CLINICAL STAGE BIOTECH IN NEUROLOGY

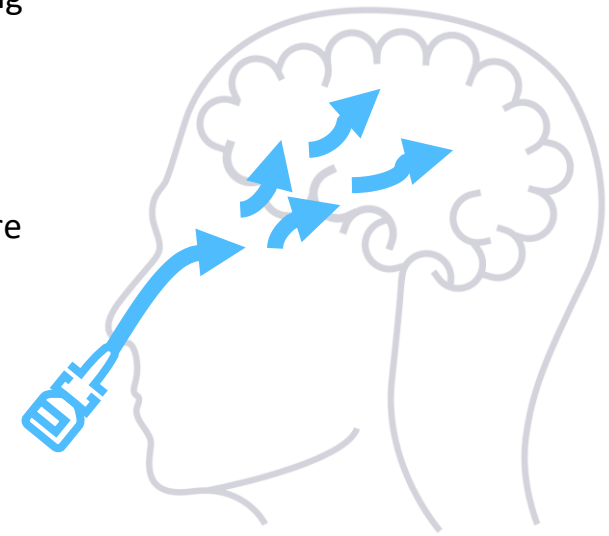
Investment Summary

Company

French biotechnology company developing therapies targeting neuronal energy metabolism, focusing on neurological diseases where impaired mitochondrial function drives disease progression.

Product

CBT101 – Intranasal prodrug of creatine. A patented new chemical entity and formulation designed to reach neurons directly via the nose-to-brain pathway, bypassing the blood-brain barrier, to restore cellular energy homeostasis in the brain.



Validation

- Strong preclinical evidence demonstrating delivery of CBT101 and creatine into the brain and neurons after nasal dosing.
- Improved neuronal metabolism and cognitive performance observed in disease models.
- Phase 1 completed in healthy volunteers, demonstrating good tolerability and biological activity measured through qEEG and cognitive tests.

Market & Value Proposition

Initial focus on two neurological indications with high unmet need:

- Creatine Transporter Deficiency (CTD) – rare genetic disorder (up to 16,000 patients EU/US) with no approved treatments.
- Amyotrophic Lateral Sclerosis (ALS) – progressive neurodegenerative disease affecting >~80,000 patients.

These indications represent a combined market opportunity exceeding €2.5B and provide a pathway to expand into additional neurodegenerative diseases.

Investment Summary (Cont'd)

Competitive Advantage & IP

- First therapy designed to deliver creatine directly into neurons.
- Proprietary nose-to-brain drug delivery technology.
- Strong patent portfolio supporting CBT101 and the delivery platform.
- Platform potential to enable delivery of other drugs unable to cross the blood-brain barrier.

Regulatory & Development Status

- Orphan Drug Designation granted for CTD by both FDA and EMA.
- Pediatric designation granted by FDA.
- Phase 1 clinical study completed.
- Preparing Phase 2 trials in ALS and CTD.

Investment Opportunity

The company is raising €20M to advance Phase 2 clinical trials in ALS and CTD.
A further €40M would support pivotal Phase 3 development in ALS and broader pipeline expansion.

Team

Led by Thomas Joudinaud, MD, PhD (CEO, Co-founder), with clinical and scientific expertise in neurological diseases and drug development, and Henri Bénech, PharmD, PhD (COO, Co-founder), an experienced pharmaceutical scientist with deep expertise in translational research and drug development. The leadership team is supported by experienced scientists, clinicians, and advisors specializing in neurodegenerative diseases and mitochondrial biology.

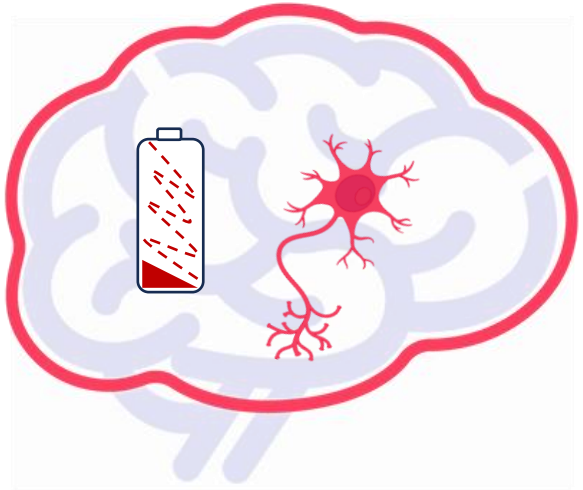
Targeting the unbalance of neuronal energy

ALS, CTD, Parkinson's, Huntington's…

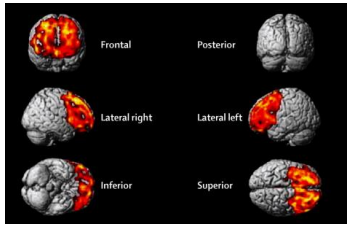
In neurologic and degenerative disorders, the energy homeostasis of neurons deteriorates progressively resulting in neuronal dysfunction

This further promotes the energetics imbalance, establishing a vicious feedback loop and a downward spiral of disease progression

→ Improving, preserving or rescuing brain energetics are key components of therapeutic strategies



Brain hypometabolism in patients with ALS
(assessed by ^{18}F-fluorodeoxyglucose PET)
Lancet Neurology, 2014



Chio et al. 2014 Lancet Neurol. Dec;13(12):1228-40
Cunnane et al. Nat Rev Drug Discov. 2020 September 19(9): 609–633
Zilberter et al. J. Neurosci. Res. 95, 2217–2235 (2017)
Camandola et al. EMBO J. 36, 1474–1492 (2017)
Cheng et al. Nat Neurosci. 2025 Apr;28(4):748-756.

Creatine, key natural component of bioenergetic homeostasis of neurons
A "promising disease modifying agent" with untapped potential

Bioenergetic failures associated with creatine dysregulation in many neurodiseases

Primary brain creatine deficit[1]

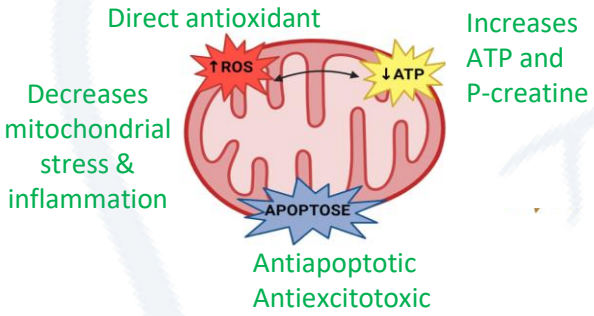
- Creatine transporter deficiency
- Creatine synthesis deficit

Neurodegenerative diseases: mitochondria dysfunction and P-Cr variations[2]

- ALS [3] , Alzheimer [4] , Parkinson[5], Huntington [6]

Indeed, Creatine is essential in the energy homeostasis of neurons …

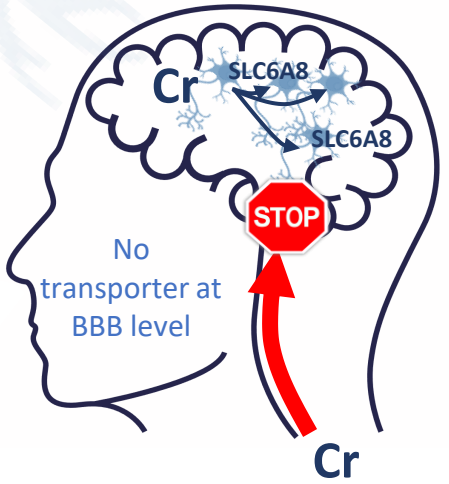
Protects & boost mitochondria, Acts as energy Shuttle & Buffer



… but cannot be supplemented easily

Oral creatine stopped at BBB explaining failure of previous clinical studies[7]

Intrinsic brain creatine pool available only in limited amount



How to deliver creatine to Neurons?

*= SLC6A8 gene coding for creatine transporter

1. Salomons et al. 2001 Am. J. Hum. Genet ; Stockler et al, 2007 Creatine and Creatine Kinase in Health and Disease
2. Alqahtani et al 2023 Mitochondrio.
3. Sassani et al, 2020 Brain ; Westeneng et al, 2025 eBioMedicine
4. Das et al. 2021, Frintiers in Neuroscience
5. Payne et al, 2024 Brain
6. Lowe et al . 2022 Brain communications
7. Bender et al. 2016 Amin Acids

Introducing CBT101: Patented Creatine Prodrug Nasal Spray

“the Neuro Booster”

→ Leveraging Nose-to-Brain pathway to target neurons with an innovative creatine prodrug enabling neuronal energy restoration

Unique ability to boost the mitochondria and restore energy levels

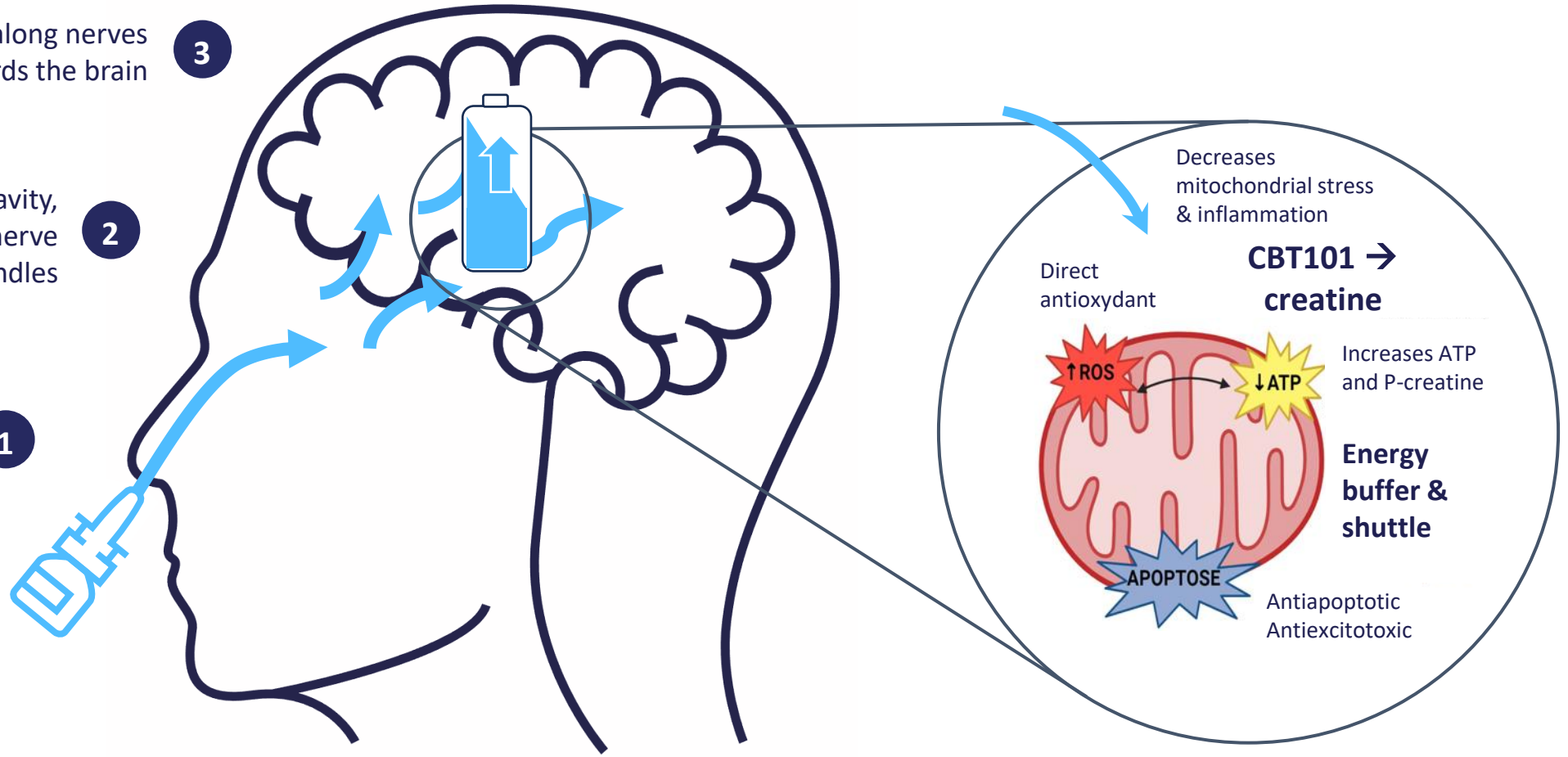
Diffuses from neurons to neurons to all brain areas 4

Releases creatine within neurons 5

Migrates along nerves towards the brain 3

Within nasal cavity, enters passively nerve bundles 2

CBT101 nasal dosing 1



Our strategy – Address neuronal energy deficit in two rare neurological diseases with major unmet medical needs

Expand secondarily in societal diseases

Development priorities

1 Rare diseases

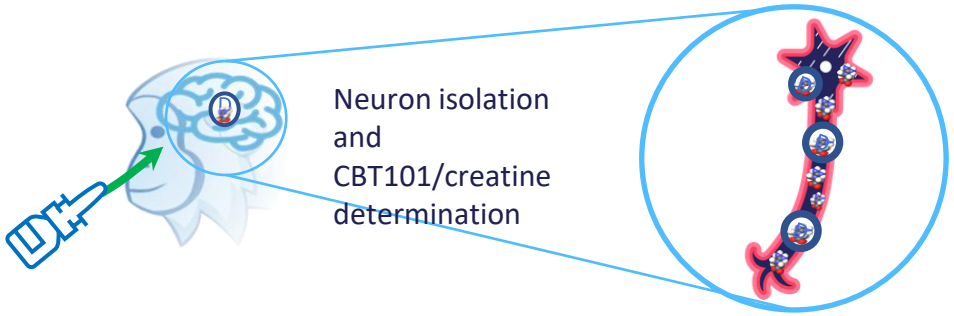
2 Societal diseases

	CTD*	ALS	Parkinson	Epilepsia, Autism, ADHD, schizophrenia…
Pathophysiology	SLC6A8 Gene defect → creatine transporter deficit =no creatine in neurons	Degeneration of motor neurons – associated mitochondrial dysfunction	Degeneration of dopaminergic neurons –mitochondrial dysfunction	Brain energy dysregulation and deficits
Clinical symptoms	**Severe intellectual deficiency, autism, seizure**	Progressive paralysis of all muscles including respiratory	Tremor, akinesia, dyskinesia	-
Preclinical	Completed	Completed	6OHDA / MPTP mice model → need NHP experiments	-
# of patients (US/EU) / market size	Up to 16,000 >€ 1B	~80,000 >€1.5B	>10,000,000 >€10B	>100 milliions
ODD	Granted FDA/EMA	To be filed in Q2 26	NA	NA
Market access requirement	Conditional approval after Phase 2	Phase 3 required Early access potential	Large phase 3 required (>€ 200-400m)	Phase 3 required
Add. Reg. Benefits	High price Access to PRV**	High price	-	-
Time to market	3-y	5-6y Early access potential in 2030	>8y	
Competition	Low (Ultragenyx no information since 2021)	High	High depending on targeted disease	
Needed Clinical study to validate CBT101 in patients	Pivotal Phase 2	Phase 2a target engagement	Phase 2 target engagement	
	→ Normal dev. in children	**→ Stop progression**		

Preclinical and clinical evidences of neuronal biodistribution and efficacy

1 **CBT101 distributed into neurons and delivers creatine**

WT monkeys



2 **CBT101 demonstrated Biological & clinical efficacy in models of CTD**

WT & SLC6A8
KO mice

Brain plasticity increased (Synaptic biomarkers)
Brain metabolism increased (FDG test PET Scan)
Cognition improved (NOR test)

3 **CBT101 achieved neuroprotection in toxic-induced mitochondriopathies including specific ALS model**

6-0HDA
or MPTP

30 days / 5 days
CBT101

Amphetamine Turning Test
Beam Walking Test
Dopamine
Survival increase

SOD1 mice

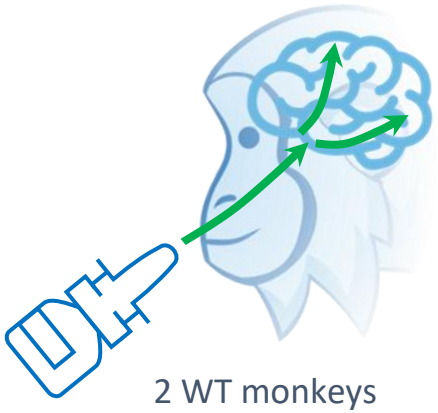
Survival increase after first symptoms
(Median 24,5 d vs. 16 d for control)

4 **CBT101 achieves biological activity in Human's brain**

Healthy volunteers
Phase 1

qEEG showing CBT101 biological activity in healthy volunteers (Increase in Beta Power)

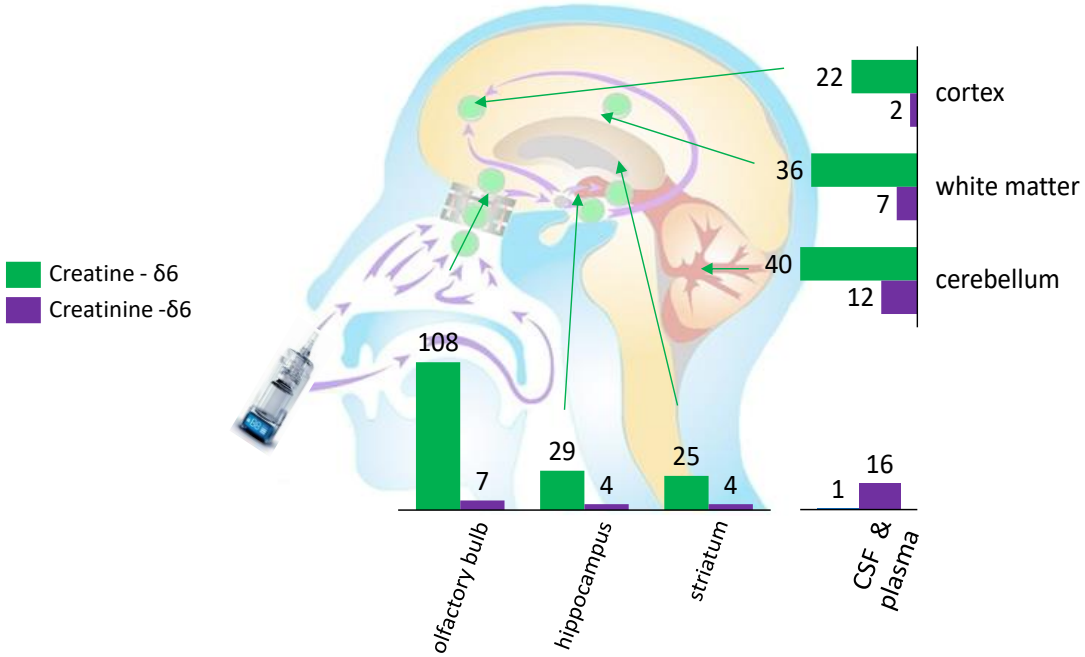
1 CBT101 delivers creatine to the brain through the nose-to-brain pathway and more specifically into the neurons…



2 WT monkeys (male & female)
Repeated nasal administration of CBT101 labelled with stable isotopes

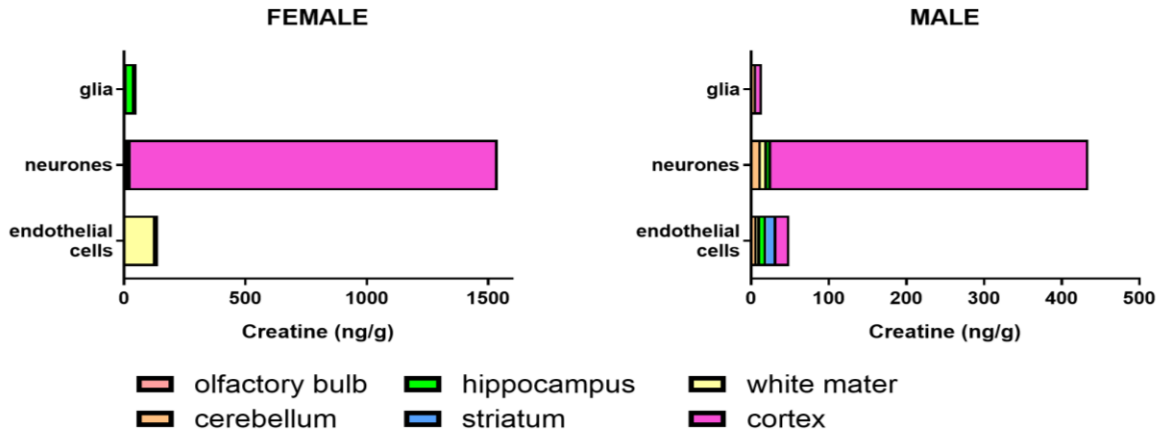
→ Creatine gradient follows olfactory & trigeminal nerves pathway and projection

Measures in brain areas (ng/g) & CSF (ng/ml) using LC-MS/MS



→ CBT101 delivers creatine into the neurons

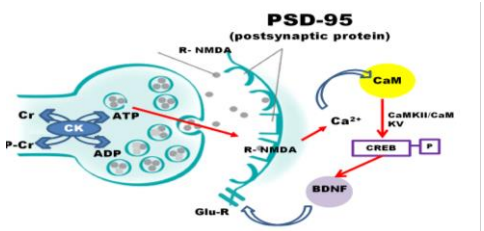
Cell isolation using Anti-PE MicroBeads and magnetic separation

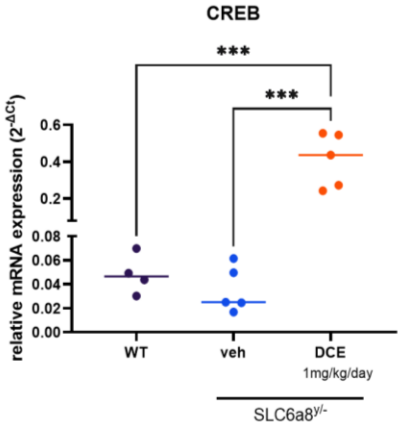


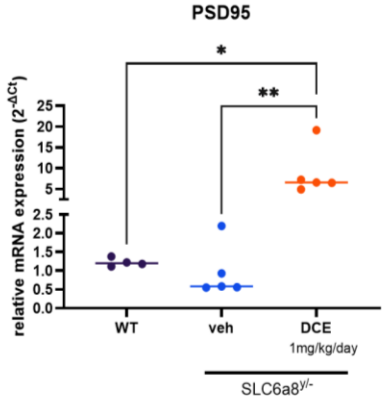
Disdier et al, 2025 Eur J med Chem Feb 15:284:117195

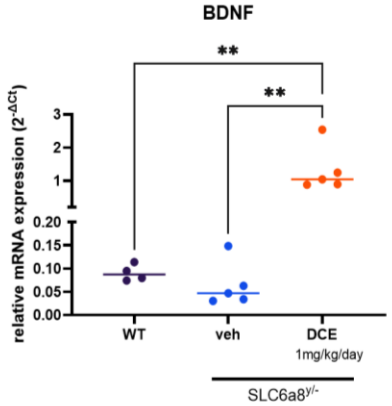
2 Strong preclinical evidences of CBT101 efficacy in creatine brain deficient mice models

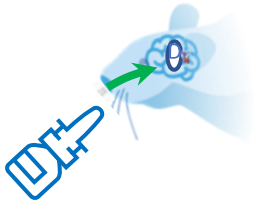
→ **CBT101 increases plasticity** Synaptic biomarkers







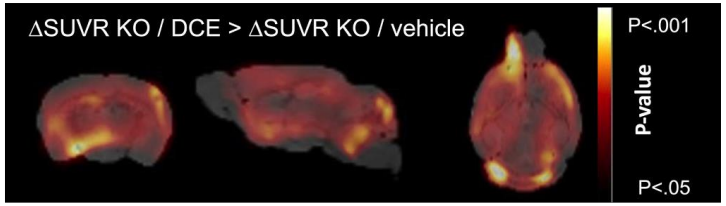




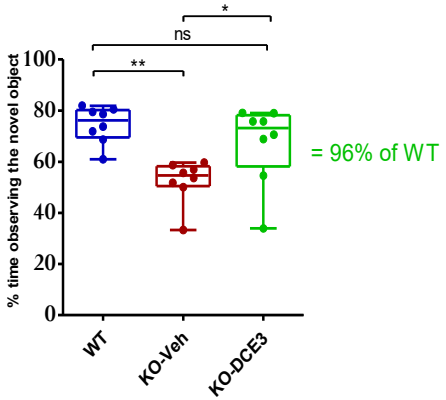
SLC6A8-KO mice
CBT101 intra nasal administration for 30 days

→ **CBT101 "increases" brain metabolism**

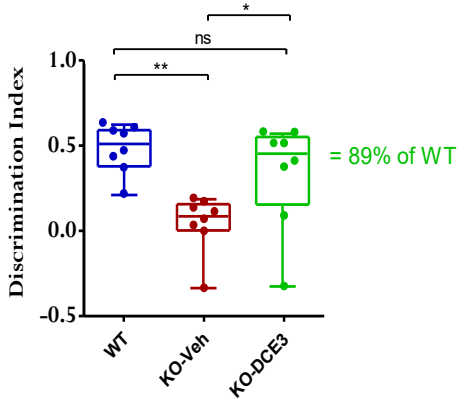
FDG test PET SCAN



→ **CBT101 improves cognition** NOR test



= 96% of WT



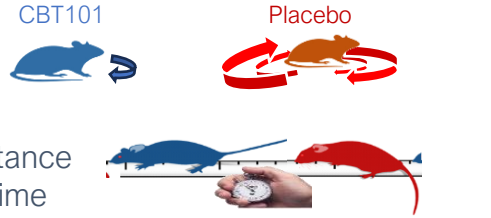
= 89% of WT

Ulio Gamboa et al. Nanomedicine (Lond) 2019 Jun;14(12):1579-1593
Mabondzo et al (2023). Frontiers in Molecular Neuroscience 16
Disdier et al, 2025 Eur J med Chem Feb 15:284:117195

3 CBT101 demonstrated neuroprotection in toxic model targeting mitochondria and in SOD1 mice model (tbc)

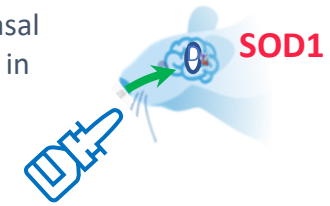
CBT101 intra nasal administration for 30 days in mice

CBT101 nasal dosing protects dopamine production in correlation with neuro behavior



Groups	Initial # of animals	# of survivors at D1
SHAM (Veh + Saline IP)	12	12
Vehicle Intra-nasal	12	3
CBT101 Intra-nasal	12	7
Creatine Per Os	12	2

CBT101 intra nasal administration in SOD1 mice



- N=48 ; 3 groups (Controls, Formulation w/o CBT101
- & CBT101)
- Neuroscore analysis

CBT101 nasal dosing protects SOD1 mice from neuromotor symptoms evolution

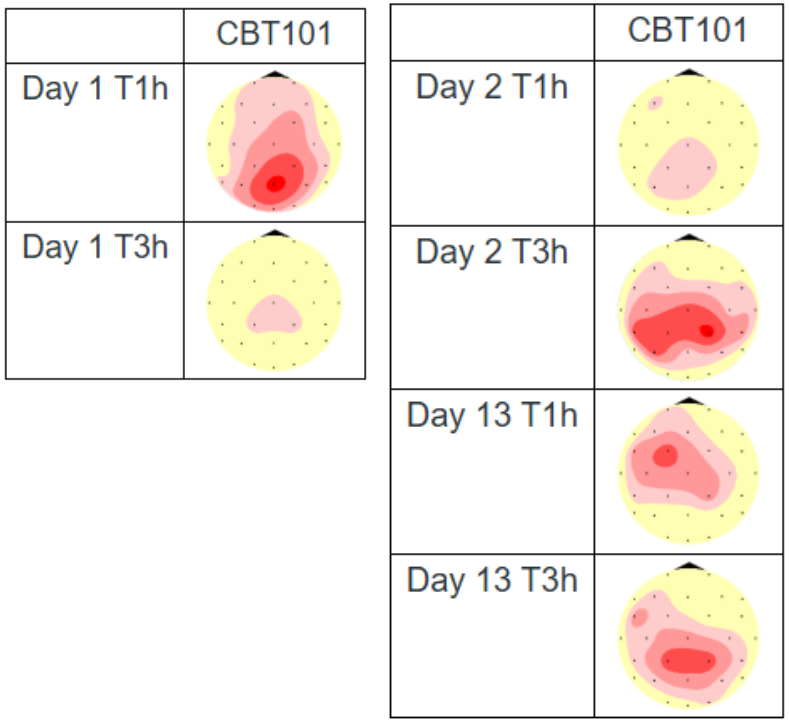
Group	Median survival– all gender (d)	Median survival -females (d)	Median survival - males (d)
Control	16	17	16
Placebo	+50% 21	+47% 20	+75% 28
CBT101	24 +14%	25 +25%	28 +0%

Bénech *et al.* Mitonice September 2022, Nice France
Disdier *et al.* 14th World Congress on Targeting Mitochondria berlin Oct 11-13, 2023
Bénech et al, Front Aging Neurosci. 2025 Jul 11;17:1597263

4 Preliminary efficacy results following Phase 1 → qEEG demonstrates CBT101 biological activity in healthy volunteers

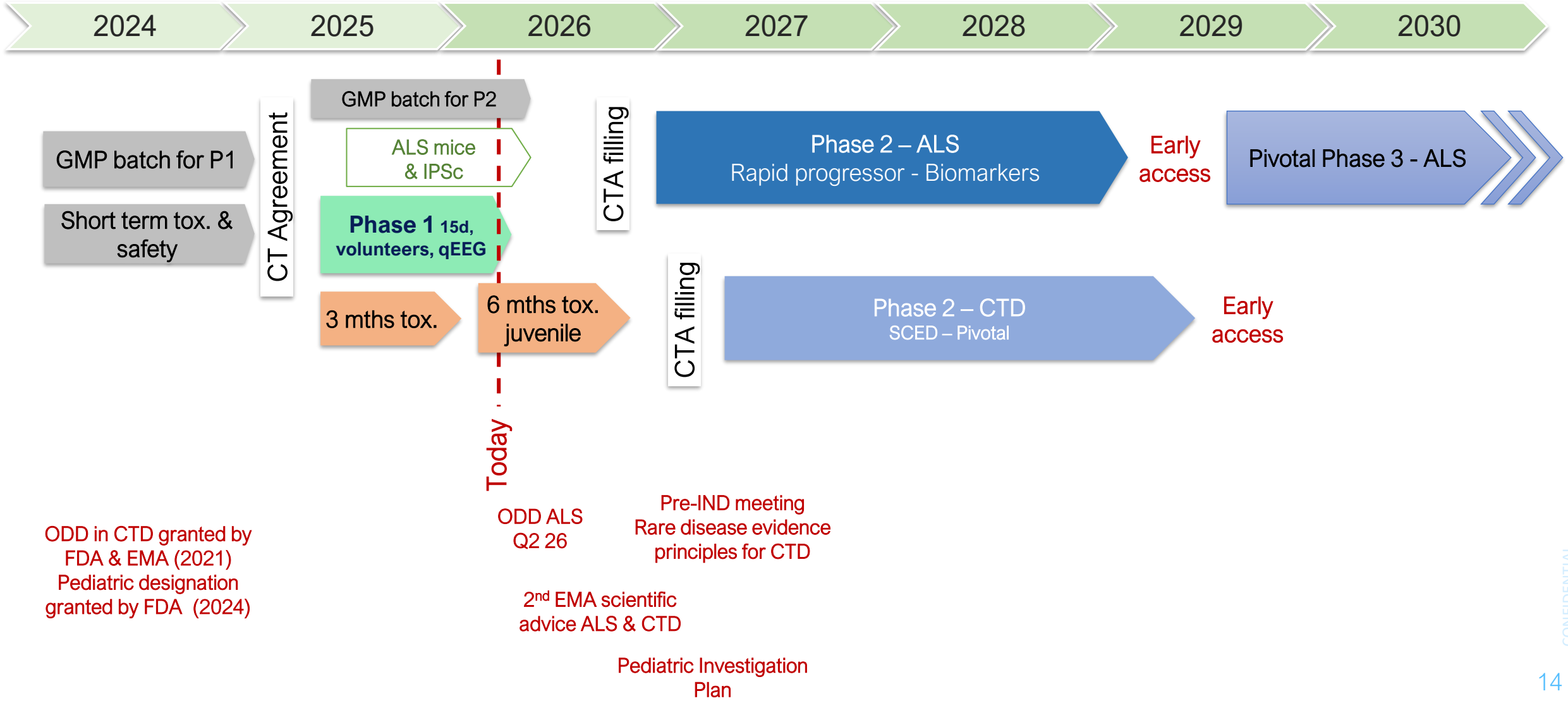
Quantitative EEG (qEEG) conducted at Day1 in SAD, D2 and D13 in MAD

- **Increase in beta-band power (**and gamma-band power after multiple dosing)**, supporting enhanced alertness and improved attention control (ie, cortical activation)**
- **Memory testing conducted in parallel** (preliminary analysis)
  - **Slight improvement observed in N-Back** test (working memory)
  - **Improved hit reaction time in the continuous performance task**



qEEG on the beta bands
(red area shows a statistical difference between treated and placebo group)

CBT101 development plan – raising USD20m to conduct clinical Phases 2 in ALS and CTD + USD40m€ to conduct Pivotal Phase 3 in ALS



Focus on key clinical studies – Rare disease opportunities

Phase 2 protocol – preliminary

Phase 2 – ALS

Randomized, Double-Blinded, Placebo-Controlled study to evaluate the Safety, Tolerability, and Pharmacokinetics of Multiple Doses of CBT101 given intra-nasally in ALS Subjects for 6 months

- Multicentric, France
- ~50-60 ALS patients (TBC)
  - Randomization 3 CBT101 / 1 placebo (TBC)
  - Definition of synthetic patients to increase study power and even treated and placebo groups
  - Selection of patients presenting high neuronal metabolism (clinical, External energy consumptions, MRS)
- Primary endpoints: safety and tolerability
- Secondary endpoints on efficacy:
  - Biomarkers including neurofilaments decrease, MRS
  - Clinical assessment (ALS clinical score, Grip test, pulmonary vital capacity test, EMG to assess motoneuron conduction)

Phase 2 – CTD

Randomized, Double-Blinded, Single Case Experimental Design study to evaluate the safety, tolerability and efficacy of CBT101 given intranasally for 6 months in CTD male pediatric and adult patients

- Multicentric (Paris and Lyon)
- 24 CTD patients
- 3-25 y-old (30%<7y-old and 30% >12y- old)
  - 2,4,6 weeks observation with placebo followed by 6 months of CBT101
  - Randomized and double blinded introduction of treatment
- Primary endpoint: safety, tolerability and efficacy
- Repeated tests to assess Bruun's composite score (cognition, autism, seizure)
  - Nasal tolerance monitoring
  - Use of specific tests on tablets and questionnaires at home every 2-3 weeks
  - Vineland and MRS at Baseline and end of studies

Strong portfolio of patents to serve Ceres' strategy

	Main Patents – related to creatine prodrugs	Patent number	Owner
Chemistry	**Crystalline form** of dodecyl creatine ester (the one tested in clinic including therapeutic applications)	Filed in **2025**	CERES
	Method for preparing creatine fatty ester, creatine ester thus prepared and uses thereof (chemical synthesis process including therapeutic applications)	Filed in **2012** (WO2014019855A1)	**CERES** – exclusive license from CEA
Formulations	Composition suitable for the administration of creatine esters (composition of matter, **final formulation used in clinic**)	Filed in **2023** (WO2024184433A12024)	**CERES**
	Composition containing creatine fatty ester for use in medicine (**preliminary** formulations for pro-creatine and therapeutic applications)	Filed in **2019** (WO2020221780A1)	**CERES** – exclusive license from CEA
Biomarkers	DNA methylation as a biomarker for cerebral creatine deficiency syndromes	Filed in **2023** (WO2025132568A1)	CEA - **CERES**

	Secondary patents	Patent number	Owner
Other formulations	Formulations for nasal administration of antivirals	Filed in **2020** (PCT/EP2021/069761)	**CERES**
Brand	"Ceres Brain Therapeutics"	N/A (Trademark)	**CERES**
Brand	"Creatine-to-Neurons"	N/A (Trademark)	**CERES**

Led by a highly skilled team in science and business surrounded by KOL physicians and researchers

Executive team

Thomas Joudinaud
MD, PhD, CEO, co-founder

Henri Bénech
Pharm.D., PhD, COO, co-founder

R&D

Camille Roucairol
PhD, Pharmaceutical Dev. Director

Clara Lhotellier
MSc Analytical Chemist

Florence Bénech
PharmD, Formulation

Thibault Anani
PhD, Data scientifs

Victoria Flament
Engineer, Biotech

Florence Guillaud
Pharm.D, Microbiology

Xavier Salançon
Pharm.D
CMC advisor

Sophie Dezard
MsC Organic Chemist

Jean-Paul Briffaux
DVM, Toxicology

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MD, PhD, Medical Director

Pr Andreas Schulze
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Dr PF Pradat
MD, PhD, ALS Paris, La Pitié-Salpêtrière, Paris

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Scientists

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Clémence Disdier
Pharm.D, PhD

Anne-Cécile Guyot
MsC, Laboratory

Scientific advisor

Luc Dupuis
Inserm research director
University of Strasbourg

Regulatory

Linda Lebon
Global Regulatory

Board members

Charles Billard
CFO Greater China

Marie Humblot-Ferrero
VP Strategy & Marketing
Land & Air systems

Aurélien Chaufour
CEO

Advisors

Marc Vincenti
PharmD, Global Optim. Director

Leveraging first successes with CBT101 to fuel pipeline

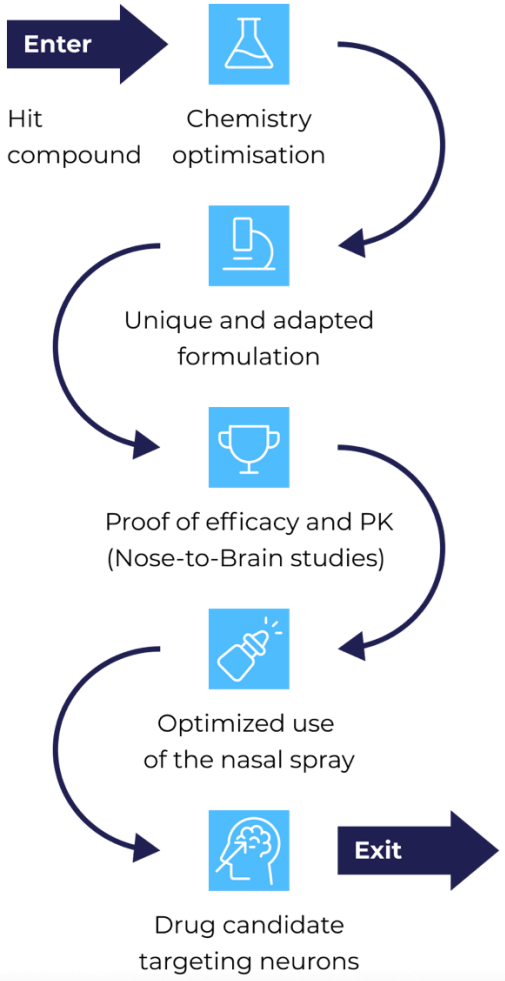
Platform	Use of the platform	Program	Indication	Preclinic	CMC	IND-Enabling Regulatory Engagement	Phase 1	Phase 2a	Phase 3
Nose-to-neurons	Creatine-to-neurons™	CBT101	Creatine Transporter Deficiency	Paediatric indication				Multicentric (tolerance & efficacy)	
			Amyotrophy Lateral sclerosis	Indication in adults				Multicentric (tolerance & efficacy)	
		CBT102 (Same CBT101 drug substance)	Parkinson's disease	Limited package for Phase 2				Monocentric & Target Engagement	
	Glucose/ Creatine to Neurons	CBT401	Glucose Transporter Deficiency	→					
	Therapeutic antibody to brain	CBT301	Brain tumor	→					
R&D collaboration agreement		CBT201	Tauopathies	→					

CBT101 success will open new indication in other neurodegenerative diseases and validate Ceres'Nose-to-Neurons® platform

1 Amyotrophic Lateral sclerosis

Validation of CBT101 as a therapeutic platform against neurodegerative diseases

2 Parkinson's disease, Huntington's disease, …



Nose-to-Neurons™ platform to develop neuro-drugs

Why investing in / partnering with Ceres ?

- First-in-class nose-to-neuron asset reenergizing the brain

- Human efficacy demonstrated in Phase 1

- Rare disease indications (ALS, CTD) with regulatory incentives maximizing value for investor

- CBT101, a scalable platform

- Robust IP portfolio securing strategic advantage

CERES

brain therapeutics

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