



## **Trophos announces results of phase 3 study of olesoxime in Amyotrophic Lateral Sclerosis**

**MARSEILLE, FRANCE – December 13 2011.** Trophos SA announces today the results from the phase 3 study of Trophos' lead compound, olesoxime, in 512 patients with ALS. Olesoxime did not demonstrate a significant increase in survival versus placebo in patients receiving riluzole (Rilutek®). A trend was seen on patients' function as measured by the ALSFRS-R functional rating scale. Olesoxime was very well tolerated.

Following receipt of these results, Actelion has informed Trophos of its decision to not exercise its exclusive option under the July 2010 Acquisition Option Agreement between Trophos and Actelion (see Actelion release of 13 December 2011).

Trophos continues its ongoing programs and has financing secured to at least the end of 2013. These programs include:

- An ongoing pivotal trial of olesoxime in Spinal Muscular Atrophy (SMA) with results due in the second half of 2013;
- An ongoing phase 2a proof-of-concept study of TRO40303 in cardiac ischemia-reperfusion injury (IRI), with results due before end 2012;
- A planned phase 2 proof-of-concept trial of olesoxime in Multiple Sclerosis (MS) disease progression (subject to securing outside funding);
- A research collaboration with Actelion to screen and characterize Actelion compounds using Trophos' proprietary CNS assay technology.

The inability of olesoxime to show a greater effect on survival for ALS patients above that of riluzole in the phase 3 trial is most likely because the disease process is already so severe and rapidly progressing by the time of diagnosis that any further benefit of olesoxime over that of riluzole cannot be detected. Indeed, it is known that in the most widely used ALS model, over 50 per cent of the motor neurons and neuromuscular connections have already been lost by the time the first symptoms appear. Of Trophos' other target indications for olesoxime, SMA type 2 and 3, being studied in an ongoing trial, differ in that disease progresses slowly over many years. Progressive MS is again different as neuronal degeneration correlated with disease progression only sets in after symptoms appear.

"The results of this study in ALS are disappointing, above all for the ALS community, who urgently require new therapies that can prolong survival and improve function. We are genuinely proud to have worked closely with this community and our international partners in the MitoTarget project on this important and very well run study," said Damian Marron, CEO, Trophos. "We remain convinced of the promise of our cholesterol-oxime, mitochondrial pore modulator compounds. We have ensured that Trophos is financed until at least the end of 2013 so that we continue to move forward on our other programs, which address high medical need orphan or niche indications with no existing treatments."

### **Details of the study**

The study was an 18-month randomized, parallel group, double-blind, placebo-controlled trial evaluating the efficacy and safety of olesoxime against placebo in patients treated with riluzole. The study was conducted in 512 patients diagnosed with

ALS between six and 36 months before enrollment and receiving standard of care. Olesoxime was dosed orally at 330 mg once-a-day.

Olesoxime did not demonstrate significant benefit on the primary endpoint of survival after 18 months of treatment over that of riluzole. A trend was seen on the secondary criteria of ALSFRS-R on a pre-specified analysis after nine months of treatment. Olesoxime was very well tolerated with a side effect profile similar to riluzole plus placebo. Full results will be published in scientific journals and congresses in due course.

The study was undertaken in 15 centers in France, Germany, UK, Belgium and Spain as part of a three-year collaborative project named MitoTarget (Grant Agreement No: HEALTH-F2-2008-223388) for which the European Commission has awarded a grant of nearly EUR 6 million.

#### **About Olesoxime**

Olesoxime is Trophos' lead compound of a proprietary mitochondrial pore modulator series. Preclinical studies have demonstrated that olesoxime promotes the function and survival of neurons and other cell types under disease-relevant stress conditions, through interactions with the mitochondrial permeability transition pore (mPTP).

Olesoxime is in an ongoing pivotal efficacy and safety study in Spinal Muscular Atrophy (SMA), substantially funded by the AFM patient association (see Trophos release of October 15, 2010), with results due in the second half of 2013. Olesoxime is also at entry to phase 2 development for multiple sclerosis.

#### **About TRO40303 and cardiac ischemia-reperfusion injury**

Use of thrombolytics and balloon angioplasty to rapidly reperfuse heart tissue with oxygen following a MI has greatly reduced morbidity and mortality. Paradoxically, about 50 per cent of the damage to heart tissue following MI is due to re-oxygenation leading to a burst of reactive oxygen species as energy production by mitochondria is reactivated. The mechanism of action of TRO40303 involves prevention of stress-induced mitochondrial permeability transition, a target implicated in cardiac reperfusion injury. In a model of MI, treatment with TRO40303 at the time of reperfusion was shown to significantly reduce infarct size. This innovative program was supported by a grant of nearly EUR 1 million by the French Agence Nationale pour la Recherche (ANR) in a project named IRIstop, (see release of February 28 2008).

TRO40303 has successfully completed a phase 1 study to assess the safety, tolerability and pharmacokinetics of single escalating doses of TRO40303 as an intravenous infusion at different rates compared with placebo in 72 healthy volunteers. The results demonstrated that TRO40303 can be safely administered by the iv route in humans at doses expected to be pharmacologically active. Full results of this study were recently presented at the European Society of Cardiology 2011 held in Paris from 27th-31st August (Schaller et al., ESC 2011 Paris, N88427, Phase I clinical trial of TRO40303, a new mPTP inhibitor for reducing reperfusion injury).

The ongoing phase 2 study of TRO40303 is part of a collaborative project named MitoCare (Grant Agreement Number: Health-2010-261034). The European Commission has awarded a grant of EUR 6 million to MitoCare, a 2.5 year international, translational medicine project led by Trophos.

#### **About Trophos SA – [www.trophos.com](http://www.trophos.com)**

Trophos is a clinical stage pharmaceutical company developing innovative therapeutics for indications with under-served needs in neurology and cardiology. The company has a novel and proprietary cholesterol oxime based chemistry platform generating a pipeline of drug candidates. The lead product, olesoxime (TRO19622), is in a pivotal clinical study for Spinal Muscular Atrophy (substantially funded by the AFM patient

association). A second product, TRO40303, is in phase 2 clinical development to treat cardiac reperfusion injury (as part of an EU funded project, MitoCare). Trophos' mitochondrial pore modulator compounds enhance the function and survival of stressed cells via modulation of dysfunctional mitochondria through interactions at the permeability transition pore (mPTP). Recently published clinical studies support the therapeutic rationale for mitochondria targeted drugs, which Trophos is uniquely placed to exploit.

Trophos was founded in 1999, is based in Marseille, France and currently has 37 employees.

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