

DISRUPTIVE COMBINATION  
AGAINST NEUROLOGICAL DISORDERS

PRESENTATION OF THE RESULTS  
OF THE PHASE 2 STUDY OF THN102  
IN PARKINSON'S DISEASE

March 31st 2020

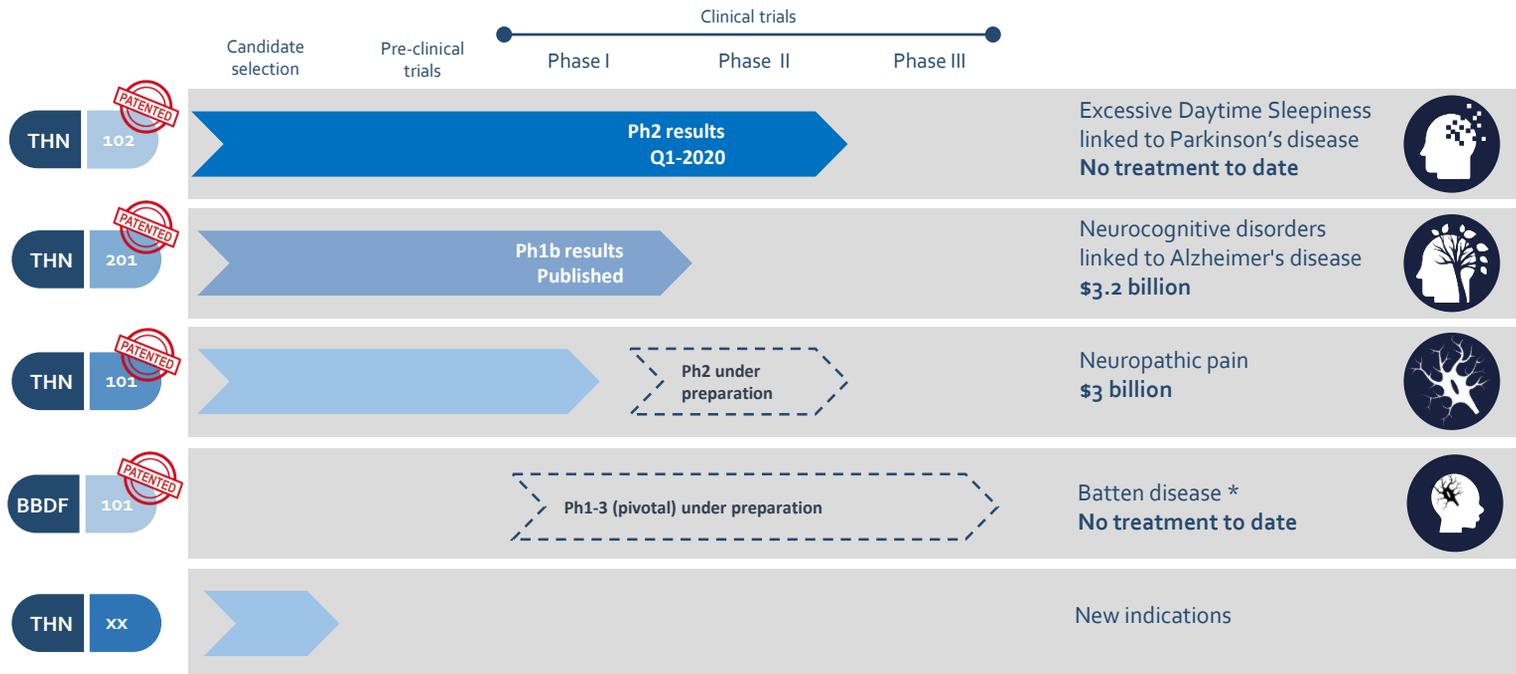


▲ NEURONAL NETWORK  
● GLIAL NETWORK

 Theranexus



## 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 1<sup>ST</sup> LINE-TREATMENT

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

*CNS drugs  
1<sup>st</sup> 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



## 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**

<sup>1</sup> European Parkinson's Disease Association

<sup>2</sup> Market research study performed by LSA Partnering & Analytics



## 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)**



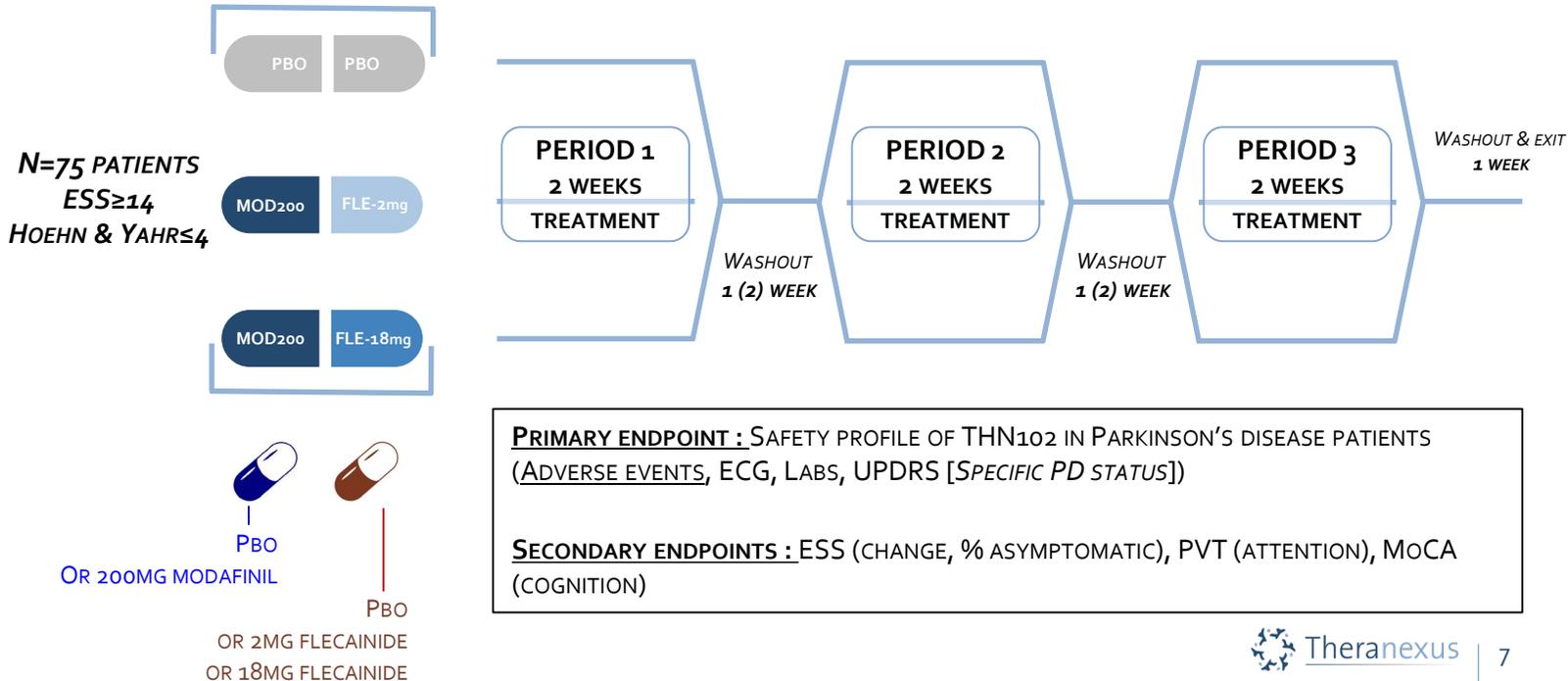
## AGENDA

- 1 RESULTS OF THE P<sub>2</sub> STUDY OF THN<sub>102</sub> IN PARKINSON'S DISEASE
- 2 ACTION PLAN AND PERSPECTIVES FOR THE DEVELOPMENT OF THN<sub>102</sub>
- 3 NEWSFLOW



## 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





## 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<sup>(1)</sup> : 27,4  $\pm$  3,4 kg/m<sup>2</sup>
  - Hoehn & Yahr score<sup>(1)</sup> : 2,3

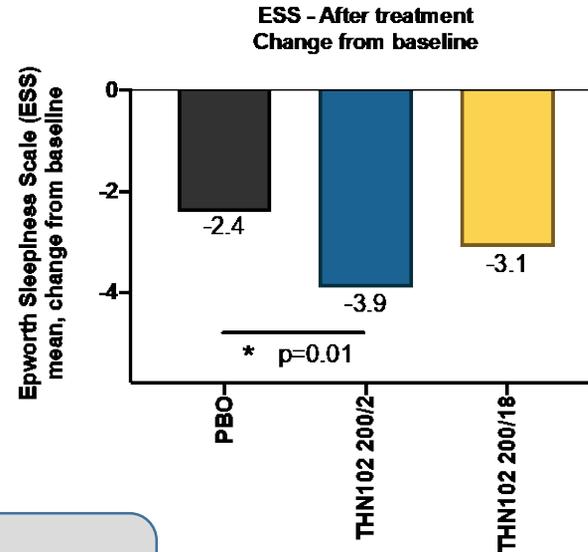
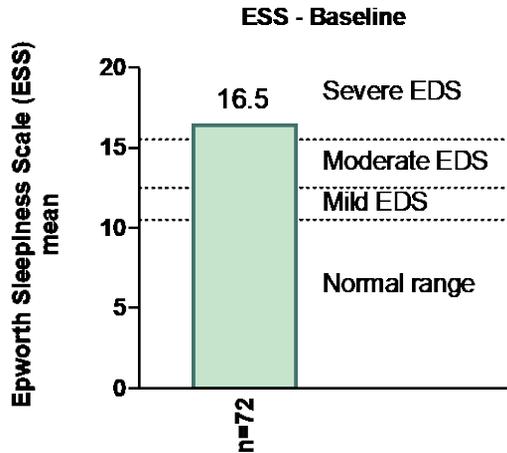
<sup>(1)</sup> Body Mass Index

<sup>(2)</sup> Scale of severity of symptoms of Parkinson's disease (0-4)



## 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)



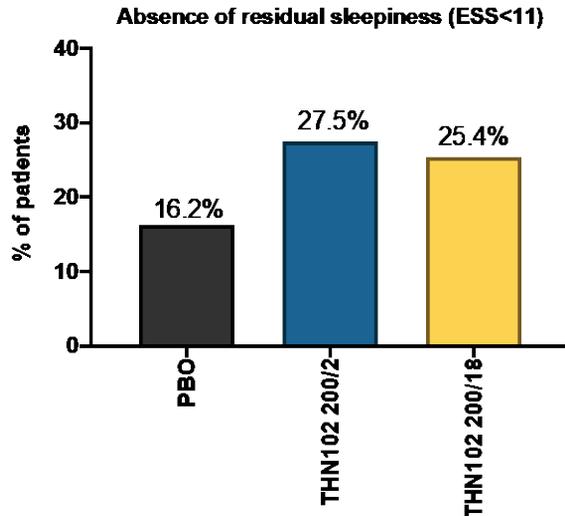
### Conclusion :

- 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 : A VERY SATISFACTORY SAFETY PROFILE

### **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<sup>(1)</sup> , 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



## THN<sub>102</sub>: SUMMARY OF THE FINDINGS FROM THE CLINICAL STUDY

- ✓ THN<sub>102</sub> **significantly reduces excessive daytime sleepiness** in Parkinson's disease patients
- ✓ THN<sub>102</sub> 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.
- THN<sub>102</sub> 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

1

RESULTS OF THE P<sub>2</sub> STUDY OF THN<sub>102</sub>  
IN PARKINSON'S DISEASE

2

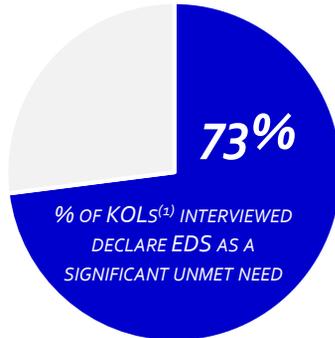
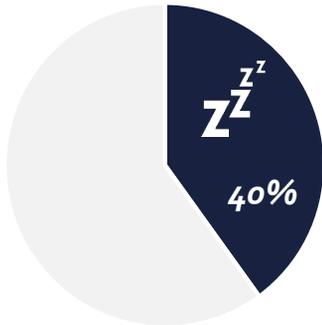
ACTION PLAN AND PERSPECTIVES  
FOR THE DEVELOPMENT OF THN<sub>102</sub>

3

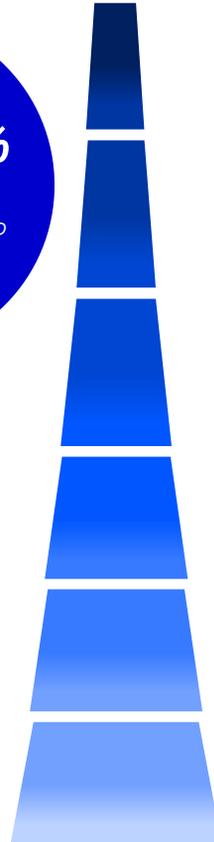
NEWSFLOW



## 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 <sup>(2)</sup> – 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<sup>(3)</sup>



### 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	<b>Northera™</b> (droxidopa) Capsules 100 mg-200 mg-300 mg	\$70'250	Neurogenic orthostatic hypotension	midodrine	\$900
2016	<b>NUPLAZID™</b> (pimavanserin) tablets	\$38'230	Psychosis	clozapine	\$560
2017	<b>XADAGO®</b> (safinamide) tablets	\$11'900	ON/OFF fluctuations	rasagiline	\$6'840
2018	<b>GOCOVRI™</b> (amantadine) extended release capsules 68.5 mg   137 mg	\$33'140	Levodopa induced dyskinesia	amantadine	\$780
2019	<b>Inbrija™</b> (levodopa inhalation powder) 42 mg capsules	\$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 <sup>(1)</sup>	ON/OFF fluctuations	China	3	14	??%
2017			NDA <sup>(1)</sup>	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**



## A FAVORABLE MARKET AND INDUSTRIAL ENVIRONMENT

- ✓ Excessive daytime sleepiness affects about **2M patients** suffering from Parkinson's in the major markets
- ✓ There is **no treatment labelled** for the management of this **significant unmet medical need**.

### **The management of non-motor symptoms represents a major challenge for players specializing in Parkinson's disease:**

- Highly priced treatments: Exceeding \$10k/patient/year in the US
- High-value deals after a demonstration of efficacy
- A pool of prospective partners groomed ahead of the results and ready to jump into a competitive partnering process



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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 March 30<sup>th</sup> 2020 : 2,50 €

Market cap : €9M

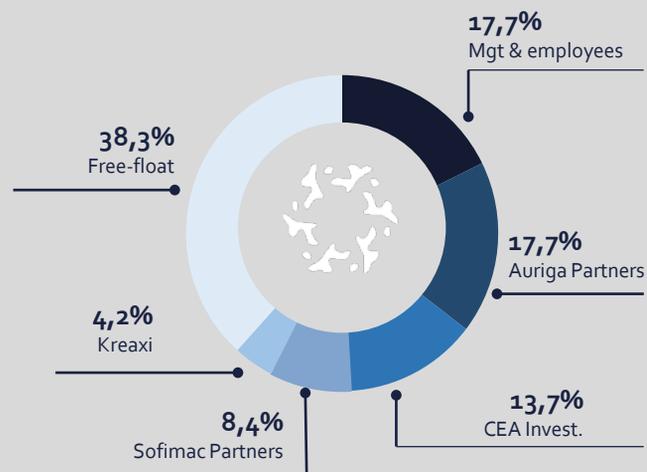
Liquidity contract : Portzamparc

Cash at Dec. 31<sup>st</sup> 2019 : €9.5M



### SHAREHOLDERS

Number of shares : 3 622 413





## INVESTOR RELATIONS AND MEDIA CONTACTS



**Thierry LAMBERT**

Chief Financial Officer

- 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

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