



**Quels modèles d'entreprises pour les maladies rares ?  
Quels sont les leviers financiers existants ?**

**Damian Marron  
CEO**

# *TROPHOS at a glance*

- *2000: Founding of Trophos, a Univ Aix-Marseille spin out*
- *2002: establish novel screening technology, including proprietary analyser, Plate Runner HD®*
- *2003: Discovery of cholesterols, including olesoxime*
- *2005: Olesoxime enters the clinic*
- *2009: Trophos led Mto Target consortium starts AD phase 3 study with olesoxime*
- *2010 Starts olesoxime pivotal SMA study and first-in man with TRO40303 in cardiology*
- *2010 Signs strategic agreements with Actelion Ltd.*
- *To day: late stage biopharmaceutical company focused on orphan and niche with 32 employees + an extensive network of academic collaborators*

# TROPHOS Pipeline Chart

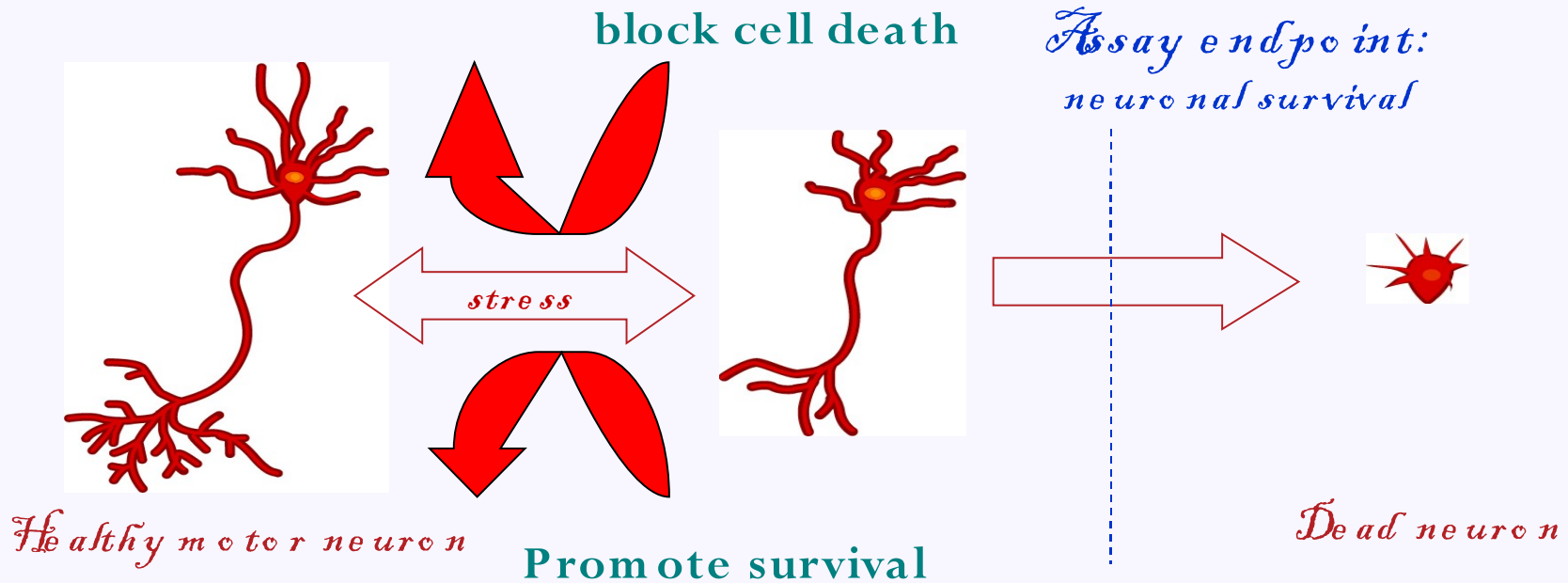
Compound/Indication	Preclinical	Phase I/Ib	Phase 2	Phase 3	Approval
<b>Olesoxime (TRO19622)</b>					
ALS (part funded by €6M EU FP7 grant)					
SMA (funded by AFM)					
<b>TRO40303</b>					
Cardiac Ischemia-Reperfusion Injury					
<b>Undeclared</b>					
Neurodegenerative Diseases				Neurology	
Multiple Sclerosis				Cardiovascular	

# *Discovery - Where to start?*



# Trophos Phenotypic Screening Approach

To identify drugs that promote motor neuron survival



## KEY FEATURES

- ◊ Non-targeted phenotypic screen (ALS SMA other MND)
- ◊ First high-throughput screening on primary motor neurons (C. Henderson)

## *Trophic deprivation as a screen for MNDs*

- ◊ *Mimics trophic factor withdrawal consecutive to NMJ breakdown: an early event in SMA & ALS*
- ◊ *Triggers several death processes (caspase activation, oxidative stress, protein nitrosylation)*
- ◊ *Assay is highly selective*
- ◊ *Enables discovery of all known neurotrophic factors*
- ◊ *Neurotrophic factors delivered by gene transfer provided strong proof of concept in MND animal models although clinical translation has been challenging*
- ◊ *In all compounds mimicking similar protective & restorative activities (survival & neurite outgrowth) should delay motor neuron degeneration*

# *Disease models - what are they worth?*



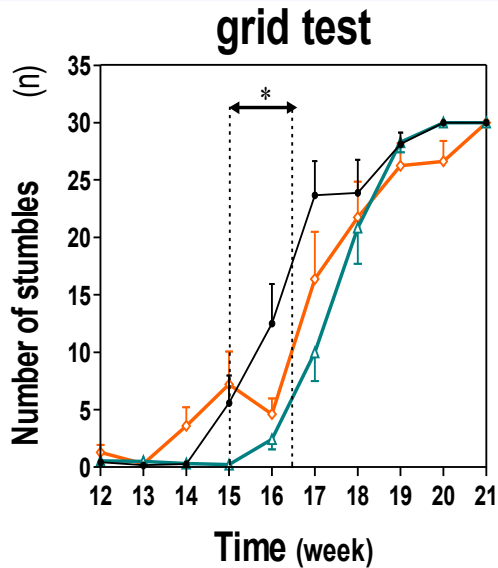
# Olesoxime: D<sub>1</sub> G<sub>93</sub> A model of familial ALS

Significant effects on multiple parameters

vehicle sc     
  Olesoxime 3 mg/kg sc     
  riluzole 8 mg/kg po (n=11)

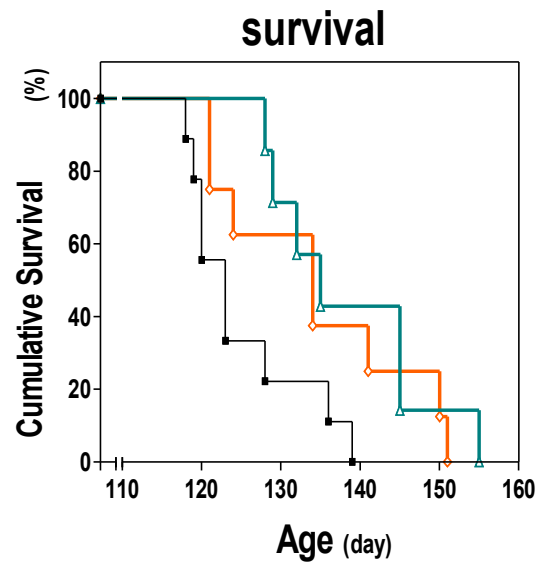
SOD1G93A

treatment from d60

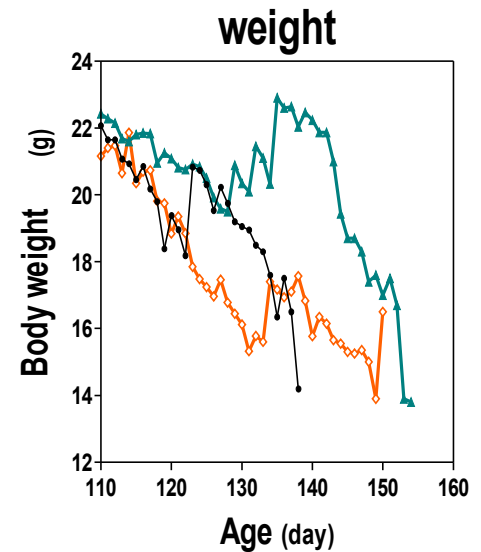


Two-way Anova test from W14to W21

Groups	p (vs Vehicle)
Olesoxime	0.003
Riluzole	0.172



Vehicle (n=9)  
 Olesoxime (n=7); Logrank p = 0.018  
 riluzole (n=8); Logrank p = 0.050

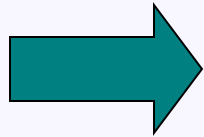


Two-way Anova test from D106 to D135

Groups	p (vs Vehicle)
Olesoxime	0.002
Riluzole	0.003

## Disease and market

- ◇ *Motor neuron degeneration leads to progressive paralysis*
- ◇ *Survival < 5 yrs.*
- ◇ *90 000 patients WW; orphan disease*
- ◇ *Riluzole only approved treatment; modest efficacy only (2 - 4 months ↑ survival)*
- ◇ *Goal is to demonstrate life-span extension by more than 6 months;*
- ◇ *Survival improvement to justify premium pricing*
- ◇ *Limited number of diagnosing/prescribing physicians in specialist centres, easy to target*



*Olesoxime nearest product in development to market*

- *With data on survival in long duration pivotal trial in 2011*
- *Nearest competitor to enter phase 3 in 2011*

# Olesoxime: Ongoing AD Phase 3 study

- ◇ ODD status in USA & EU
- ◇ A single pivotal trial required for registration (EMA protocol advice)
- ◇ Double-blind placebo-controlled study of olesoxime 330mg once per day as add-on to riluzole
- ◇ Primary endpoints: survival  $\Delta=12\%$  at 18 months (6-9 months improvement in median survival)
- ◇  $N=238$  per group with at 18 months; 480 patients total
- ◇ Multicenter (~15 sites) in Europe (UK, Belgium, Germany, France, Spain)
- ◇ Phase 3 ongoing; substantially funded by €6 M EU grant (MTC Target)
- ◇ Recruitment completed February 2010

**Efficacy results 4 Q 2011**

# *Ole so xim e fo r SMA*

## **Disease and market**

- ◇ *Progressive paralysis of striated muscles caused by SMN1 gene deletion; infant onset*
- ◇ *20 000 patients WW<sup>o</sup>; 1 new case/6.000 births; orphan disease;*
- ◇ *Limited number of diagnosing/prescribing physicians in specialist centres*
- ◇ *Product slowing or preventing loss of muscle function would be widely used*
- ◇ *Single trial expected to support registration*
- ◇ *No approved product; products approved for other indications are tested but without strong rationale*

# Ole so xim e fo r SMA

## Development – Pivotal study underway

- ◇ *Orphan Drug status in EU & USA*
- ◇ *Pivotal efficacy study design discussed with KOLs and EMA*
- ◇ *Double-blind, placebo-controlled, 24 month study in non ambulant SMA patients aged > 3 years*
- ◇ *Primary endpoint MM functional scale*
- ◇ *Secondary endpoints Hamman-Rich scale, electromyography (EMG/MUNE)*
- ◇ *Interim efficacy/futility analysis at 1 year*
- ◇ *EU development principally funded by AFM (EU patient association) to end of efficacy study*

**Start October 2010: results**

**2 H 2 0 1 3**

# TROPHOS strong, broad IP Portfolio

*The cholesterol-oxime chemistry platform (first medicinal use / COM method of use claims)*

- ◇ *Olesoxime (TRO19622): International Application filed in 2004*
  - *Regional/National phases entered September, 2005*
    - ◇ *Europe, Canada, USA, Japan, Australia, Israel and Brazil*
  - *WO2004/082581: scope includes,*
    - ◇ *New derivatives of the cholesterol-4-en-3-one formula (I), and their use as drugs*
    - ◇ *The use of Olesoxime (TRO19622) as a drug, notably as neuroprotectant (EU)*
    - ◇ *Methods of Use (divisional): extensive list of neurodegenerative diseases inc. ALZHEIMER (US)*
  - *Additional patent application filed on March, 2006: scope includes,*
    - ◇ *Use of these compounds (I) as cytoprotectant*
- ◇ *TRO40303: International Application filed in 2005*
  - ◇ *WO2006/027454: Includes specific claims for cardioprotection*
- ◇ *Others patents filed covering new compounds, formulation & other properties*

*It's a long and winding road...*



# *Finance: Investor equity matched by non-dilutive money*

*€68 M raised since 2000*

- ◊ *€26.7 M raised in equity in three major rounds to 2009*
- ◊ *€28 M raised in last eighteen months, incl.,*
  - *€10 M option payment from Actelion*
  - *€2.0 M convertible loan from historic investors*
  - *€1.0 M from OSO Innovation repayable in case of success*
  - *€6 M MELTP award for 'Met Target' program (incl. efficacy study in ALS)*
  - *€6.7M AFM contract No. 4 for TRO19622 SMA efficacy trial*
  - *€1 M ANR award for 'Pstop' project to advance TRO40303 to Phase 1*

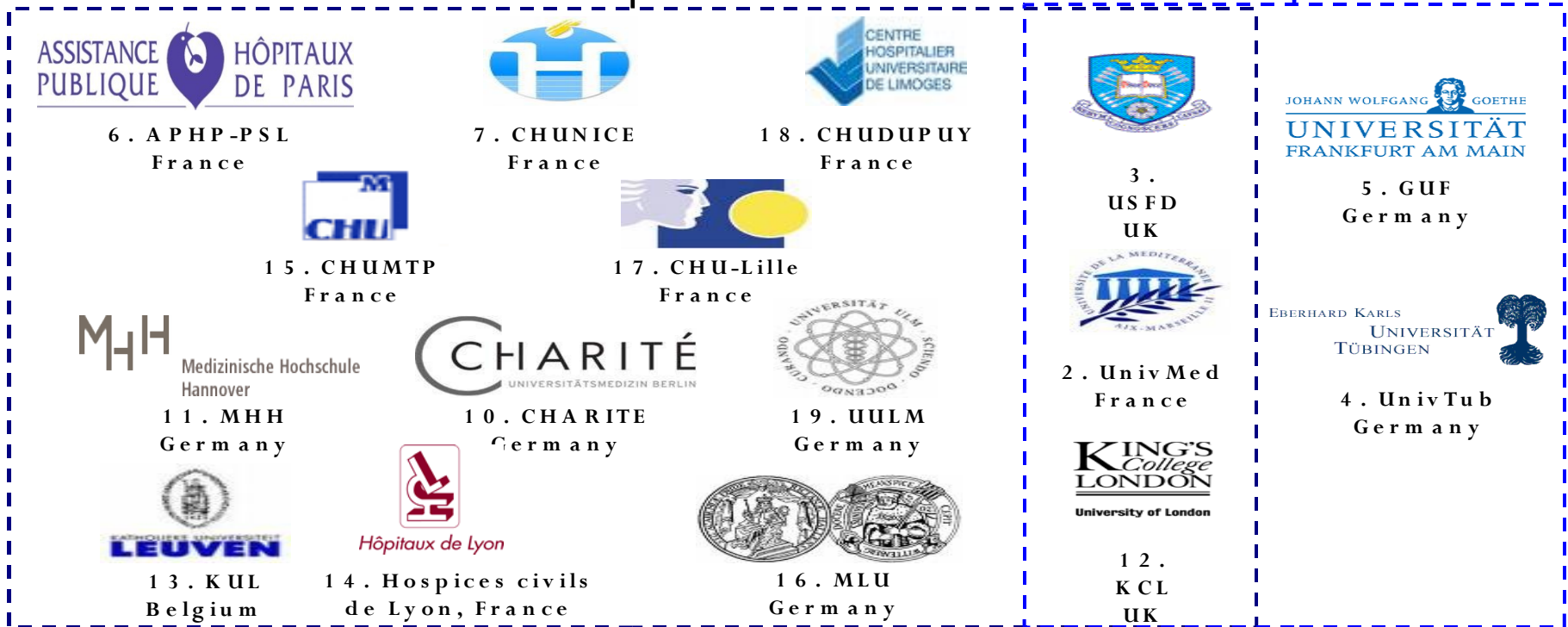
*Peer Reviewed  
translational funding*

# MITOTARGET: EUPB award of €6M



**TROPHOS**  
The neuron company  
1. TROPHOS  
France

Coordinat  
or  
SME



+ Madrid site  
Assess the efficacy in man of a  
mitochondrial targeted  
compound

Explore mitochondrial  
dysfunction in  
neurodegenerative diseases

## *Strategic deals with Actelion*

### ◇ Acquisition Option Agreement

*€10M paid for exclusive option to acquire 100% of Trophos shares*

- ◇ *Option can be exercised at any time before end 2012 and at the latest 60 days after receipt of the results of the ongoing phase 3 AD study*
- ◇ *Purchase price between €125M and €195M (including contingent milestones)*
- ◇ *Leverages Actelion's regulatory and commercialisation expertise in orphan diseases*

### ◇ Research collaboration agreement

*To exploit Trophos proprietary assay technology*

- ◇ *mimics neuronal degeneration processes in the test tube*
- ◇ *Allows screening of chemical libraries for molecules capable of blocking this process*

*Builds on Trophos and Actelion expertise in neurology*

# TROPHOS Executive Management

- ◇ *Damian Merro n, CEO*
  - *Extensive biotech and pharma experience. Raised > €175M and executed deals with big pharma and biotech. Joined Trophos June 2008*
- ◇ *Jan-Louis Abitbol, CMO*
  - *Over twenty years in clinical development and large and mid size pharma. With Trophos since 2004*
- ◇ *Patrick Berna, CDO*
  - *15 years experience in project management and non-clinical development. Joined Trophos in 2006*
- ◇ *Christine Pacet, CFO*
  - *Strong financial experience with more than twenty years in large companies and start-ups and with Trophos since 2005*
- ◇ *Rebecca Pruss, COO*
  - *16 years in pharma and responsible for discovery and entry into development of numerous drugs in CNS. Joined Trophos in 2002.*

# What next?



*Wait, Mr. Gates. Your future is becoming clear now.*



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## Support for the Trophos' discovery & development programs



## MEFOPA

