

# HERANTIS

## PHARMA

**Company presentation**

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# Company Overview

- Headquartered in Helsinki, listed on Nasdaq First North Finland (2014) and Sweden (2019)
- Pure play CNS biotech company as of 2021
- Research focus is on assets that modify disease pathology
- 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 yielding compelling dataset supporting clinical, imaging, biomarker, and genetics

# A Pure Play CNS Company Focused on Neurodegenerative Diseases

Drug Candidate/Project	Indication	Discovery	Research/ Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone	Market Potential
CDNF	#1. <b>Parkinson's Disease</b> (Intracranial surgery CED device)						Met Primary Endpoints at 12-Month Expanding to new route of administration & indications	Approx. EUR 1.6 bn <sup>a</sup>
	#2 <b>Parkinson's Disease</b> Intranasal Route of Administration:						Data on progress of new administration routes & pre-clinical	Approx. EUR 6 bn <sup>a</sup>
	#3: <b>Neurodegenerative Disease</b> Subcutaneous Route of Administration:						Data on progress of new administration routes & pre-clinical	Approx. EUR multi bn <sup>a</sup>
xCDNF	# 4. <b>Parkinson's</b> and other Neurodegenerative Diseases Subcutaneous						Lead Candidate Selection H1 2021	Approx. EUR 6 bn <sup>a</sup>

CDNF = Cerebral Dopamine Neurotrophic Factor

# CDNF & xCDNF Key Data

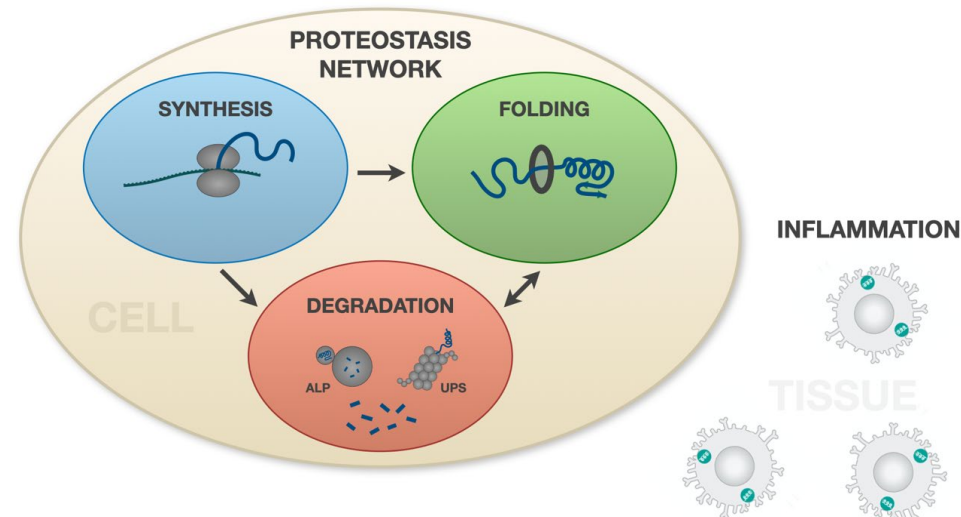
1. Mechanism of Action
2. Safety
3. Biomarkers
4. Genetics
5. Potency



# 1. Proteostasis

# CDNF and xCDNF Act Powerfully On Key System Of The Body - **Proteostasis**

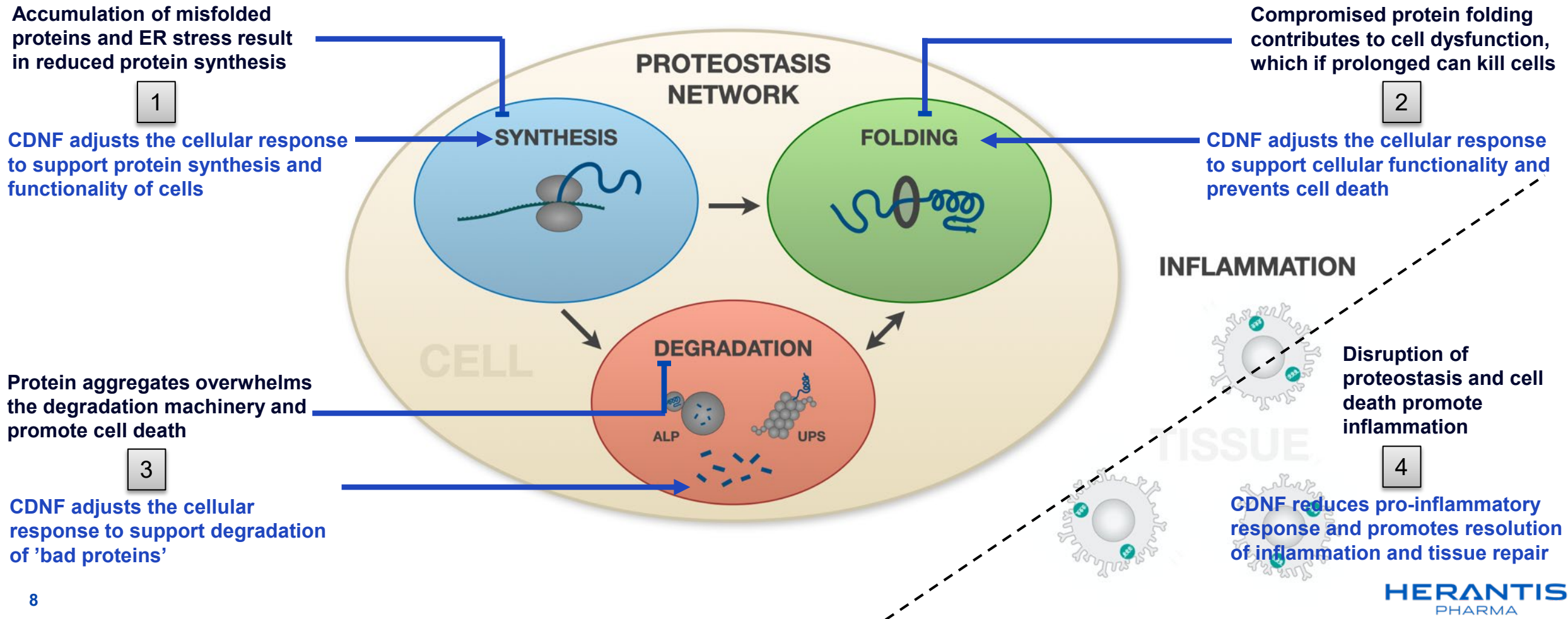
- Proteostasis regulates proteins within the body and influences the fate of every protein from synthesis to degradation
- Particularly important in nondividing, long-lived cells, such as neurons, as its failure is implicated with the development of neurodegenerative diseases such as Parkinsons.
- CDNF (a biological protein) and xCDNF (a chemically engineered molecule) are designed to restore the protective effects of proteostasis
- Highly active area of research together with major players Roche, Merck, Biogen, Calico/Google





# CDNF Targets Core Pathology Of Parkinsons Disease

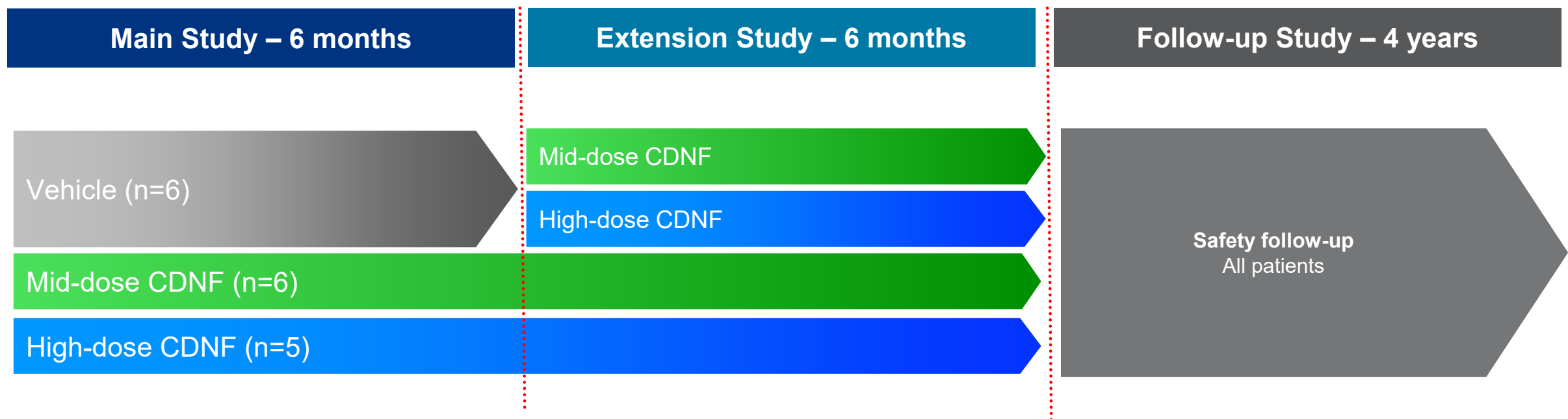
**Proteins are the building blocks of everything in the body.** Functionality of all cells (particularly neurons) depends on the balance of the three cornerstones of proteome regulation: synthesis, folding and degradation.  
**If any of these becomes dysfunctional, problems will follow**





## 2. Safety

# Phase I Safety Study Successfully Completed

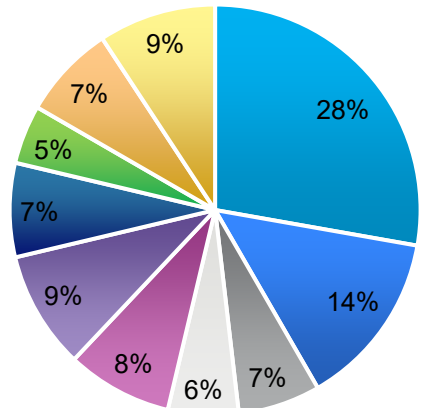


Clinical Characteristic of Enrolled Patients	Placebo n=6	CDNF (low-mid-mid) n=6	CDNF (low-mid-high) n=5
Age (years)	63.8 ± 6.4	63.2 ± 8.9	57.8 ± 6.7
Disease duration since first motor symptoms (years)	10.5 ± 2.7	10.7 ± 3.1	10.8 ± 2.3

# CDNF Safety Established

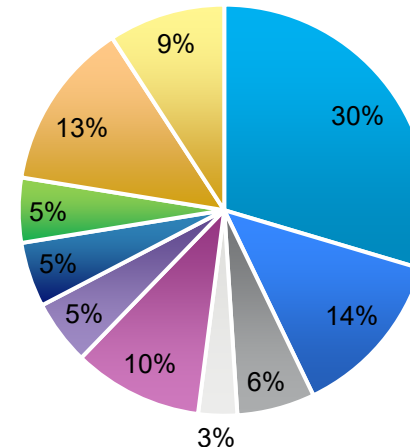
- Majority of the reported drug-related adverse events AE's were mild and transient
- Similar safety profile in Main (0 – 6 Months) and Extension (6 – 12 Months) study
- Similar safety profile between dose-groups
- No dose-limiting toxicities related to CDNF
- Serious SAE's related to surgical implantation device and procedures, not related to CDNF
- Not an efficacy study due to advanced stage of patients disease, but ...
  - no worsening of disease, and promising biological signals in some patients

**0 – 6 month Main Study**



**Adverse events profile**

**6 – 12 month Extension Study**

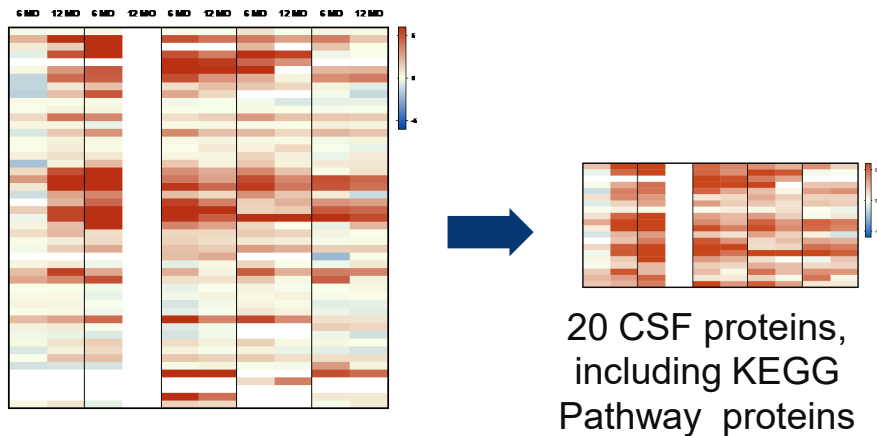


### **3. Biomarkers & Genetics**

# Emerging Evidence Of CDNF Treatment Effects On Biomarkers

- Biomarkers in Cerebrospinal Fluid (CSF) change in response to CDNF 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 CDNF treatment

## A specific CSF biomarker signature in responders

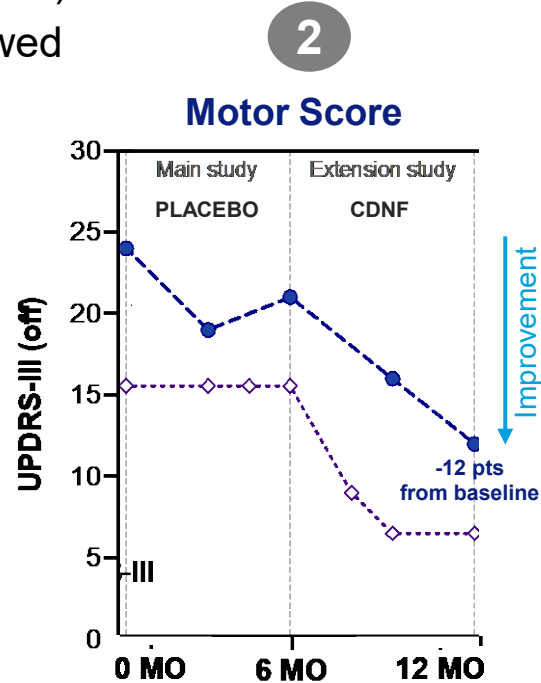


KEGG Pathway (2019 Human)	Adjusted P-value	Odds Ratio	Combined Score
Lysosome	0.01	29.21	243.46
IL-17 signaling pathway	0.05	24.28	135.02
Longevity regulating pathway	0.05	22.09	118.83
Autophagy	0.06	17.51	86.47
Cell adhesion molecules (CAMs)	0.06	15.41	72.43

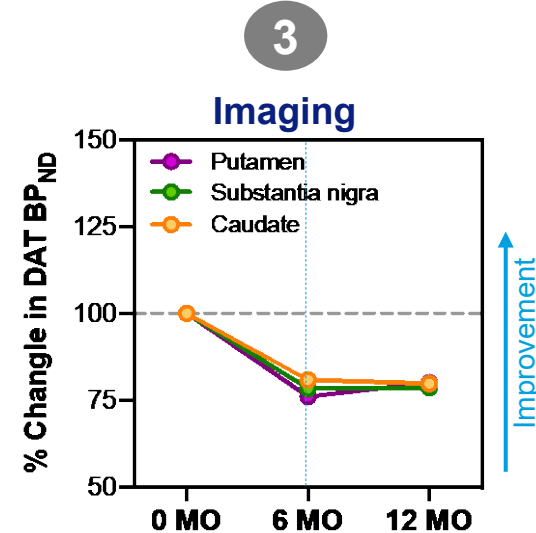
# Emerging Evidence Linking Genetic + Clinical + Imaging + Biomarker Data

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

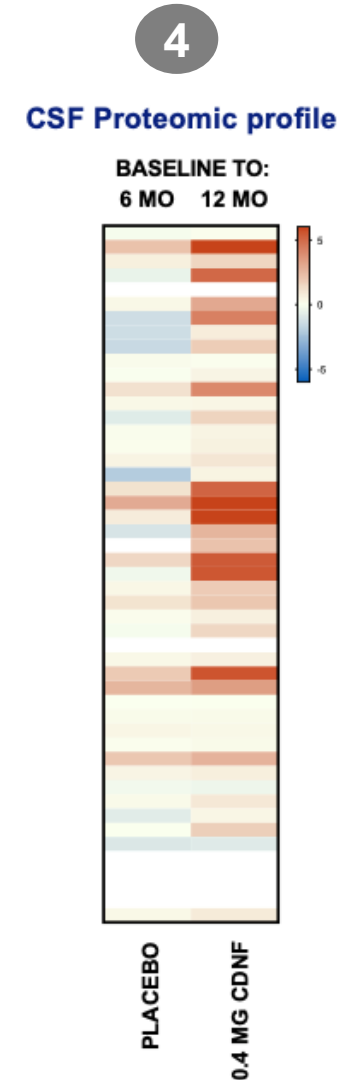
## 1 Genotype LRRK2 (G2019S)



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



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



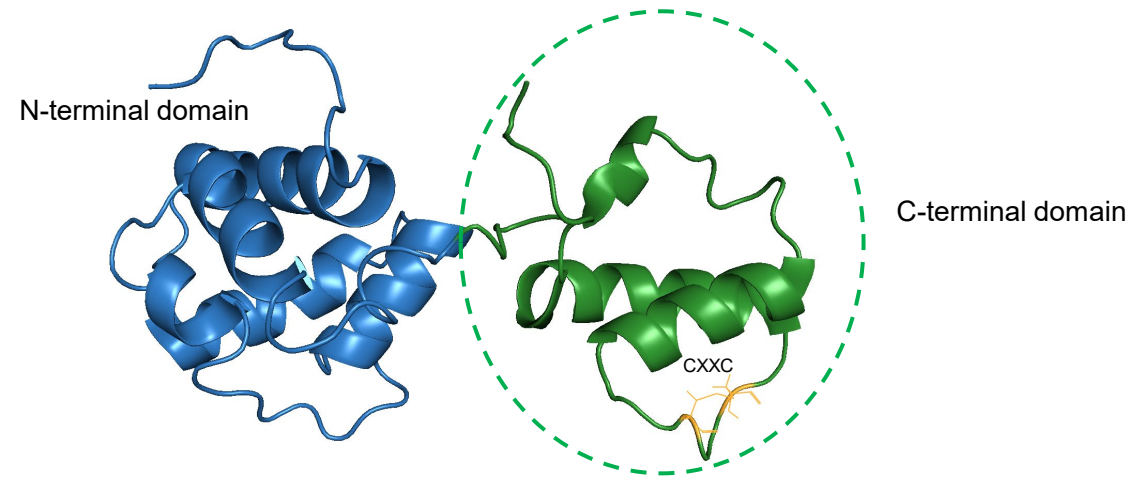
Strong response signal in disease and proteostasis relevant markers

## 4. xCDNF



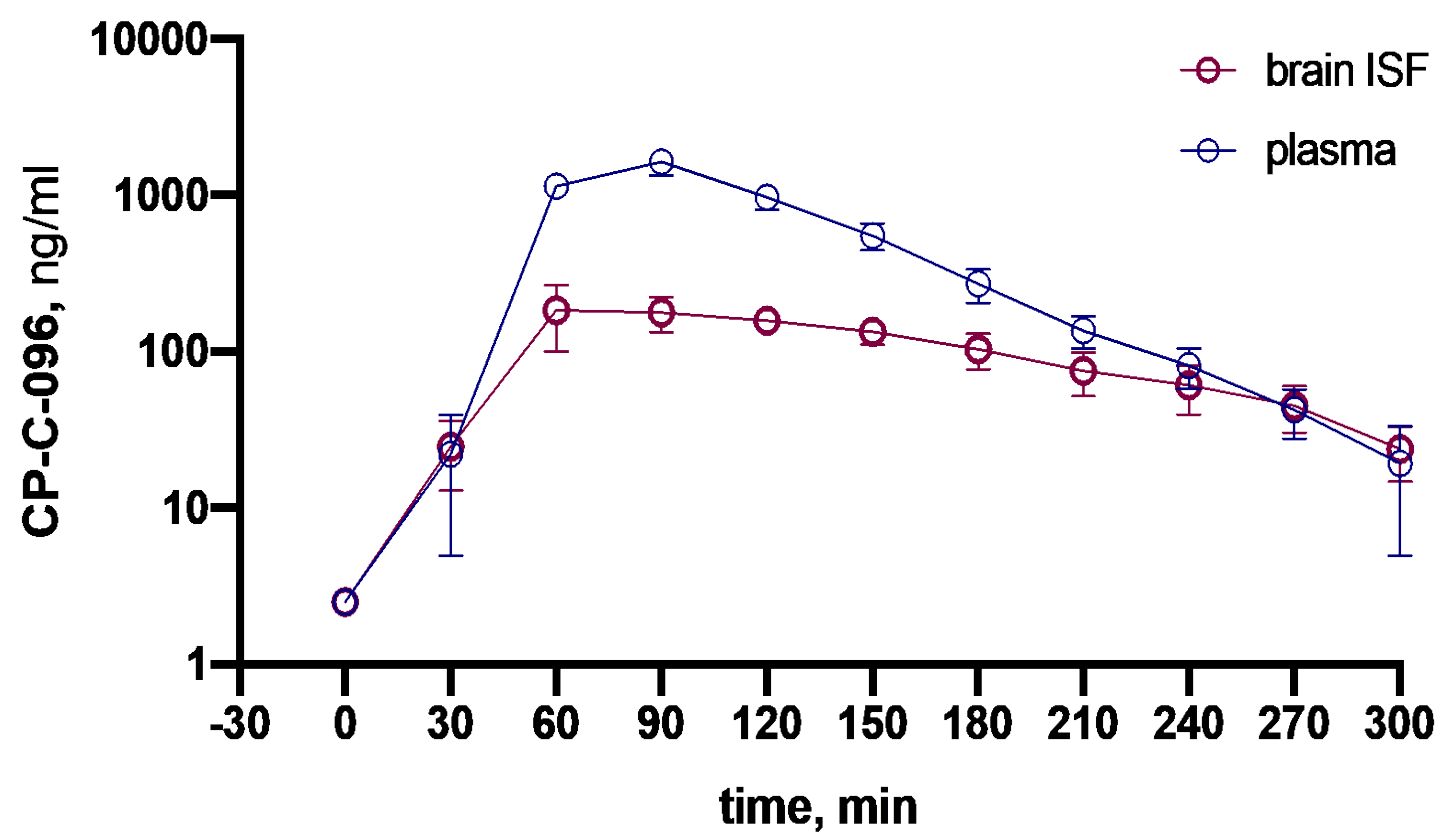
# xCDNF - Engineered To Achieve Essential Therapeutic Parameters

- Synthetic peptidomimetic compound using only smallest most potent fragments of parent CDFN
- Engineered to maintain **potency** in protecting neurons, as well as to **cross the blood brain barrier** (BBB) - both critical elements for success of this therapy
- Latest data shows impressive effect on neuronal survival, synuclein reduction, biomarker findings
- Administered via a simple skin injection
- Potential treatment of chronic and acute neurodegenerative diseases



# BBB Penetration: At Therapeutic Levels + Extended Half Life In Vivo

DUAL (BRAIN AND PLASMA) MICRODIALYSIS STUDY IN MICE

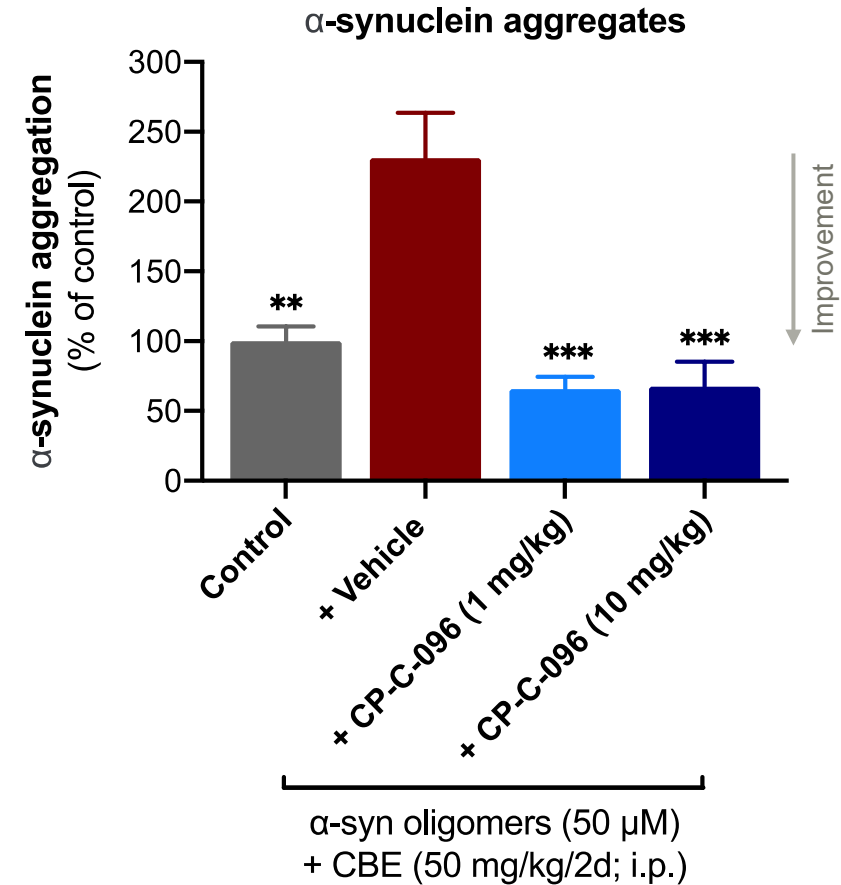
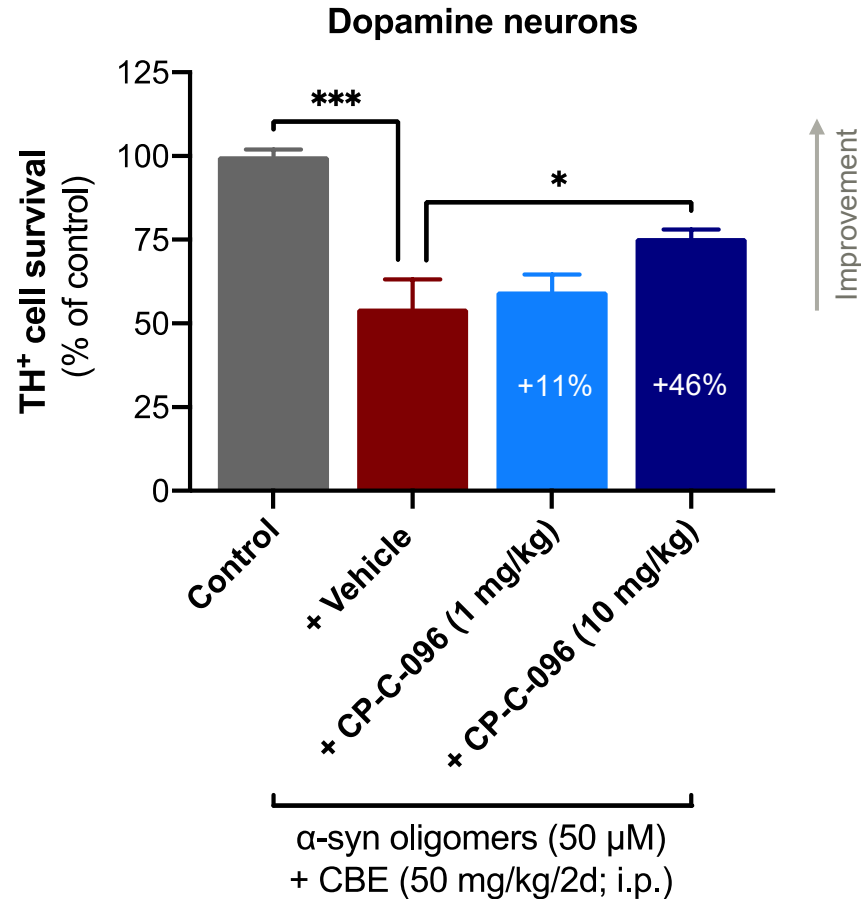


$K_{p,uu,brain} = 0.216$



# Potency: Protects Dopamine Neurons + Reduces $\alpha$ -Synuclein Aggregates In Vivo

High protection of dopamine neurons, plus almost complete eradication of  $\alpha$ -synuclein aggregates

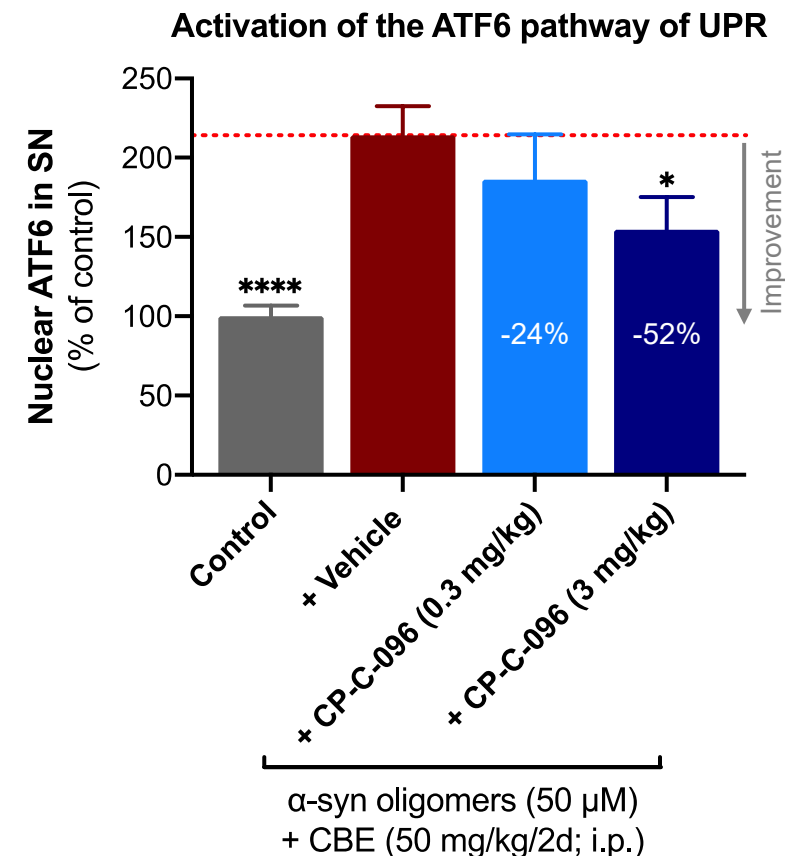
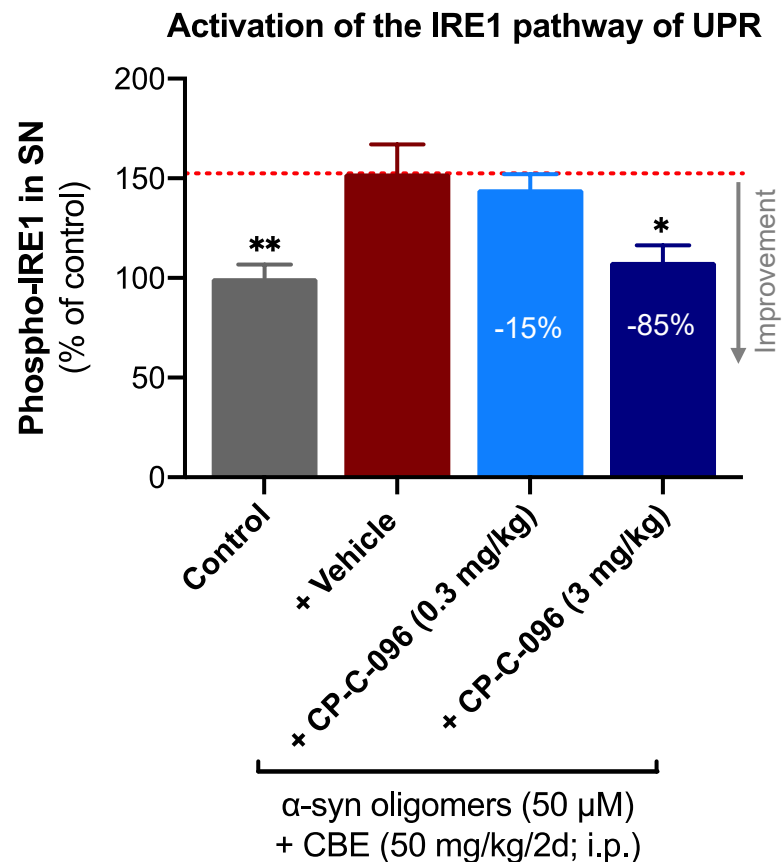
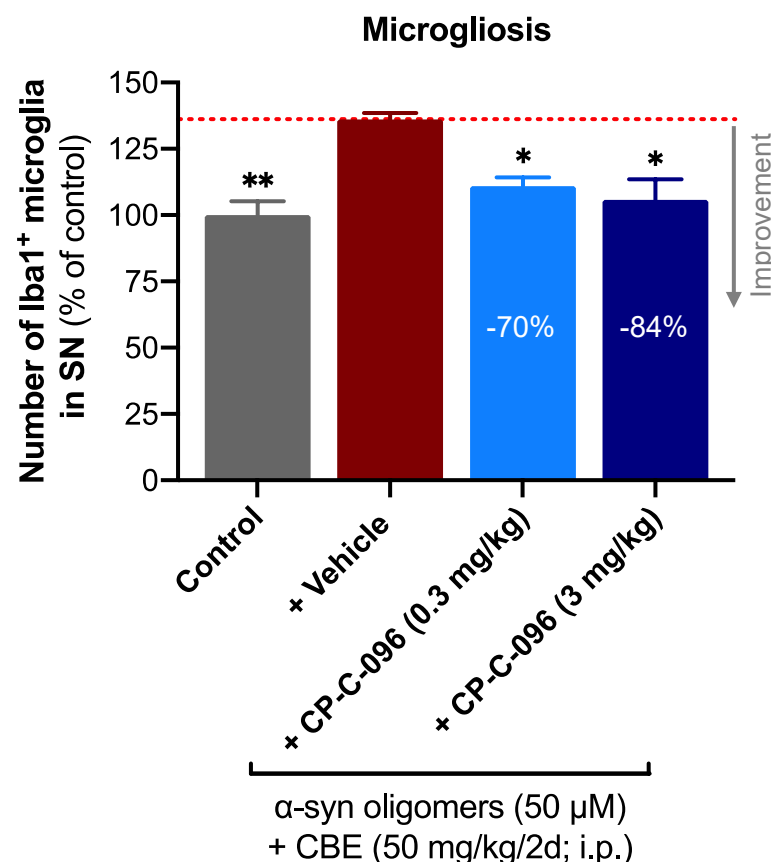


**STUDY:** Test compound CP-C-096 was administrated subcutaneously in dose 1mg/kg or 10 mg/kg three times per week for four weeks starting from the day of  $\alpha$ -synuclein oligomers injection. Animals were sacrificed at day 28 after the model initiation, and neuronal survival and alpha-synuclein 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.



# Attenuates Unfolded Protein Response And ER Stress, Reduces Cell Death

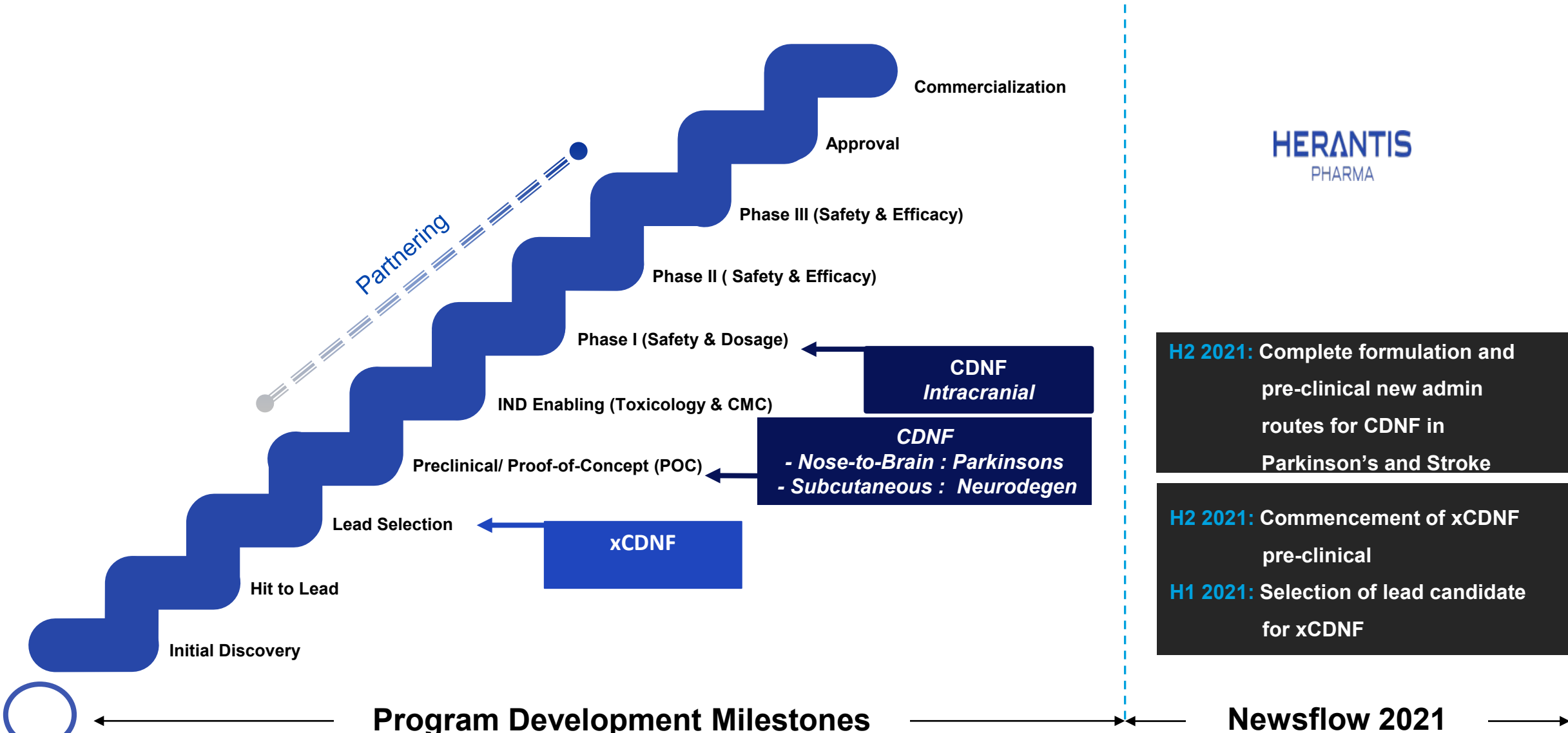
**Microglial Activation and Unfolded Protein Response Are Attenuated in the Substantia Nigra of Mice Treated with CP-C-096 >80% reduction of key neuroinflammatory/microgliosis marker, and 85% and 52% reductions of activated IRE1 and ATF6**



**STUDY:** Test compound CP-C-096 was administrated subcutaneously in dose 0.3 mg/kg or 3 mg/kg three times per week 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-IRE1α) in substantia nigra were assessed by immunohistochemistry (n=5). \*p<0.05 ANOVA with post-hoc Fisher's test versus group treated with vehicle.

# Summary

# Timelines, Newsflow, Next Steps



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# Summary CDNF and xCDNF: Persuasive Picture Emerging Across MoA, Clinical, Biomarker, Imaging And Genetic Data

1. Strong multimodal MoA for CDNF and xCDNF:
  - Restores **proteostasis** and reduces **neuroinflammation** – both key elements of Parkinsons
  - Evidence of **target engagement**
2. CDNF
  - Established **safe** in humans
  - **Biomarker** response to CDNF treatment, **correlates** with clinical and imaging findings
  - Potential **genetic and biomarker** patient subgroups emerging
  - No worsening of disease over 12 months treatment
3. xCDNF
  - Chemical **engineering** has been successful
  - Weekly **subcutaneous** dosing effectively **penetrates BBB**, **protects neurons**, and **reduces alpha-synuclein aggregation and neuroinflammation**





**Thank You!**