

DISRUPTIVE COMBINATION
AGAINST NEUROLOGICAL DISORDERS

INVESTOR PRESENTATION CF&B CONFERENCE

April 14&15 2020



▲ NEURONAL NETWORK
● GLIAL NETWORK

 Theranexus



YOUR CONTACTS



Franck MOUTHON

Co-founder and Chairman
and CEO

- Franck Mouthon holds a degree in life sciences from the École Normale Supérieure
- Joined the Life Sciences Department of the French Alternative Energies and Atomic Energy Commission (CEA) in 1995
- Founded CEA spin-off Theranexus in March 2013 with Mathieu Charvériat
- Board member of France Biotech



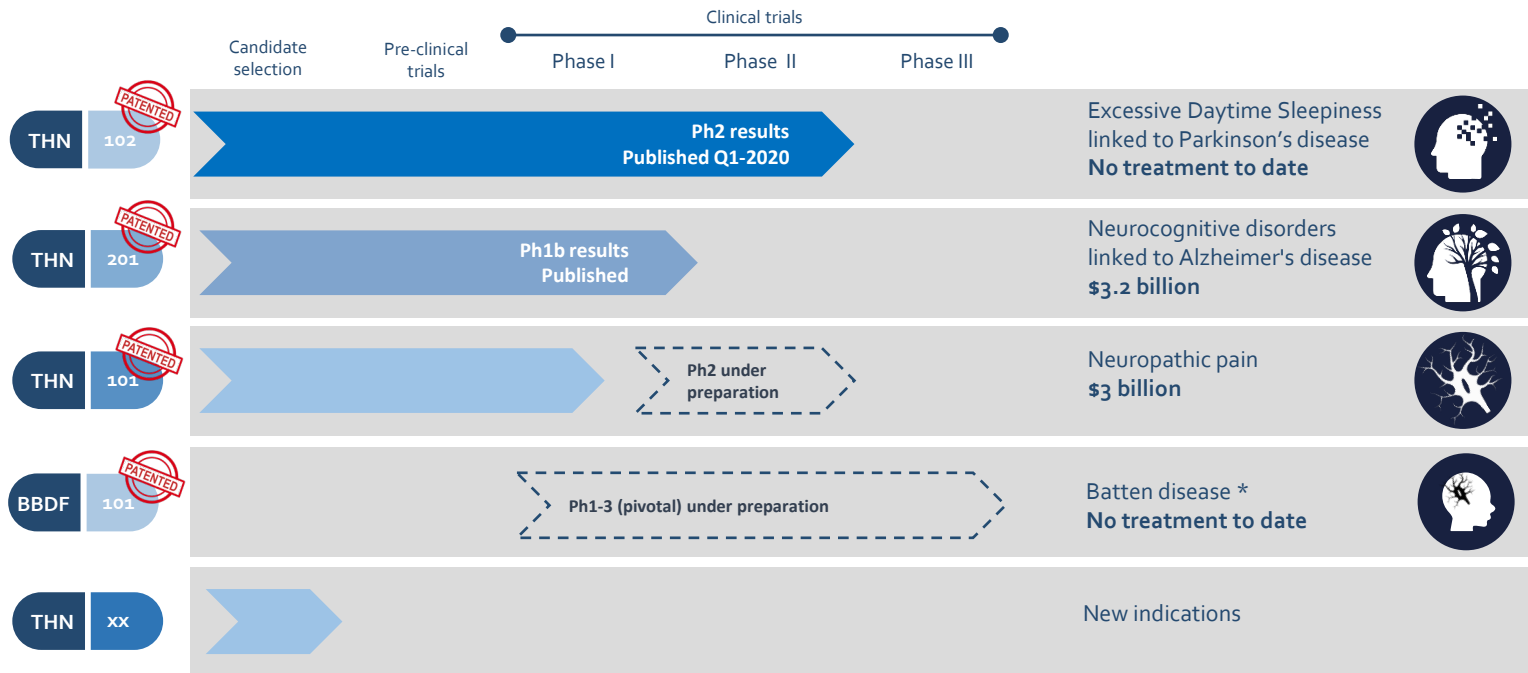
Thierry LAMBERT

CFO

- Thierry Lambert holds a degree in business administration from Birmingham University and an MBA from INSEAD
- 4 years of experience in syndicated and corporate finance
- 5 years as Chief Financial Officer for listed companies Naturex and then Safe Orthopaedics
- Joined Theranexus in 2017



A DIVERSIFIED PIPELINE



*All figures are derived from Datamonitor reports (ND, dementia); company annual reports (Jazz Pharmaceuticals, Teva)



THERANEXUS PLATFORM: PROPRIETARY, SCALABLE & VERSATILE

CNS DRUGS

DRUG SEEN AS THE 1ST LINE-TREATMENT

Condition with a strong unmet need for improved efficacy (with the current therapeutics arsenal)

*CNS drugs
1st line- treatment
for CNS* conditions*



Action on the neuron

GLIAL CELL MODULATOR

DRUG REPOSITIONED AS A MODULATOR

Optimization of the glial network



Theranexus library of 27 glial cell modulators

THN

XXX



3 major advantages



Ambition to achieve superiority at all stages (*Best in class*)



New monopoly on use (*patent*)



Higher probability of success, greater flexibility and shorter time-to-market

*Central Nervous System



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- 5 NEWSFLOW



EXCESSIVE DAYTIME SLEEPINESS IN PARKINSON'S DISEASE: A STRONG NEED



Excessive daytime sleepiness
in Parkinson's disease

40% of Parkinsonians
More than **1 million patients** (G7)

One of the most debilitating symptoms of the disease

Increases the **risk of accidents**

Amongst the largest causes of **institutionalisation** of patients

No approved treatment
No efficacy of other pharmaceutical developments to date

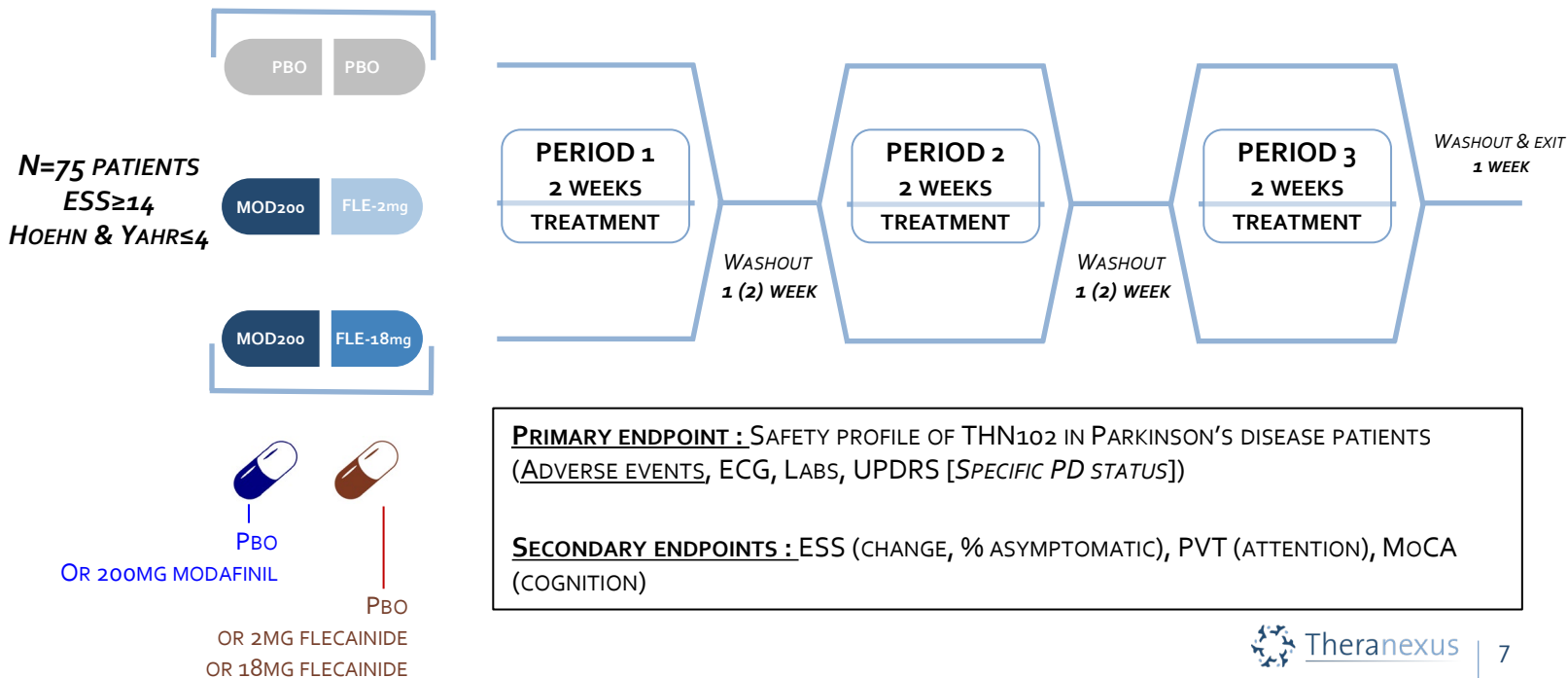
¹ European Parkinson's Disease Association

² Market research study performed by LSA Partnering & Analytics



THN102 : STUDY DESIGN

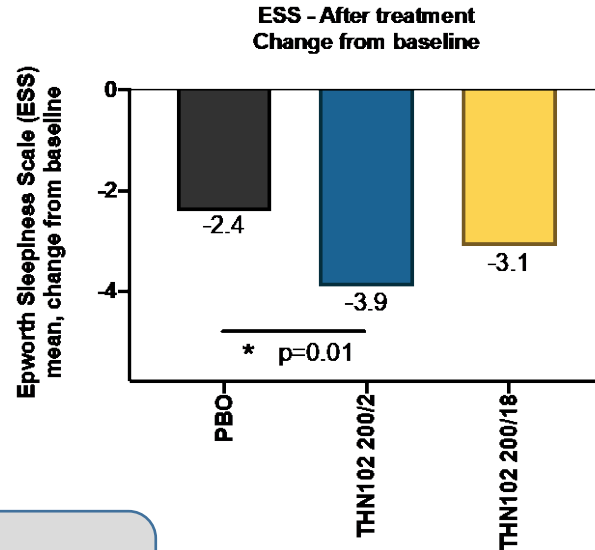
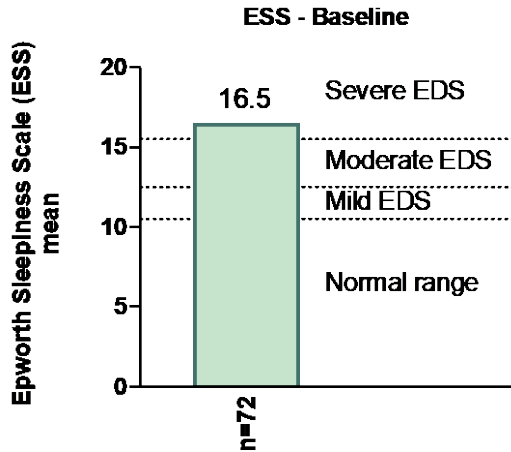
Randomised, double-blind, placebo-controlled, complete 3-way cross-over phase IIa trial to investigate safety and efficacy of two THN102 doses in subjects with excessive daytime sleepiness associated with Parkinson's disease, PI: Prof JC Corvol, ICM, Paris





EPWORTH SLEEPINESS SCALE: CLEAR SUPERIORITY VS. PLACEBO

- Excessive daytime sleepiness (EDS) is assessed using the Epworth Sleepiness Scale (ESS)
- The « normal » range of ESS scores is up to 10. ESS scores of 11-24 represent increasing levels of excessive daytime sleepiness (Johns, 1991 ; Chen et al, 1995 ; Johns and Hocking, 2004 ; Manni et al, 1999 ; Izci et al, 2008)



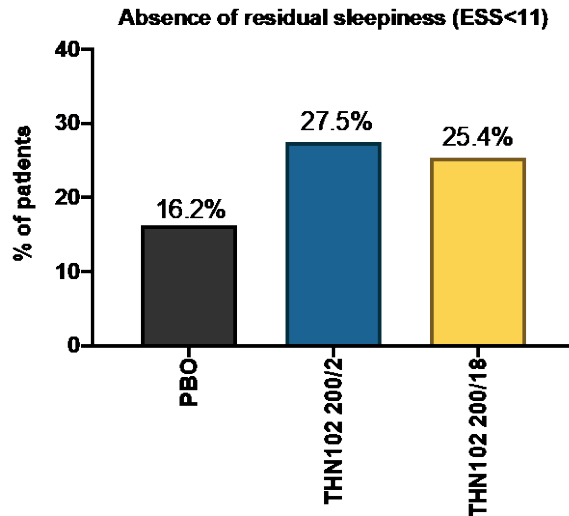
Conclusion :

- High ESS score at baseline, indicating severe EDS in patients
- Significant reduction of ESS in THN102 200/2 group (p=0.010)



EPWORTH SLEEPINESS SCALE: ABSENCE OF RESIDUAL SLEEPINESS

- Absence of residual sleepiness is generally defined as $ESS < 11$, as it is reported that the « normal » range of ESS scores is up to 10 (Johns, 1991 ; Chen et al, 1995 ; Johns and Hocking, 2004 ; Manni et al, 1999 ; Izci et al, 2008)



No clear trend on two exploratory efficacy measures:

- Psychomotor Vigilance Test (PVT) (Dinges & Powell, 1985)
- Montreal Cognitive Assessment scale (MoCA)

More detailed data from the study will be presented at an upcoming a scientific conference

Conclusion :

Increase in the % of patients with absence of residual sleepiness after treatment with THN102 200/2 ($P=0,05$) and THN102 200/18 ($P=0,10$)



THN102: SUMMARY OF THE FINDINGS FROM THE CLINICAL STUDY

- ✓ THN102 **significantly reduces excessive daytime sleepiness** in Parkinson's disease patients
- ✓ THN102 is **well tolerated** in Parkinson's disease patients

Highly meaningful result in the context of Parkinson's disease:

- Over the past few years, 3 other products targeting EDS were tested in the clinic in phase 2 / 3 studies in Parkinson's patients
- None of them could show efficacy on EDS symptoms in this population.
- THN102 is the first treatment to show a significant improvement of daytime sleepiness v. placebo in such a well-controlled clinical trial
- The absence of residual sleepiness in more than 25% of severe patients (mean ESS of 16,5) holds the promise for a meaningful medical benefit to be confirmed in phase 3 trials.

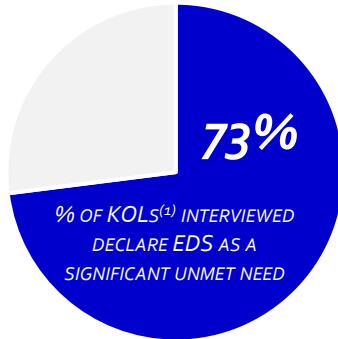
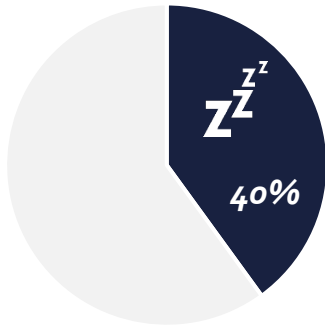


AGENDA

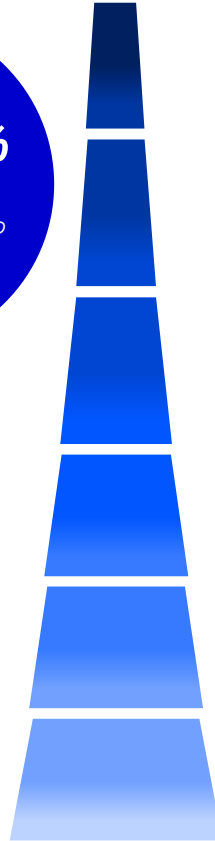
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EDS IS A SIGNIFICANT UNMET NEED WITH A LARGE MARKET POTENTIAL



- In non depressed PD patients, the risk of falls increases by 20% per unit change on the ESS ⁽²⁾ – falls are among the first causes of institutionalization of PD patients
- The costs of institutionalization of Parkinson's disease patients in the US are estimated to \$ 7Bn⁽³⁾



DEPRESSION

“There is a significant association between depression and sleep disorders with the two symptoms worsening each other” [US KOL]

COGNITIVE IMPAIRMENT

“Any effects on cognition would be a key driver for prescription” [US KOL]

EDS

“It is a major issue – many elderly are “healthy aged” and therefore have the legitimate desire to be as active as before in spite of the disease” [UK KOL]

FATIGUE

“I just don't have energy is the number one complaint I am hearing from my patients and I just have no treatment to propose to them” [US KOL]

PSYCHOSIS

“Psychosis is an emergency situation when it happens but it's rare” [Canadian KOL]

SLEEP FRAGMENTATION

“This is indeed an issue, but it is just so closely associated with the disease that the patients have to cope with it” [French KOL]

RBD

“Not a real issue now – definitely the less impactful” [US KOL]



(1) Interviews of 23 KOLs in Europe and in the US

(2) Spindler et al., 2013

(3) Lewin Group report / Michael J. Fox Foundation 2019















THE VALUE IN THE MARKET OF NON-MOTOR SYMPTOMS IS DEFINED BY THE US MARKET – THIS TERRITORY MUST BE THE CENTRAL ELEMENT OF OUR BD STRATEGY

FDA approval	Brand	WAC/patient/yr* (\$US as of 03/2020)	Symptom treated	Original SOC /comparator	WAC/patient/yr (\$US as of 03/2020)
2014	Northera [™] (droxidopa) Capsules <small>100 mg-200 mg-300 mg</small>	\$70'250	Neurogenic orthostatic hypotension	midodrine	\$900
2016	NUPLAZID [™] (pimavanserin) tablets	\$38'230	Psychosis	clozapine	\$560
2017	XADAGO [®] (safinamide) tablets	\$11'900	ON/OFF fluctuations	rasagiline	\$6'840
2018	GOCOVRI [™] (amantadine) extended release capsules <small>68.5 mg 137 mg</small>	\$33'140	Levodopa induced dyskinesia	amantadine	\$780
2019	Inbrija [™] (levodopa inhalation powder) <small>42 mg capsules</small>	\$12'000	ON/OFF fluctuations	levodopa/ carbidopa ER	\$4'130

*WAC: Wholesale Acquisition Cost – estimated based on list price available on GoodRx and Drugs.com websites



TRANSACTIONS OF PRODUCTS TARGETING « NON CORE SYMPTOMS » IN PARKINSON'S DISEASE WITH CLINICAL DATA AVAILABLE

Year	In-Lic.	Out-Lic.	Dev phase	Symptom	Territory	Upfont	Mil.	Roylt.%
2020			P1	Circadian rythm disorder	WW	75	635	X%-1X%
2018			P2	Levodopa induced dyskinesia	M&A	100	805	N/A
2018			NDA ⁽¹⁾	ON/OFF fluctuations	China	3	14	??%
2017			NDA ⁽¹⁾	ON/OFF fluctuations	US	30	115	37%
2017			P3	ON/OFF fluctuations	M&A	1'100	N/A	N/A
2016			P3	ON/OFF fluctuations	M&A	624	N/A	N/A

(1) NDA: New Drug Application (dossier d'Autorisation de Mise sur le Marché)

=> HIGH-VALUE TRANSACTIONS



THN102: PARTNERSHIP STRATEGY FOR THN102



Market and dimension

Excessive Daytime Sleepiness linked to Parkinson's disease
No treatment to date



Specialists in EDS or CNS



Generalists and "big pharma"



INTRINSIC COMMERCIAL POTENTIAL OF PRODUCT: > €1Bn

ADDITIONAL OPPORTUNITIES FOR PARTNERSHIPS:

- + OPTIMIZATION OF SALES FORCES USED FOR PARKINSON'S
- + POSSIBILITY TO REACH NEW MARKET FOR EDS SPECIALISTS

BLOCKBUSTER POTENTIAL FOR AN INDICATION WITH A GROWING BUT UNTREATED NEED



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Batten disease or juvenile neuronal ceroid lipofuscinosis (NCL₃)

A rare genetic disease that is fatal between the ages of 20 and 30

EPIDEMIOLOGY AND PHYSIOPATHOLOGY OF NCL₃



c. 3,000 patients
(all NCL types)



Autosomal recessive



Diagnosis in children
aged 4 to 8



Blindness



Cognitive decline



Loss of motor skills



No registered
treatment

FOUNDATION

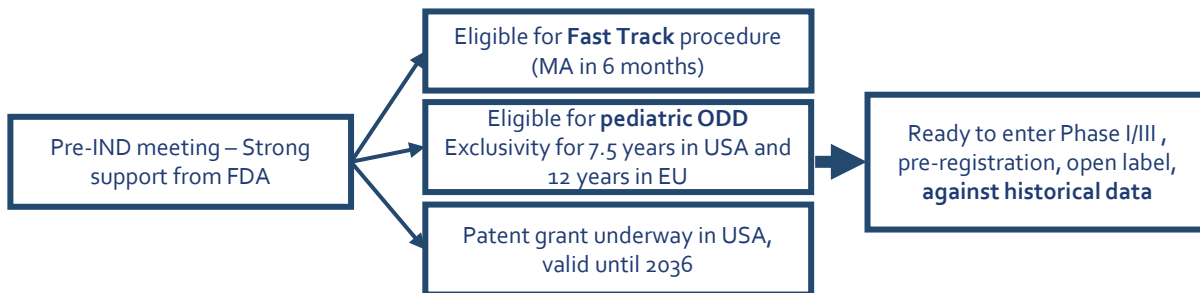


Created in 2008 by Craig Benson

USD 30 million R&D investment leading
to identification of **BBDF101**

BBDF101

Trehalose + Miglustat combination





Competitive environment and market opportunity

COMPARABLES

ZAVESCA¹⁰⁰
(miglustat) capsules

Myozyme
(alglucosidase alfa)

elaprased
(idursulfase)

Brineura[®]
(cerliponase alfa)

6,000 cases USA
5,000 cases EU

5,000 cases USA
1,800 cases EU

500 cases USA
400 cases EU

500 cases USA
250 cases EU

Gaucher disease

Pompe disease

Hunter syndrome

NCL2

\$240,000/yr/patient
€55,000/yr/patient

\$300,000/yr/patient

\$375,000/yr/patient

\$700,000/yr/patient

Peak (2014): \$113m

Peak (2018): \$947m

Peak (2018): \$634m

Peak (2027): \$359m
(f)

Notes: All drugs have 'Orphan Drug Designation' status and Brineura obtained a pediatric voucher (sold for \$120m)

COMPETITION IN CLINICAL DEVELOPMENT

NCL3 AAV9 gene therapy
Amicus Therapeutics

Phase I/II: Recruitment underway

Duration: 36 months' control
Completion due in December 2022

Design: n=7

Open IND **Polaryx Therapeutics**
No clinical plan announced to date

MARKET ACCESS

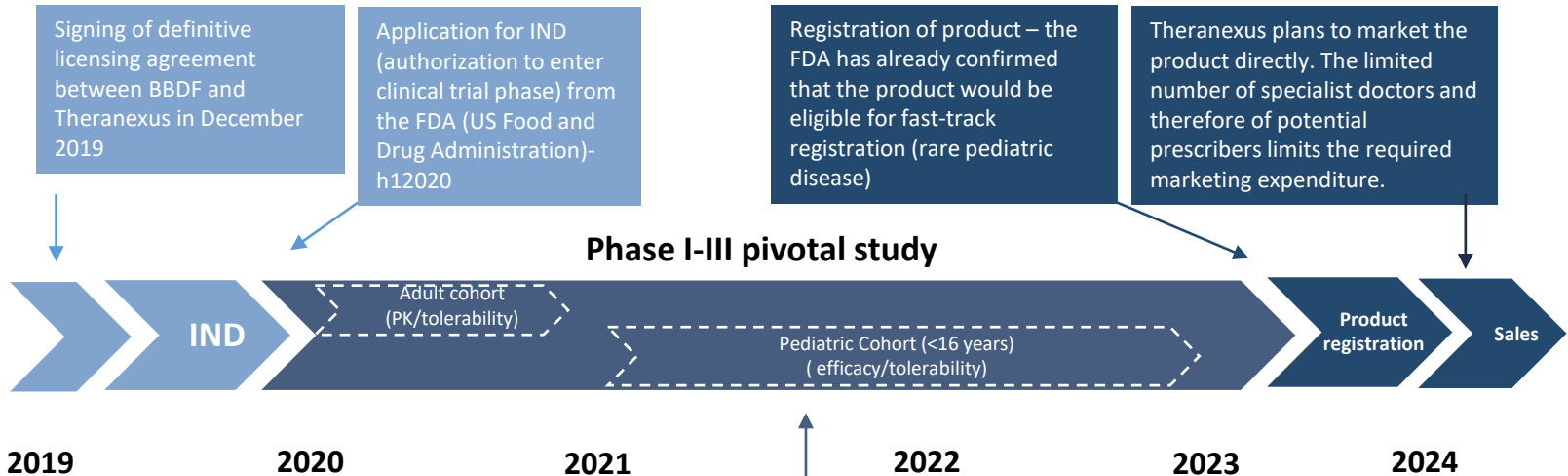
Access to patients highly structured – Direct sales force of limited size

USA: Two main associations (BBDF and BDSRA)
and 18 hospitals taking care of Batten patients

EU: 7 primary centers (France, UK, Germany, Norway)



BBDF 101 development plan



Clinical trials:

- Phase I-III (leading directly to product marketing)
- On 36 patients in the USA :
 - adolescent/adult cohort of six patients over a period of 5 month
 - pediatric cohort of 30 patients over a period of two years with an intermediate assessment at 12 month
- Open label
- The evaluation is based on comparing the disease progression in patients recruited for the trial against the natural course of the disease as described by several existing groups of NCL3 patients – similar to the trials conducted by Biomarin for Brineura™



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THN₂₀₁: A HIGH-POTENTIAL CANDIDATE FOR DEMENTIA

DONEPEZIL | MEFLOQUINE



Neurocognitive disorders
linked to **Alzheimer's disease**

THN

201



Phase Ib clinical trial complete
On the lookout for an industrial partner

Impaired memory, reasoning and orientation

15 million patients in 2015 (G7)
19 million by 2030
45% of patients undiagnosed

DONEPEZIL

\$3.2 billion
(annual cost of treatment per patient €4,000-5,000)

23 drug candidates at
clinical trial stage

Under the CX-COG project funded by the
French "**Fonds Unique Interministériel**" (FUI AAP22)

**Double-blind randomized study
comparing placebo and standard of care drug**
(Donepezil), conducted on 152 healthy volunteers
in a parallel group design in 10 centers in France
and abroad

Trial conducted on three parallel groups
evaluating the cognitive activity,
tolerability and pharmacokinetic profile of THN₂₀₁

Key efficacy criteria:
measurement of pro-cognitive activity
through a scopolamine test

Results published 15/01/2020
Reinforcement of the profile of Donepezil by
Mefloquine favouring executive processes (speed
of memory and EEG power in the gamma band)



THN₁₀₁: DRUG CANDIDATE READY FOR PHASE II TRIALS: PAIN

AMITRIPTYLINE | MEFLOQUINE



Neuropathic pain

Chronic pain with occasional stabbing pain, sensations of burning or electric shocks

70 million patients
(Europe, USA, Japan)

AMITRIPTYLINE

\$3 billion
(annual cost of treatment per patient \$3,000-4,000)

32 drug candidates at clinical trial stage

THN

101



Preparation stage for Phase II clinical trial

Key efficacy criteria: pain scale

Double-blind randomized study comparing placebo with standard of care drug (Amitriptyline)

Trial conducted on three parallel groups:
Amitriptyline 25 mg/day and mefloquine 10 mg/day vs. Placebo and vs. active comparator (amitriptyline).
Regular evaluation of pain and analysis of multiple secondary markers and tolerability.

Patients suffering from neuropathic pain caused by diabetes or post-herpetic neuralgia (following shingles)

Multi-center international trial conducted on **370 patients**
Conducted in parallel at **40-45 centers in Europe.**

Phase II trial program at preparation stage



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A STRONG NEWSFLOW IN 2020

Success of Phase 2 : Q1-2020 ✓

Industrial partnership to continue developing THN102



Obtaining an IND for BDF 101 in Batten's disease: H1-2020

Obtaining the ODD: H1-2020

Recruitment of the first patient in the study: H2-2020



Continuing programs stemming from the platform





SOMMAIRE

APPENDICES



INVESTOR RELATIONS

FINANCIAL DATA

ISIN : FR0013286259 - Mnemo: ALTHX

Market : Euronext Growth

Stock price as at April 9th 2020 : 6,90 €

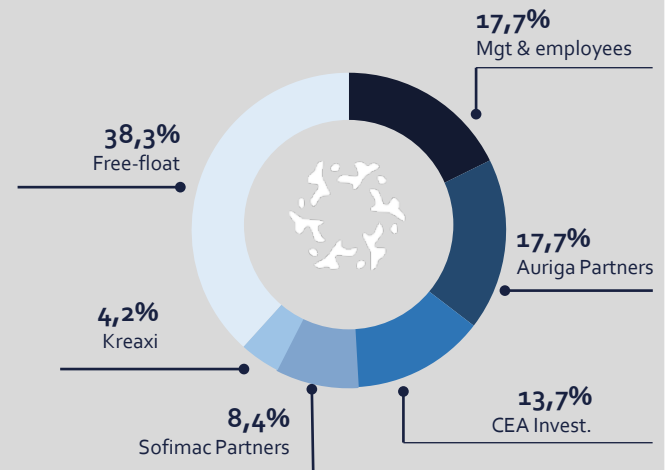
Market cap : €25M

Liquidity contract : Portzamparc



SHAREHOLDERS

Number of shares : 3 622 413





P&L 2019

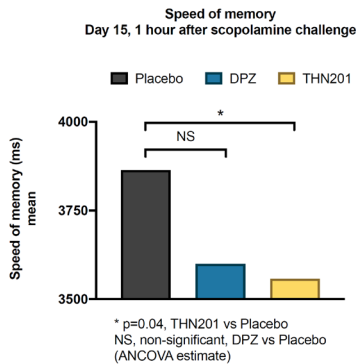
In K€ (French GAAP)	2018	2019
Operating income	175	617
Other purchases and external charges	4 969	5 426
Salaries and benefits	2 117	2 353
Depreciation and amortization	55	154
Other operating expenses	24	61
Operating result	(6 990)	(7 377)
Net financial income	(31)	(241)
Corporate tax	1 721	2 038
Net income	(5 301)	(5 580)

CASH AS AT MARCH 31ST 2020: 7.8 M€



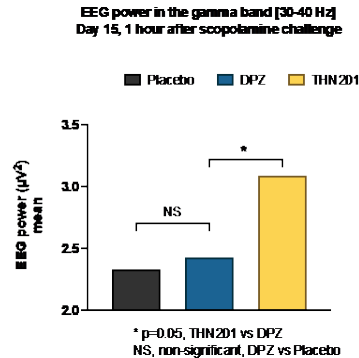
THN201 :KEY RESULTS

Significant increase of speed of memory by THN201 vs Placebo ($p=0.04$) at 1 h post scopolamine challenge
No significant effect of DPZ vs Placebo



Composite endpoint of the CDR assessment ; this endpoint is typically considered to be one of the most sensitive to decline in AD patients over time (Wesnes et al, 2010).

Significant increase of EEG power on gamma band by THN201 vs DPZ ($p=0.05$) at 1 h post scopolamine challenge



EEG gamma band is recognized as a marker of cognitive activity (Herrmann et al, 2001 ; Fitzgibbon et al, 2004) ; an increase in this band is considered as beneficial for AD patients (Herrmann et al, 2005).

Similar profile to Donepezil on other pharmacodynamic parameters

- ➔ ENLARGEMENT OF THE EFFECT OF DONEPEZIL BY MEFLOQUINE IN FAVOUR OF A REINFORCEMENT OF EXECUTIVE PROCESSES
- ➔ THE TOLERANCE PROFILE OF THN201 IS SIMILAR TO THAT OF DONEPEZIL



STRONG INTELLECTUAL PROPERTY PROTECTION AND AN ACCELERATED REGISTRATION PATH

Strong patent protection until 2036

Territories delivered:



International patent number:
WO/2017/009472

Expiry date:
15/07/2036



Accelerated registration path already secured

- The FDA has already confirmed the **505 (b)(2) status** of THN102
- **IND already open** (phase II was Europe/US)

505(b)(2)

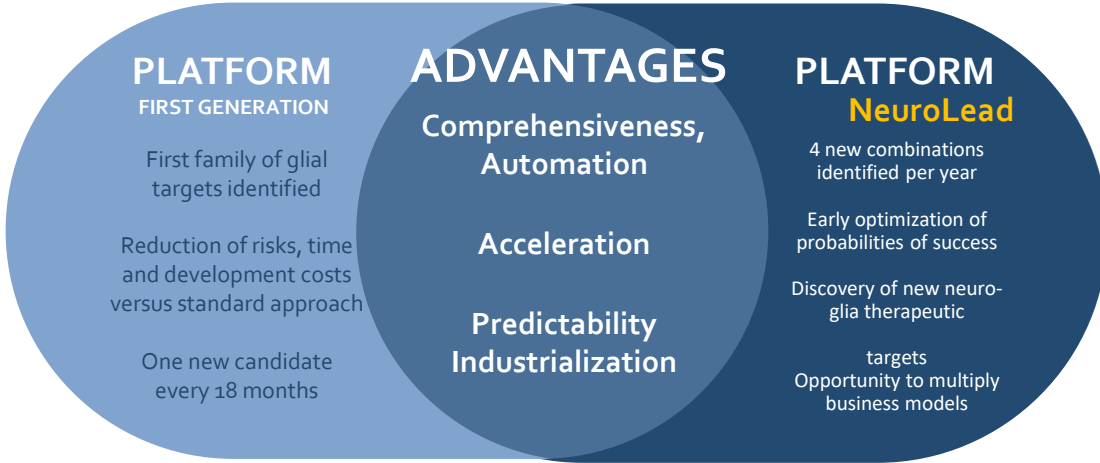


NEUROLEAD : STRENGTHENING THE LEAD GENERATION PLATFORM

A NEW PLATFORM FOR DRUG CANDIDATE GENERATION FOCUSED ON MEDICAL AND INDUSTRIAL VALUE

NeuroLead

- Development of a drug candidate generating platform based on neuron-glia interactions
- Prestigious partners:
 - 
 - 
- Capacity to build on the latest innovations in neuroscience and Deep Learning
- Funding package of €6.2m from BpiFrance, for the consortium managed by Theranexus



FROM PIONEER TO REFERENCE PLAYER IN NEUROLOGY



No adverse impact on other symptoms of the disease:

- No change in UPDRS scores

The treatment was well tolerated:

- No treatment-related serious adverse events reported
- No cardiovascular safety issues (vital signs, ECG)
- No safety issues in lab values
- Overall low incidence of TEAEs⁽¹⁾ , mainly of mild to moderate severity. TEAEs correspond to the known profile of modafinil:
 - Placebo: 19 pat (27,9%)
 - 200/2: 23 pat (31,9%)
 - 200/18: 29 pat (39,7%)

(1) Treatment Emergent Adverse Events



THN102 : STUDY PATIENT POPULATION

- **Multicentric study (EU/US) in 5 countries: 30 sites distributed in France (7), Hungary (5), Czech Rep.(7), Germany (8), USA (3)**
- **75 patients included (Safety set)**
- **Efficacy population (n=72):**
 - **Age 63.3 years \pm 9,4 (min 38 ; max 80)**
 - **Gender : Male 66.7% ; female 33.3%**
 - **BMI⁽¹⁾ : 27,4 \pm 3,4 kg/m²**
 - **Hoehn & Yahr score⁽¹⁾ : 2,3**

⁽¹⁾ Body Mass Index

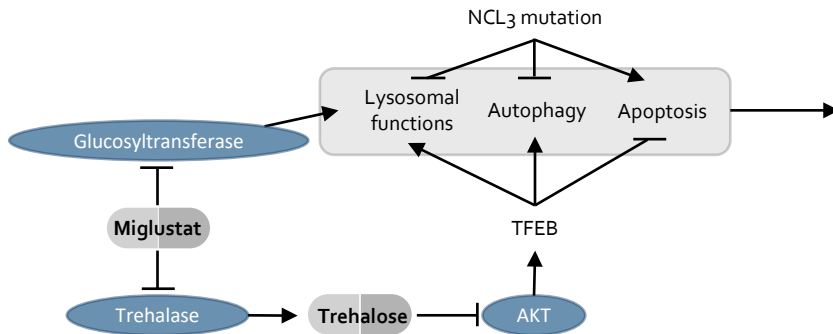
⁽²⁾ Scale of severity of symptoms of Parkinson's disease (0-4)



Batten disease or juvenile neuronal ceroid lipofuscinosis (NCL₃)

A rare genetic disease that is fatal between the ages of 20 and 30

MECHANISM OF ACTION



PRECLINICAL DEMONSTRATION

NCL₃ transgenic mice

↑ Cell survival

↓ Neuroinflammation

↓ Lysosomal signaling pathway deficiency

STRONG IMPACT ON MECHANISMS RESPONSIBLE FOR NCL₃ SYMPTOMS