

DISRUPTIVE COMBINATION
AGAINST NEUROLOGICAL DISORDERS

INVESTOR ACCESS PRESENTATION

September 27th-28th , 2021



▲ NEURONAL NETWORK
● GLIAL NETWORK

 Theranexus



THERANEXUS: A UNIQUELY POSITIONNED BIOTECH IN THE CNS SPACE

Our speakers

Franck Mouthon **CEO & founder**



Top researcher at leading research organization CEA

Co-founder of Theranexus

President of France Biotech



Thierry Lambert **CFO**



5 years in Transaction Services with PWC UK

ACA-trained (Institute of Chartered Accountants in England and Wales)

8 years as CFO in listed companies mainly in the healthcare sector



Our model

Targets: Innovative targets in the Central Nervous System (CNS) based on unique science of neuroglia interactions

Approach: Combinations of registered compounds driven by robust business cases and capacity to rapidly demonstrate clinical value

Our pipeline:

- ✓ *Strong and diversified portfolio of clinical-stage assets*
- ✓ *Lead candidates in Parkinson's and Batten disease, indications with no treatment available*



A STRONG AND DIVERSIFIED CLINICAL PIPELINE



A phase 2 –Parkinson’s Disease asset with positive clinical efficacy data in EDS

THN 102 Ph2a results Published Q1-2020

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

A uniquely positioned rare-disease asset, entering clinical development in 2021

BBDF 101 Obtaining the IND PH1-2 Sept. 2021

Ph1-2 (Starting Q4-2021)

Ph3 (Starting H2-2022)

Batten disease *
No treatment to date

Additional clinical-stage programs

THN 201 Ph1b results Published Q1-2020

Neurocognitive disorders linked to Alzheimer’s disease

THN 101 Ph1 results Published Q4-2019

Neuropathic pain

* Exclusive worldwide agreement and license in place with Beyond Batten Disease Foundation (inventor and owner of intellectual property)

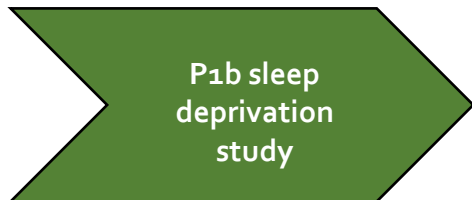
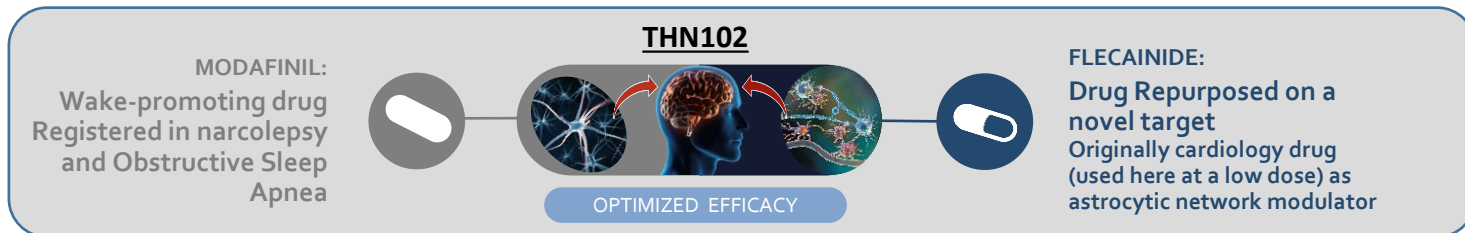


AGENDA

- 1 THN₁₀₂ (PARKINSON'S DISEASE)
- 2 BBDF-101 (JUVENILE BATTEN DISEASE)
- 3 NEWSFLOW
- 4 FINANCIAL SITUATION



THN₁₀₂ CLINICAL DEVELOPMENT SUCCESS



Demonstrated:

- Potentiation of the wake-promoting effect of modafinil
- Enlarged spectrum of effect v. modafinil



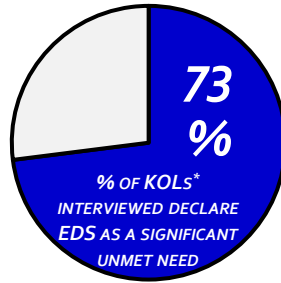
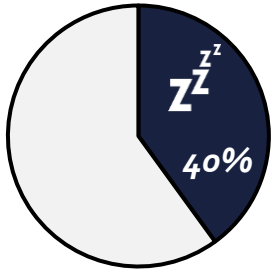
Focus on untreated patients with moderate to high EDS
Successful at significantly reducing EDS symptoms



THN₁₀₂ IS A UNIQUELY POSITIONED ASSET IN EDS IN PARKINSON'S DISEASE



Excessive daytime sleepiness in
Parkinson's disease



More than **2 million patients (G7)**
One of the most debilitating symptoms of the disease

- The **risk of falls** increases by 20% per unit change on the ESS** in PD patients
- The **costs of institutionalization** of Parkinson's disease patients in the US are estimated to \$ 7Bn**

Previous EDS candidates failed in Parkinson's

- 3 recent attempts in P2/P3 by pharmas/biotechs ***
- All candidates failed to show any effect even though two of these have shown efficacy in other pathologies

=> There is something specific/different to EDS in PD

A unique opportunity for THN₁₀₂

*Interviews of 23 KOLs in Europe and in the US (2)

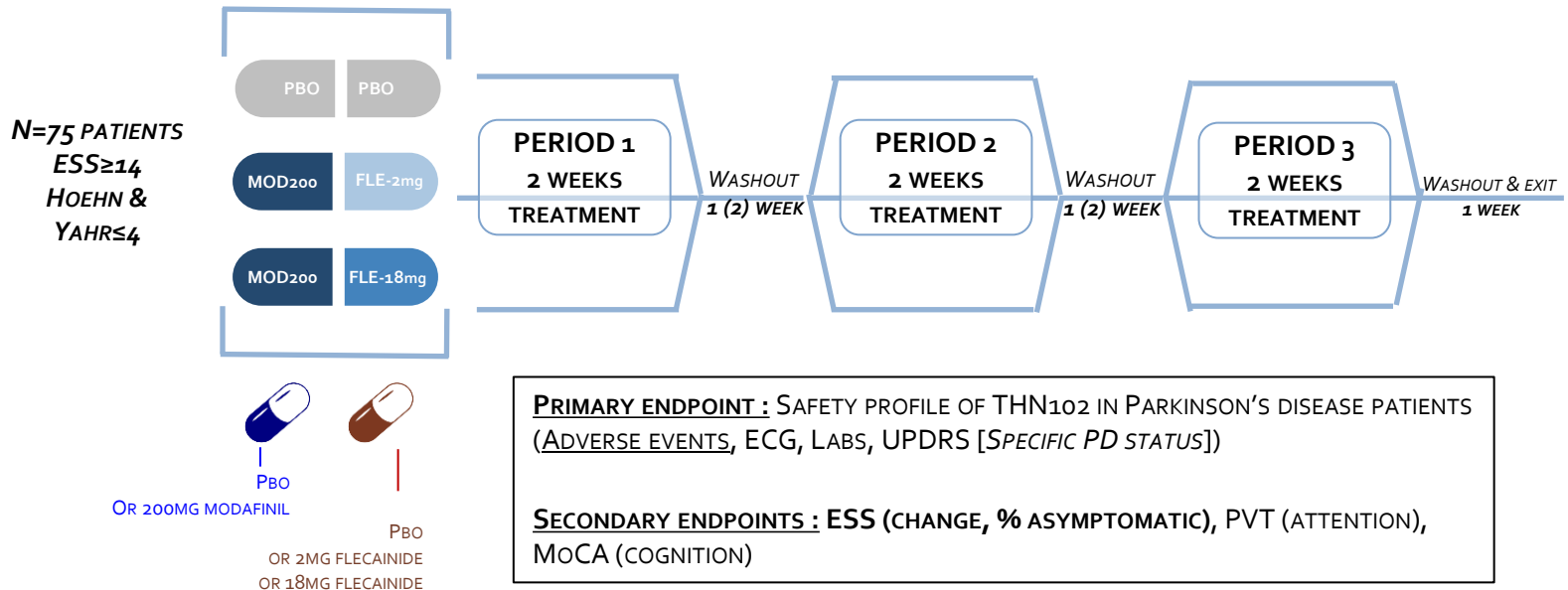
**Lewin Group report / Michael J. Fox Foundation 2019

*** In addition to THN₁₀₂ - JZP-110 (now Solriamfetol) from JAZZ, Pitolisant from Bioprojet Bavisant from Benevolent AI



THN₁₀₂ IN EDS IN PARKINSON'S DISEASE: 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

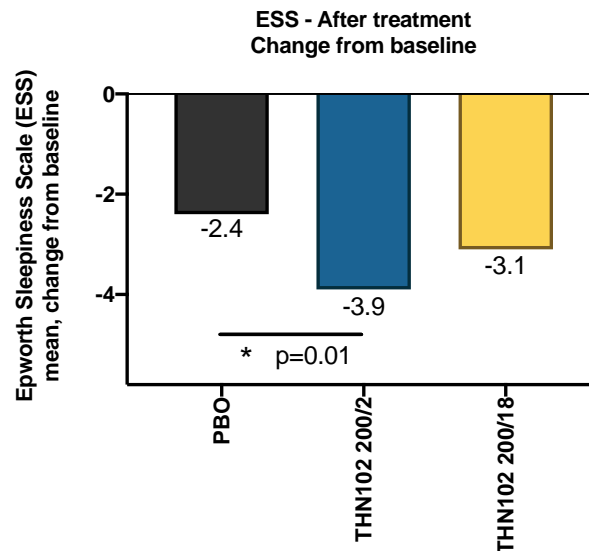
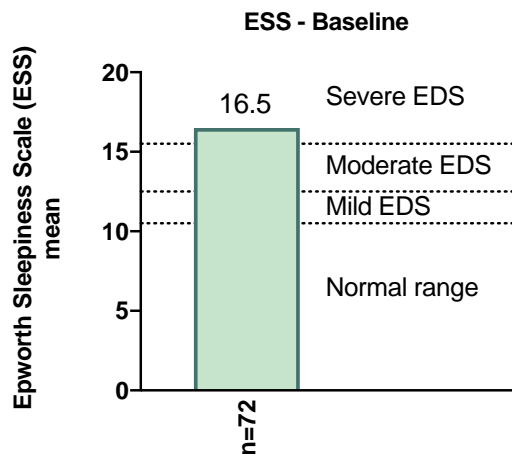


- Key objective: dose exploration, safety and efficacy in PD patients v. placebo
- Crossover with short exposure the most cost-efficient way to achieve this
- Main drawback: likely to underestimate the size of the response



THN₁₀₂ IN EDS IN PARKINSON'S DISEASE PATIENTS: 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)

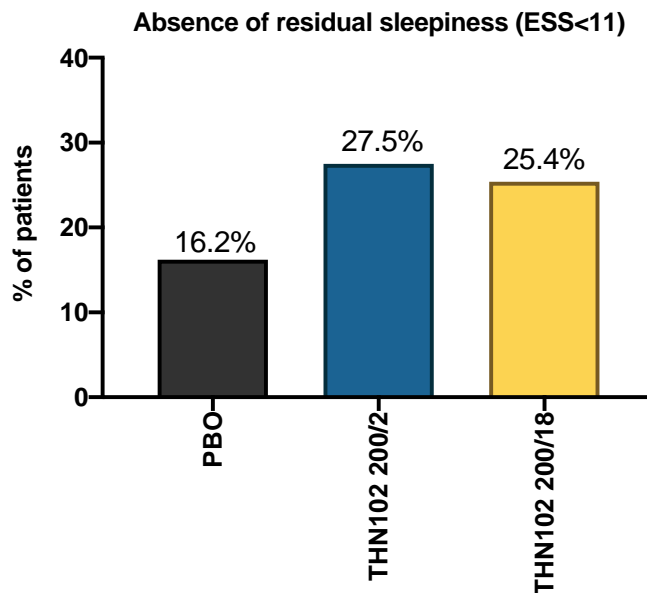


- Significant reduction of ESS in THN₁₀₂ 200/2 group (p=0.012)
 - Trial design (short exposure and crossover) enabled exploration of 2 doses v. placebo, but likely to underestimate the full effect of THN₁₀₂
- ⇒ **THN₁₀₂ demonstrates significant improvement v. placebo in EDS in PD patients**



THN₁₀₂ IN EDS IN PARKINSON'S DISEASE PATIENTS: IMPROVED REMISSION RATE WITH THN₁₀₂

- Remission 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)



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

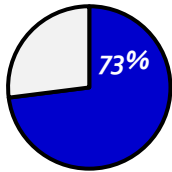
⇒ **Indicates a strong medical benefit**



THN₁₀₂ IN EDS IN PARKINSON'S DISEASE PATIENTS: A LARGE MARKET POTENTIAL

1 - A large patient pool

2 - KOLs already convinced of the medical needs



73% of KOLs interviewed declare EDS as a significant unmet need

3 - Favourable medico-economics

- EDS increases the risk of falls (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*

4 – No treatment currently on the market

5 – Favourable pricing benchmarks

Typical prices > 10k\$ per patient p.a. in the US

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>40mg (40mg/100mg)</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 [®] (levodopa inhalation powder) <small>40.5 mg 107 mg</small>	\$33'140	Levodopa induced dyskinesia	amantadine	\$780
2019	Inbrija [®] (levodopa inhalation powder) <small>40 mg inhalation</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

A strong blockbuster potential > 1Bn\$**



*Lewin Group report / Michael J. Fox Foundation 2019

**Clarivate analytics report



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"



DIFFERENT OPTIONS WITH THE AIM OF MAXIMISING VALUE FOR THE COMPANY AND ITS SHAREHOLDERS

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

DISCUSSIONS ONGOING WITH SEVERAL POTENTIAL PARTNERS



AGENDA

1 THN₁₀₂ (PARKINSON'S DISEASE)

2 BBDF-101 (JUVENILE BATTEN DISEASE)

3 NEWSFLOW

4 FINANCIAL SITUATION



BBDF-101 : DISCOVERY AND DEVELOPMENT UNTIL THE AGREEMENT BETWEEN THERANEXUS AND THE FOUNDATION

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

Discovering the mechanics of the disease

Discovering the drug candidate

Development plan design

Agreement with Theranexus



Created in 2008
by Craig Benson
Investing on average
c. 2M\$ p.a.
in academic research
in CLN₃

Financing academic
studies
Discovery of disease
mechanisms by Dr
Sardiello
of Baylor College of
medicine (*Palmieri et al.*
Nat Com 2017)

BBDF-101 discovered by
Dr Sardiello's team at
Baylor College
Trehalose IV + Miglustat
combination
Patent granted in USA,
valid until 2036

Development plan
design
Pre-IND meeting

Global exclusive
license,
December 2019



BBDF-101 AMBITION : REDUCE NEURONAL DEATH AND SLOW THE PROGRESS OF THE DISEASE

Discovery by Dr Sardiello of Baylor College of Medicine

Nature 8 May 2010 • Accepted 11 Dec 2009 • Published 4 Feb 2010
 OPEN
 mTORC1-independent TFEB activation via Akt inhibition promotes cellular clearance in neurodegenerative storage diseases

Michela Palmieri¹, Ritaia Paf¹, Hannah K. Nakagaki¹, Parisa Lant¹, Gary B. Stenmet¹, Michela L. Scymoni¹, Anand Chaudhuri², Lakshya Baghel¹, Vikash V. Bhatia¹, Luca Bernardi¹, Laura Salani¹, Denis Y. Spigel¹, Diego Serrano-Santesteban¹, Samuel M. Wu¹, Joel R. Ninkovic¹, Susi A. Perrotti¹, Roba G. Pauter¹, George G. Robay^{1,3}, Jonathan D. Cooper¹ & **Mario Sardiello**



Src regulates amino acid-mediated mTORC1 activation by disrupting GATOR1-Rag GTPase interaction

Ritang Paf¹, Michela Palmieri¹, Anand Chaudhuri², Tameh Birgin Kibar¹, Alberto di Ronza¹, Joel R. Ninkovic¹, George G. Robay¹ & **Mario Sardiello**

Src-dependent impairment of autophagy by oxidative stress in a mouse model of Duchenne muscular dystrophy

Ritang Paf¹, Michela Palmieri¹, James A. Lindor¹, Shantanu L. Bhami¹, Ramon Aliza-Zabala¹, Saverio Di Muzio¹, Francesco B. Thirumangalakudi¹ & **George G. Robay**



CLNB is an endoplasmic reticulum cargo receptor that regulates lysosome biogenesis

Alberto di Ronza¹, Lakshya Baghel¹, Jayaprakash Sivaraman¹, Deepthi Saragadam¹, Parisa Lant¹, Carolyn Joy Adams¹, John Colletta¹, Michela Palmieri¹, Abdallah Amawi¹, Lauren Papp¹, Kevin Tommy Chang¹, Maria Chiara Menchini¹, Hui-Chiu Eastwood Leung¹, Luca Serrano-Santesteban¹, Alexander Somenzi¹, Richard Norman Sifers¹, Filippo Maria Santoro¹ and **Mario Sardiello**

TFEB Links Autophagy to Lysosomal Biogenesis



Carmine Settembre^{1,2,3}, Chiara Di Malta^{1,2,3}, Vincenza Alessio Pallo^{1,2,3}, Matteo Garcia Arancibia¹, Francesco Verzi^{1,2}, Susanna Erdos^{1,2}, Sergio Uchida^{1,2}, Young Hwang^{1,2}, Diego Medina¹, Pasquale Colatta¹ & **Mario Sardiello**

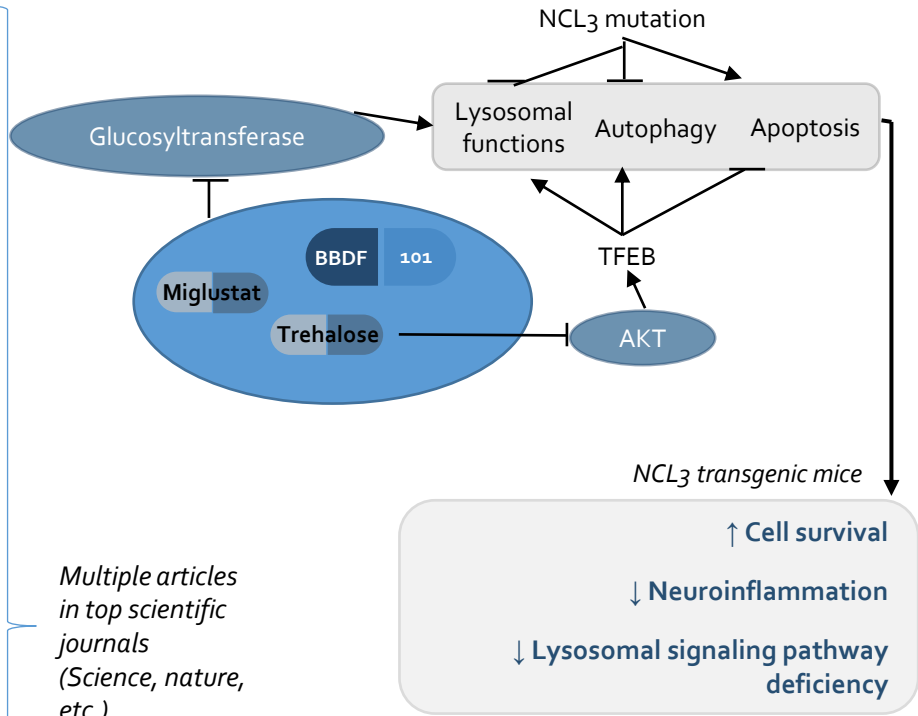
A Gene Network Regulating Lysosomal Biogenesis and Function

Mario Sardiello¹, Michela Palmieri¹, Alberto di Ronza¹, Diego Luis Medina¹, Marta Valenza¹, Vincenzo Alessandro Geniarino¹, Chiara Di Malta¹, Francesca Donaudy¹, Valerio Embrione¹, Roman S. Polshchuk¹, Sandro Banti¹, Giancarlo Parenti¹, Elena Cattaneo¹, Andrea Ballabio^{1,2,3,4}

Abnormal glycogen storage in tuberous sclerosis complex caused by impairment of mTORC1-dependent and -independent signaling pathways



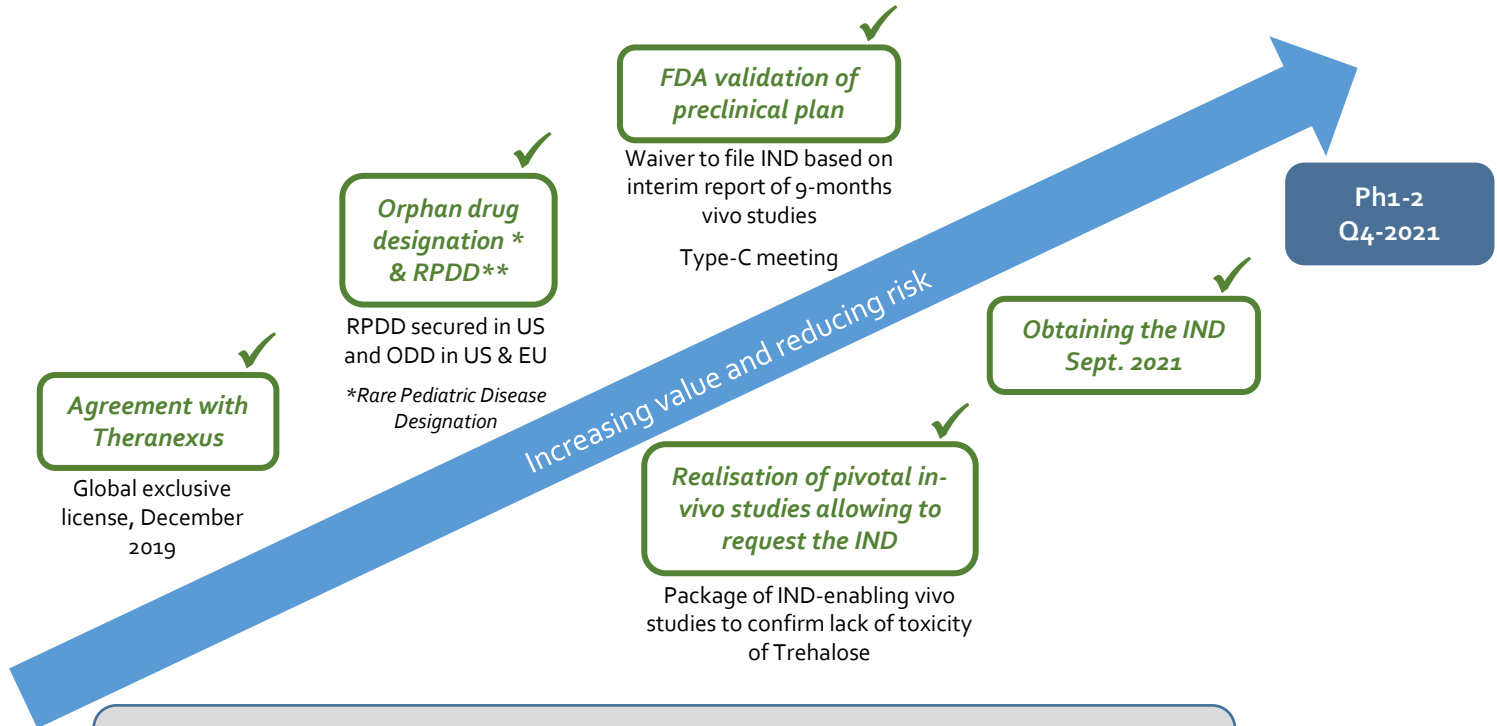
Ritang Paf^{1,2,3}, Van Hoang^{1,2,3}, and **Mario Sardiello**



Multiple articles in top scientific journals (Science, nature, etc.)



REGULATORY ACHIEVEMENTS AND DEVELOPMENT SINCE AGREEMENT WITH BBDF

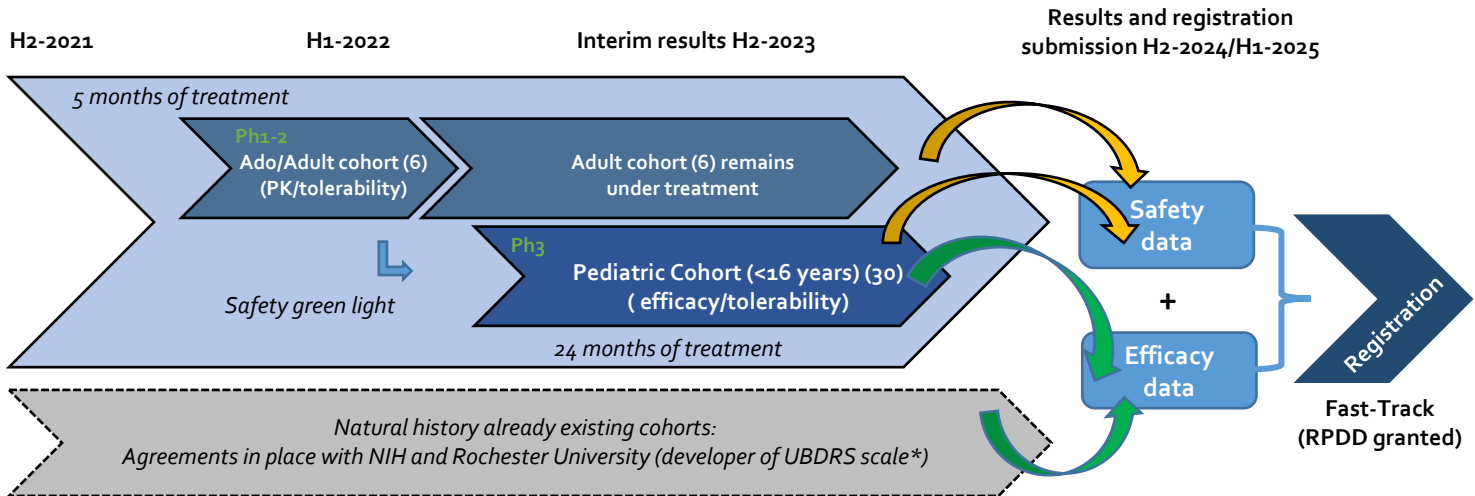


* ODD : 7-year very strong protection
**RPDD: fast-track registration + transferable rare disease voucher (obtained from the FDA at the time of registration, market value c. \$100M)



BBDF-101 : PHASE I-III PIVOTAL PROGRAM

- Adolescent/adult cohort of 6 patients over a period of 5 month : Ph1-2 (launching Q4 2021)
- Pediatric cohort of 30 patients over a period of two years with an intermediate assessment at 12 month : Ph3 (launch H2-2022)
- **Open label:** Evaluation 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
- Budget until full results : c. €15m



* Reference scale for Batten disease patients evaluation



COMPETITIVE ENVIRONMENT AND MARKET OPPORTUNITY

COMPARABLES



6,000 cases USA
5,000 cases EU

Gaucher disease

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

Peak (2014): \$113m



5,000 cases USA
1,800 cases EU

Pompe disease

\$300,000/yr/patient

Peak (2018): \$947m



500 cases USA
400 cases EU

Hunter syndrome

\$375,000/yr/patient

Peak (2018):
\$634m



500 cases USA
250 cases EU

NCL2

\$700,000/yr/patient

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

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

MARKET ACCESS

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

Partnership already in place with main US patient association (BBDF)
Batten disease KOLs involved in clinical study

COMPETITION IN CLINICAL DEVELOPMENT

NCL3 AAV9 gene therapy (Amicus Therapeutics)

- Aim = treat very young patients (3-10 years old)
- Currently in P1/2 (completion expected Dec 2022)

Open IND Polaryx Therapeutics

No clinical plan announced to date

Rochester University review of treatments potential
(Masten et Al. 2020)

"[...] a combination of multiple therapeutic approaches may be necessary to provide optimal benefit"

"combination therapy may provide the best chance for meaningful disease modification"

⇒ Gene therapy not a 'silver bullet' in this indication

⇒ All patients (even those young enough to be benefit from gene therapy) likely to require additional treatment

- ➔ Easy market access and strong peak sales potential
- ➔ BBDF-101 very likely to fit within treatment even if other solutions emerge



AGENDA

- 1 THN₁₀₂ (PARKINSON'S DISEASE)
- 2 BBDF-101 (JUVENILE BATTEN DISEASE)
- 3 NEWSFLOW
- 4 FINANCIAL SITUATION



A STRONG NEWSFLOW OVER THE NEXT 12 MONTHS

THN102 partnership agreement



THN 102

First patient In Ph1-2 : Q4-2021

Launch of Ph3 : H2-2022



BBDF 101

Continuing programs stemming from the discovery platform



THN XX



AGENDA

- 1 THN₁₀₂ (PARKINSON'S DISEASE)
- 2 BBDF-101 (JUVENILE BATTEN DISEASE)
- 3 NEWSFLOW
- 4 FINANCIAL SITUATION



P&L 2020

In K€ (french GAAP)	2019	2020
Operating income	617	315
Other purchases and external charges	5 426	3 568
Salaries and benefits	2 353	2 422
Depreciation and amortization	154	376
Other operating expenses	61	48
Operating result	(7 377)	(6 099)
Net financial income	(241)	307
Corporate tax	2 038	994
Net income	(5 580)	(4 797)

REDUCED EXPENSES : END OF CLINICAL STUDIES ESPECIALLY ON THN₁₀₂

MAINLY RESEARCH TAX CREDIT

Cash at June 30, 2021 : €13.5m

Including eight drawdowns (total €5.6m) under Equity line concluded with IRIS during the first semester of 2021 (maximum of €8.4m over 12 months)



CAPITAL MARKETS SNAPSHOT

FINANCIAL DATA

ISIN : FR0013286259 - Mmemo: ALTHX

Market : Euronext Growth



Stock price as at Sept. 22th, 2021 : €8.2

Market cap : €38.4m

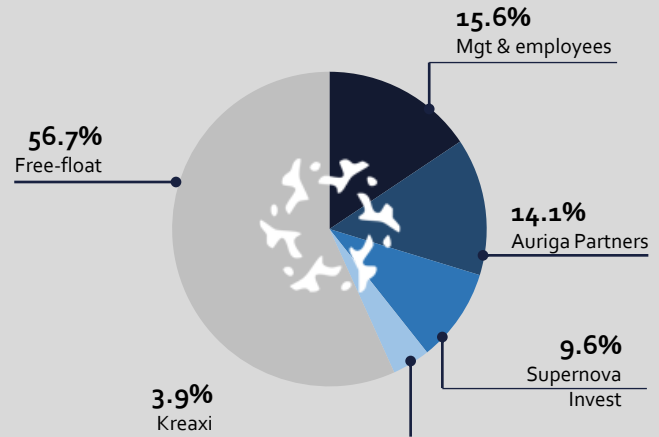


Brokers coverage : Bryan, Garnier & Co, Portzamparc, ODDO BHF

Liquidity contract : Portzamparc

SHAREHOLDERS

Number of shares : 4 686 513





AGENDA

APPENDICES



NEUROLEAD : STRENGTHENING THE LEAD GENERATION PLATFORM

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

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



PLATFORM FIRST GENERATION

- First family of glial targets identified
- Reduction of risks, time and development costs versus standard approach
- One new candidate every 18 months

ADVANTAGES

- Comprehensiveness, Automation
- Acceleration
- Predictability Industrialization

PLATFORM NeuroLead

- 4 new combinations identified per year
- Early optimization of probabilities of success
- Discovery of new neuro-glia therapeutic targets
- Opportunity to multiply business models

FROM PIONEER TO REFERENCE PLAYER IN NEUROLOGY



THERANEXUS ORGANISATION



Franck Mouthon CEO & founder

Top researcher at leading research organization
CEA

Co-founder of Theranexus

President of France Biotech



Mathieu Charvériat CSO & founder

PhD in Neuroscience

Ex-researcher at leading research organization CEA

Co-founder of Theranexus



Julien Veys CBDO

Business Developer specialized in CNS sector

As head of BD negotiated sale of Trophos
(French CNS biotech to Roche)



Werner Rein CMO

Ex global VP of CNS clinical development for Sanofi

MD in neurology and psychiatry – was resident in
Tübingen University Hospital



Thierry Lambert CFO

5 years in Transaction Services with PWC UK

ACA-trained (Institute of Chartered Accountants in
England and Wales)

8 years as CFO in listed companies mainly in the
healthcare sector



19 employees, mostly R&D
scientists, clinical operations
managers and business developers

In-house vitro capabilities

Vivo capabilities in partnership with
leading academic institutions

Structured partnerships with
leading institutions

