered directly into the brain. In addition, although these studies were carried out in PD patients with advanced dopaminergic loss, the patients remained relatively stable over the 12-month assessment period, which is a promising result in a disease that normally deteriorates over time.

Biomarkers: Even more significantly, these studies revealed biomarker changes in the cerebrospinal fluid suggesting a biological response to CDNF treatment. Notably, these biomarker changes were correlated with improvements in motor function and enhanced dopamine signalling in several patients. Biomarkers specific to proteostasis were also found to be modulated following CDNF treatment, supporting the mechanism of action of CDNF.

Genetics: Around one-third of patients treated with CDNF were found to have relevant mutations in genes implicated in the pathogenesis of PD, including LRRK2 and GBA. A LRRK2 mutation patient showed substantial motor improvement as well as enhanced dopamine imaging, together with biomarker response, when switched from placebo to CDNF therapy. Herantis is evaluating these genetic patient subpopulations in more detail.

Administration: Getting PD therapies into the mid-brain remains a challenge; the BBB prevents large molecules including CDNF from entering the brain, which effectively rules out subcutaneous and intravenous administration. In the first CDNF clinical study, CDNF was administered directly into the brain via a surgical mechanical device, but this is highly invasive and places a considerable burden on patients and limits the target patient populations. To address these delivery challenges, Herantis is developing CDNF formulated for intranasal administration, which previous data has suggested can achieve pharmacologically active concentrations in the brain.

xCDNF—a smartly engineered peptide

Herantis is also working on another solution to the delivery obstacles through its xCDNF program. Driven by insights gained from studying natural CDNF, Herantis has generated several peptidomimetic compounds based on endogenous CDNF that can cross the BBB while retaining the neuroprotective effects of CDNF. Because xCDNF peptides can penetrate the BBB, they open up the possibility of easy and effective subcutaneous delivery. By running both programs, with comparable potency but different routes of delivery, Herantis has balanced and de-risked its CDNF portfolio.

In animal models, xCDNF administered subcutaneously penetrates the BBB and achieves therapeutic concentrations in the brain, including basal ganglia, with a long half-life that increases its therapeutic effects. xCDNF has also been shown to protect dopaminergic neurons against the PD-inducing neurotoxin MPP+, and also strongly reduces and even normalizes α-synuclein aggregates and neuroinflammation in a mouse model of PD based on intranigral injection of α-synuclein oligomers. Herantis is currently taking the lead xCDNF peptide into formal development.

Herantis has established a compelling science base that has been safely translated into humans, and increasing evidence that CDNF and xCNDF therapeutically affect key biological systems. The company is in a strong position to leverage its assets to meet the therapeutic needs of patients through strategic out-licensing collaborations with big pharma partners to advance CDNF and xCDNF through to market where independent projections suggest the CDNF opportunity could reach peak sales of $8 billion.

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Thank You!